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Table of Contents

<table>
<thead>
<tr>
<th>Abstracts</th>
<th>S1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials I (abstract 1LBA)</td>
<td>S1</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials II (abstracts 2LBA, 3LBA)</td>
<td>S1</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials III (abstract 4LBA)</td>
<td>S2</td>
</tr>
<tr>
<td>Proffered Papers</td>
<td></td>
</tr>
<tr>
<td>Breast Cancer (abstract 5LBA)</td>
<td>S3</td>
</tr>
<tr>
<td>Proffered Papers</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Malignancies – Upper GI (abstract 6LBA)</td>
<td>S3</td>
</tr>
<tr>
<td>Proffered Papers</td>
<td></td>
</tr>
<tr>
<td>Health Economics of Cancer (abstract 7LBA)</td>
<td>S4</td>
</tr>
<tr>
<td>Poster Spotlight Session 1</td>
<td></td>
</tr>
<tr>
<td>Poster Spotlight Session 1 (abstract 8LBA)</td>
<td>S4</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials III (abstract 1BA)</td>
<td>S4</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials I (abstract 2BA)</td>
<td>S5</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials III (abstract 3BA)</td>
<td>S5</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials I (abstract 4BA)</td>
<td>S6</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials III (abstract 5BA)</td>
<td>S6</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials II (abstract 6BA)</td>
<td>S7</td>
</tr>
<tr>
<td>Plenary Session</td>
<td></td>
</tr>
<tr>
<td>Practice Changing Trials III (abstract 7BA)</td>
<td>S7</td>
</tr>
<tr>
<td>Proffered Papers</td>
<td>Poster Session</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Breast Cancer (abstracts 101–106)</td>
<td>S7</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Breast Cancer (abstracts 157–264)</td>
<td>S10</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Central Nervous System (abstracts 315–330)</td>
<td>S45</td>
</tr>
<tr>
<td><strong>Proffered Papers</strong></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Malignancies – Colorectal Cancer (abstracts 379–382)</td>
<td>S49</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Malignancies – Colorectal Cancer (abstracts 433–491)</td>
<td>S50</td>
</tr>
<tr>
<td><strong>Proffered Papers</strong></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Malignancies – Upper GI (abstracts 540–544)</td>
<td>S71</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Malignancies – Upper GI (abstracts 596–639)</td>
<td>S73</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Gynaecological Cancer (abstracts 688–720)</td>
<td>S87</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Haematological Malignancies (abstracts 763–773)</td>
<td>S98</td>
</tr>
<tr>
<td><strong>Proffered Papers</strong></td>
<td></td>
</tr>
<tr>
<td>Head and Neck Cancer (abstracts 822–826)</td>
<td>S101</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Head and Neck Cancer (abstracts 877–915)</td>
<td>S103</td>
</tr>
<tr>
<td><strong>Proffered Papers</strong></td>
<td></td>
</tr>
<tr>
<td>Health Economics of Cancer (abstracts 966–972)</td>
<td>S113</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Health Economics of Cancer (abstracts 1023–1033)</td>
<td>S116</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Health Policy (abstracts 1083–1091)</td>
<td>S119</td>
</tr>
<tr>
<td><strong>Proffered Papers</strong></td>
<td></td>
</tr>
<tr>
<td>Melanoma (abstracts 1141–1146)</td>
<td>S122</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Melanoma (abstracts 1197–8LBA)</td>
<td>S124</td>
</tr>
<tr>
<td><strong>Poster Session</strong></td>
<td></td>
</tr>
<tr>
<td>Organisation of Cancer Care Delivery (abstracts 1259–1273)</td>
<td>S129</td>
</tr>
<tr>
<td>Poster Session</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Outcome Research (abstracts 1322–1346)</td>
<td>S134</td>
</tr>
<tr>
<td>Paediatric Oncology (abstracts 1395–1410)</td>
<td>S142</td>
</tr>
<tr>
<td>Preclinical (abstracts 1460–1466)</td>
<td>S148</td>
</tr>
<tr>
<td>Rare Cancers – NET (abstracts 1516–1518)</td>
<td>S150</td>
</tr>
<tr>
<td>Rare Cancers – Sarcoma (abstracts 1568–1573)</td>
<td>S152</td>
</tr>
<tr>
<td>Rare Cancers – Sarcoma (abstracts 1624–1629)</td>
<td>S154</td>
</tr>
<tr>
<td>Screening (abstracts 1679–1686)</td>
<td>S156</td>
</tr>
<tr>
<td>Supportive Care (abstracts 1734–1738)</td>
<td>S159</td>
</tr>
<tr>
<td>Palliative and Supportive Care (abstracts 1789–1825)</td>
<td>S160</td>
</tr>
<tr>
<td>Survivorship (abstracts 1874–1877)</td>
<td>S171</td>
</tr>
<tr>
<td>Survivorship (abstracts 1928–1941)</td>
<td>S172</td>
</tr>
<tr>
<td>Thoracic Cancer (abstracts 2046–2065)</td>
<td>S178</td>
</tr>
<tr>
<td>Urology (abstracts 2114–2118)</td>
<td>S186</td>
</tr>
<tr>
<td>Urology (abstracts 2169–2200)</td>
<td>S188</td>
</tr>
<tr>
<td><strong>Author index</strong></td>
<td>S199</td>
</tr>
</tbody>
</table>
Abstracts

Plenary Session (Saturday 28 January 2017)
Practice Changing Trials I

1LBA LATE-BREAKING ABSTRACT
Eight-year follow up results of the OTOSOR Trial: The Optimal Treatment Of the Axilla – Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer.
A randomized, single centre, phase III, non-inferiority trial
1National Institute of Oncology, Department of Breast and Sarcoma Surgery, Budapest, Hungary; 2Norfolk and Norwich University Hospital, Department of General Surgery, Norwich, United Kingdom; 3National Institute of Oncology, Center of Radiotherapy, Budapest, Hungary; 4National Institute of Oncology, Department of Pathology, Budapest, Hungary; 5National Institute of Oncology, Department of Diagnostic Imaging, Budapest, Hungary; 6Hungarian Academy of Sciences, MTA TTK Momentum Cancer Biomarker Res. Group, Budapest, Hungary; 7National Institute of Oncology, Department of Breast and Sarcoma Surgery, Budapest, Hungary

Introduction: The National Institute of Oncology, Budapest conducted a single centre randomized clinical study. The OTOSOR (Optimal Treatment Of the Axilla – Surgery Or Radiotherapy) trial compares completion of axillary lymph node dissection (cALND) to regional nodal irradiation (RNI) in patients with sentinel lymph node metastasis (pN1sN1) in stage I–II breast cancer.

Patients and Methods: Patients with primary invasive breast cancer (cN0 and cT<3 cm) were randomized before surgery for cALND (standard treatment) or RNI (investigational treatment). Sentinel lymph nodes (SN) were investigated with serial sectioning at 0.5 mm levels by haematoxylin-eosin staining. Investigational treatment arm patients received 50 Gy RNI instead of cALND. Adjuvant treatment and follow up were performed according to the actual guidelines. Between August 2002 and June 2009, 1,054 patients were randomized for cALND and 1,052 patients for RNI. SN was evaluated in 2,073 patients and was positive in 526 patients (25.4%). 474 cases were evaluable (244 in the cALND and 230 in the RNI arm), and in the cALND group 94 of 244 patients (38.5%) who underwent completion axillary surgery had additional positive nodes. The two arms were well balanced according to the majority of main prognostic factors. Primary endpoint was axillary recurrence and secondary endpoints were overall survival (OS) and disease-free survival (DFS).

Results: Mean follow-up was 97 months (Q1–Q3 80–120). Axillary recurrence was 2.0% in cALND arm vs. 1.7% in RNI arm (P = 1.00). OS at 8 years was 77.9% vs. 84.8% (P = 0.060), and DFS was 72.1% in cALND arm and 77.4% after RNI (P = 0.51). The results show that RNI is statistically not inferior to cALND treatment.

Conclusions: The long term follow-up results of this prospective-randomized trial suggest that RNI without cALND does not increase the risk of axillary failure in selected patients with early-stage invasive breast cancer (cT<3 cm, cN0) and pN1sN1. Axillary radiotherapy should be an alternative treatment for selected patients with sentinel lymph node metastases.

No conflict of interest.

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2LBA LATE-BREAKING ABSTRACT
Efficacy and safety of ribociclib (LEE011) + letrozole in elderly patients with hormone receptor-positive (HR+), HER2-negative (HER2–) advanced breast cancer (ABC) in MONALEESA-2
1The Netherlands Cancer Institute and BOOG Study Center, Medical Oncology, Amsterdam, Netherlands; 2Floridoson Cancer Specialists & Research Institute; Sarah Cannon Research Institute, Hematology-Oncology, Fort Myers, USA; 3Institut de Cancérologie de l’Ouest – René Gauducheau Centre de Recherche en Cancérologie, Medical Oncology, Nantes, France; 4Zuyderland Medical Center, Internal Medicine, Sittard-Geleen-Herpen, Netherlands; 5University, Obstetrics and Gynecology, Ulm, Germany; 6Tom Baker Cancer Centre, Oncology, Calgary, Canada; 7University Hospital of Besançon-Hospital Jean-Minjoz, Medical Oncology, Besançon, France; 8Lillebaell Hospital, Clinical Oncology, Belgium; 9Hospital Peryla Byington Centro de Referência da Saúde da Mulher, Gynecology and Obstetrics, São Paulo, Brazil; 10University of Ottawa, Medical Oncology, Ottawa, Canada; 11Novartis Pharma AG, Basel, Switzerland; 12Novartis Pharma S.A.S., Paris, France; 13Novartis Pharmaceuticals Corporation, East Hanover, USA; 14Sarah Cannon Research Institute, Clinical Operations, Nashville, USA

Background: Over 40% of patients (pts) diagnosed with breast cancer are aged ≥65 years. First-line endocrine therapy (ET) remains the standard of care for elderly pts with HR+, HER2– ABC, but ET resistance and subsequent disease progression frequently occur. Addition of targeted agents may extend the treatment benefit derived from ET and delay disease progression; however, physiologic functioning, comorbidities, and concomitant medications may impact the tolerability of combination regimens in elderly pts. In the randomized Phase 3 MONALEESA-2 study (NCT01958021), first-line ribociclib (a selective cyclin-dependent kinase 4/6 inhibitor) + letrozole significantly prolonged progression-free survival (PFS) vs placebo + letrozole in postmenopausal women with HR+, HER2– ABC, with a hazard ratio (HR) of 0.556 (95% confidence interval [CI] 0.429–0.720). Here we present results from a subgroup analysis in pts aged ≥65 years.

Material and Methods: Postmenopausal women (N = 668) with HR+, HER2– ABC with no prior systemic treatment for ABC were randomized 1:1 to receive ribociclib (600 mg/day, 3-weeks-on/1-week-off) + letrozole (2.5 mg/day, continuous) or placebo + letrozole. Pts had Eastern Cooperative Oncology Group performance status ≤1, adequate bone marrow and organ function, and no history of active cardiac dysfunction. The primary endpoint was locally assessed PFS (per Response Evaluation Criteria in Solid Tumors v1.1), with supportive analyses in pre-specified subgroups. Secondary endpoints were OS and safety (per Common Terminology Criteria for Adverse Events v4.03).

Results: In total, 295 pts aged ≥65 years (median age 71 years [range: 65–91]) received ribociclib + letrozole (n = 150) or placebo + letrozole (n = 145). At data cut-off (Jan 29, 2016), treatment was withdrawn in 14.5% (22/145) pts (ribociclib + letrozole vs placebo + letrozole arm); the most common reasons for discontinuation were disease progression (33 [22%] vs 51 [35%] pts) and adverse events (AEs; 13 [9%] vs 5 [3%] pts). Median duration of study treatment exposure was 13.1 vs 12.5 months (ribociclib + letrozole vs placebo + letrozole). In pts aged ≥65 years, median PFS was not reached (NR; 95% CI 19.3–NR) in the ribociclib + letrozole arm vs 18.4 months (95% CI 15.0–NR) in the placebo + letrozole arm, with a HR of 0.698 (95% CI 0.394–0.937). The most frequent all-cause Grade 3/4 AEs (>10% difference between ribociclib + letrozole vs placebo + letrozole).
3LBA LATE-BREAKING ABSTRACT

Pembrolizumab vs investigator-choice chemotherapy for previously treated advanced urothelial cancer: Phase 3 KEYNOTE-045 study


Background: There is no standard second-line therapy for advanced urothelial cancer. While paclitaxel, docetaxel, and vinflunine are commonly used, they provide limited clinical benefit. KEYNOTE-045 (NCT02256436) compared the efficacy and safety of the anti-PD-1 antibody pembrolizumab (pembro) vs investigator-choice chemotherapy (chemo) as second-line therapy for advanced urothelial cancer following first-line platinum-based chemo.

Methods: Eligible patients (pts) were enrolled regardless of PD-L1 expression and randomized 1:1 to pembro 200 mg Q3W for 24 mo or investigator's choice of paclitaxel 175 mg/m² Q3W, docetaxel 75 mg/m² Q3W, or vinflunine 320 mg/m² Q3W. Randomization was stratified by ECOG PS (0/1 vs 2), liver metastases (yes vs no), hemoglobin level (<10 vs >10 g/dL), and time from last chemo (<3 vs >3 mo). Primary endpoints were OS and PFS (RESCIT v1.1, blinded, independent central review). ORR was a key secondary endpoint. OS and PFS differences were assessed in the ITT population using the stratified log-rank test.

Table 1. Efficacy in KEYNOTE-045

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Pembrolizumab (N=270)</th>
<th>Chemo (N=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>155</td>
<td>179</td>
</tr>
<tr>
<td>Median (95% CI), mo</td>
<td>10.3 (9.0–11.8)</td>
<td>7.4 (6.1–8.3)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.73 (0.59–0.91)</td>
<td>P = 0.0022</td>
</tr>
<tr>
<td>PFS</td>
<td>218</td>
<td>219</td>
</tr>
<tr>
<td>Median (95% CI), mo</td>
<td>2.1 (2.0–2.2)</td>
<td>3.3 (2.3–3.5)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.98 (0.81–1.19)</td>
<td>P = 0.42</td>
</tr>
<tr>
<td>ORR (95% CI)</td>
<td>21.1% (16.4–26.5)</td>
<td>11.4% (7.9–15.8)</td>
</tr>
<tr>
<td>Treatment difference, % (95% CI)</td>
<td>9.6 (3.5–15.9)</td>
<td>P = 0.0011</td>
</tr>
</tbody>
</table>

Results: Between Nov 5, 2014, and Nov 13, 2015, 542 pts from 29 countries were enrolled: 270 in the pembro arm, 272 in the chemo arm. As of Sept 7, 2016, median follow-up was 9.0 mo; 49 (18.4%) pts remained on pembro and 3 (1.2%) pts remained on chemo. Baseline characteristics were generally balanced between arms, with 87.3% with visceral disease, 34.3% with liver metastases, 1.1% with ECOG PS 2, 10.9% with hemoglobin level <10 g/dL, and 38.2% with <3 mo since last chemo. Pembro significantly improved OS over chemo (HR 0.73, P = 0.0022; median 10.3 vs 7.4 mo) (Table 1). There was no difference in PFS (HR 0.98, P = 0.42) (Table 1). ORR was significantly improved with pembro (21.1% vs 11.4%) (Table 1). Pembro was associated with fewer any-grade (60.9% vs 90.2%) grade 3–5 treatment-related AEs (15.0% vs 48.4%). 4 pts in each arm died due to treatment-related AEs.

Conclusions: Pembro demonstrated a statistically significant OS benefit over chemo in the second-line advanced urothelial cancer setting, making it the first therapy to demonstrate a survival benefit over an active comparator in this population. The superior OS combined with the lower rate of any-grade and high-grade treatment-related AEs support pembro as a new standard of care for advanced urothelial cancer that progressed on/after platinum-based chemo.

Plenary Session (Monday 30 January 2017)

Practice Changing Trials III

4LBA LATE-BREAKING ABSTRACT

Breast conserving therapy and mastectomy revisited: Breast cancer-specific survival and the influence of prognostic factors in 129,692 patients

M. Lagendijk1, M.C. Van Maaren2,3, S. Saadatmand4, L.J.A. Strobbe4,5, P. Poortmans6, L.B. Koppert1, M.M.A. Tilanus-Linthorst1, S. Siesling1,2.

Background: This large, population-based study compared breast-conserving surgery plus radiation therapy (BCT) with mastectomy for breast cancer-specific (BCSS) and overall survival (OS). The influence of prognostic factors (age, stage, adjuvant systemic therapy, hormonal and HER2 receptor status and comorbidities) was studied in two time cohorts.

Methods: Patients with primary T1–2N0–2M0 breast cancer, diagnosed in 1999–2012, were selected from the Netherlands Cancer Registry. Two time cohorts were created: 1999–2005 (long-term follow-up, LTFU) and 2006–2012 (contemporary adjuvant systemic therapy). Cause of death was derived from the Statistics Netherlands (CBS). Multivariable analyses were performed for the two time cohorts within all T1–2N0–2 and separately for T1–2N0–1 and T1–2N2 stages. The T1–2N0–1 subgroup was further stratified for age, hormonal and HER2 receptor status, adjuvant systemic therapy and comorbidity.

Results: In total, 129,692 patients were included. In the 1999–2005 cohort BCT showed better BCSS [HR 0.72 (95% CI 0.69–0.76)] and OS [HR...
randomization (data not shown). There were no HRQoL differences when comparing the Swedish patients with the Austrian and German sample.

| Table 1. EORTC QLQ-30 and QLQ-BR23 scales by treatment and follow-up time for the Swedish sample |
|-----------------|-----------------|-----------------|
| Scale           | HRQoL At end of treatment | HRQoL At eight months |
|                 | Dose Standard P | Dose Standard P |
| QLQ-C30         |                 |                 |
|                 | **HR (95%CI)**  | **HR (95%CI)**  |
| Global health status | 41 (21) 55 (21) | **<0.001** 67 (19) 68 (20) |
| Physical functioning | 65 (22) 74 (19) | **<0.001** 82 (17) 85 (15) |
| Role functioning | 33 (29) 48 (31) | **<0.001** 65 (30) 69 (28) |
| Emotional functioning | 68 (22) 70 (23) | 0.32 73 (21) 72 (24) |
| Social functioning | 50 (28) 60 (25) | **<0.001** 75 (25) 77 (24) |
| Fatigue | 61 (26) 49 (25) | **<0.001** 34 (23) 32 (23) |
| QLQ-BR23         |                 |                 |
| Body image | 57 (29) 57 (30) | 0.91 70 (26) 69 (28) |
| Sexual functioning | 10 (16) 15 (19) | **<0.01** 21 (21) 24 (21) |
| Systemic side effects | 52 (18) 41 (19) | **<0.001** 20 (14) 17 (14) |
| Breast symptoms | 13 (15) 14 (15) | 0.81 23 (20) 22 (19) |
| Arm symptoms | 12 (16) 14 (17) | 0.24 21 (21) 23 (20) |

Conclusion: There were differences between the randomization groups during treatment, with lower HRQoL in the dose dense group during treatment. At follow-up, however, patients in that group recovered to HRQoL levels similar to the standard group. Thus, dose dense and tailored therapy appears to have negative HRQoL effects during treatment, but the patients recover fast once treatment is over.

References
No conflict of interest.
as an endoscopy triage test, the benefits to the healthcare system may include cost-saving through reducing the number of negative endoscopies. However these findings must be further validated in an un-enriched larger population of patients undergoing diagnostic endoscopy and in false negative patients. The value of repeat testing should be established.

Funding: This study was supported by the NIHR (NIHR-DRF-201407–088). Trial registration: This study has been registered on the National Institute for Health Research clinical trials portfolio (UKCRN 18063).

No conflict of interest.

Proffered Papers (Saturday 28 January 2017)

Health Economics of Cancer

9A LATE-BREAKING ABSTRACT

Recognising European Cancer Nursing (RECAN): A systematic review of nurses’ roles and interventions of nurses caring for patients with cancer

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Background: Nurses represent the largest group of healthcare professionals and play a pivotal role in developing and delivering interventions designed to improve patient experience and outcomes. However, the evidence for this claim often remains hidden and we have insufficient knowledge of the range and scope of interventions delivered by cancer nurses. This systematic review identifies, appraises and synthesises available evidence relating to the value and impact of cancer nursing and reports on the roles and contributions of cancer nurses in clinical trials of cancer nursing interventions.

Materials and Methods: 10 electronic databases searched systematically (from 01 January 2000 to 31 May 2016; including CENTRAL, MEDLINE, AMED, CINAHL, EMBASE, Epistemonikos, CDSR, DARE, HTA) and clinical trial registers (WHO ICTRP). No language restrictions were applied. Eligibility and methodological quality were independently assessed. Data were extracted in accordance with the Template for intervention Description and Replication (TiDeR) guidelines, and interventions were categorized using the Omaha System Intervention Scheme. Missing data were sought from trialists and tabulated in a narrative format.

Results: We identified 22,450 records, screened 16,169 abstracts and retrieved 925 full text articles. 325 unique trials (n = 217,221 participants) were included in final narrative synthesis. Of the included studies, 262 were Randomized Controlled Trials (RCTs); and 43 were Controlled-Before-After studies (CBA) across 26 countries. The majority of trials were focused on the phase of cancer treatment (n = 201); but cancer nurses were involved in delivering interventions across the cancer trajectory (6 trials in prevention and risk reduction; 25 screening; 9 diagnosis; 43 survivorship; 41 end-of-life care). Interventions included direct care, psychological support, teaching, assessment and monitoring, care management and coordination, and were delivered face-to-face; via telephone and online; to individuals and groups. 18 trials included active patient and public involvement in the trial design, including the co-creation of intervention materials with patients and other key stakeholders.

Conclusions: As the first study to synthesise evidence from studies across the entire cancer spectrum, this review provides crucial and important insights into the evidence base for the range of cancer nursing interventions. It will be useful for workforce planning; identifying skill sets for the delivery of complex interventions and enhancing the understanding of the research focus of nursing roles. It can also form the basis of an ongoing dialogue with policy makers across Europe in order to enhance and understanding of the contribution and future potential of specialist cancer nursing.

No conflict of interest.

Saturday 28 January 2017

Poster Spotlight Session 1

8LBA LATE-BREAKING ABSTRACT

Two year overall survival rate of all advanced melanoma patients treated with ipilimumab in Australia 2013–2014

H. Kim1, S. Comey1, Bristol-Myers Squibb, External Affairs, Mulgrave, Australia

Background: Australia has one of the world’s highest melanoma incidence rates (e.g. 2012: 34 per 100,000 in Australia vs 13.2 per 100,000 in the European Union). Until recently treatment of advanced melanoma was largely ineffective. Ipilimumab (IPI), the first registered immunotherapy for the use as an anti-cancer medicine, was approved for listing on the Australian Pharmaceutical Benefits Schedule (PBS) for treatment of advanced melanoma (any line of therapy) on 1st August 2013. There are 12 clinical trials published by Schadendorf et al. (2015). However there is still some uncertainty for clinicians and patients as to how trial results would translate into real world clinical practice. As a condition the 2 year overall survival (OS) had to be reported in the first year’s cohort of patients. The rationale was to ensure pay for performance as demonstrated in the cost effectiveness analysis presented in the reimbursement submission to the Pharmaceutical Benefits Advisory Committee (PBAC). A 2-year survival rate of 21.6% was cited in the PBAC. This cohort study reports the 2-year OS in all patients receiving PBS subsidised IPI between 01-Aug-13 to 31-Jul-14 in Australia.

Material and Methods: The main data gathering tool was a web portal integrated into the supply chain. Physicians were required to do mandatory training on treatment protocols for IPI before registration and obtaining consent from each patient. A follow-up email was sent to the physicians at the 2-year anniversary following the first exposure. Rejection of calls were placed to non-responders. A cut-off date of 23-Sep-16 was set for the data gathering allowing for 8 weeks of following up and resolve queries. Simple descriptive statistics were used to calculate the proportion alive, dead and lost to follow-up.

Results: A total of 913 patients were registered on the portal. Two patients declined to participate and 1 passed away before drug was dispatched leaving 910 patients. At the 2 year anniversary, 24.0% of patients (218/910) were confirmed alive, 52.3% (476/910) were confirmed dead and 6.3% (57/910) were confirmed lost to follow-up. The remaining 17.5% (159/910) were unconfirmed lost to follow-up, with no reply from the treating physician.

Conclusions: The 2-year OS rate of patients receiving IPI on the PBS from 01-Aug-13 to 31-Jul-14 is at least 24.0%. A large proportion were unconfirmed to follow-up and it is therefore possible that the 2-year survival rate was higher. The results from this cohort study are significant. They indicate that Australian patients initiated with IPI between 01-Aug-13 to 31-Jul-14 performed at least as well with respect to OS as those in the pivotal clinical trials presented in the PBAC submission. The results provide external validation for the OS rate seen in a clinical trial setting.

No conflict of interest.

Plenary Session (Monday 30 January 2017)

Practice Changing Trials III

1BA BEST ABSTRACT

Investigating the effect of a supportive complementary and alternative medicine (CAM) nursing intervention to improve quality of life outcomes in gynecologic oncology patients – first report of a randomized controlled trial

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Background: Increasingly, patients complement their conventional treat- ment plans with various methods from Complementary and Alternative
Materials and Methods: A two-armed randomized controlled trial was conducted and patients diagnosed with breast or gynecologic cancers were recruited at two certified cancer centers (NCT, National Center of Tumor Diseases, Heidelberg, and SKK, Community Hospital Karlsruhe). In the Intervention group, patients additionally received the symptom-guided nursing CAM intervention at each new cycle of CHT (max. 24 weeks), while control group patients received routine supportive care. Patient-oriented outcomes were measured at the following time points: T1 = baseline, prior to start of initial treatment, T2 = midline, after the first half of CHT, T3 = end of CHT, and T4 = 6 months after completion of CHT. In addition, the EORTCQLQC30 measuring quality of life as the primary outcome was completed weekly with the patient diary.

Results: From July 2014 until April 2016, 251 patients were randomized to intervention and control groups (n = 126 vs. n = 125). The sample (25–89 years, mean 51.4 ± 15.5 years) represents patients with different cancers (44% breast, 10% ovaries, 4% uterus, 2% other) under curative (84%) as well as under palliative (16%) CHT.

Data collection and databank cleansing will proceed until December 2016. Data will be analyzed with linear mixed models for the complete time span: T1 to T4 whilst considering time point T3 as having the highest impact. The models will take into account fixed group effects (e.g., intervention/ control group, interaction of treatment and time, QoL baseline scores) as well as random individual effects (repeated measurements for each patient) to provide a stronger base for quantitative analytic procedures. First results will be presented in January 2017 at the ECC.

Conclusions: The designed CAM intervention has been successfully implemented in two different cancer centers. Results from the CONGO trial will evaluate the quality of life of all patients and contribute to a better understanding of everyday coping strategies can be improved by a complex CAM nursing intervention during the arduous phase of curative or palliative cancer treatment. No conflict of interest.
had axilla RT only, 321/365 had SCF RT only and 31/365 had both axilla & SCT RT. There were no significant differences between 50 Gy/25Fr and the hypofractionated regimens for patient-assessed arm or shoulder symptoms.

<table>
<thead>
<tr>
<th>Arm/shoulder pain</th>
<th>Cumulative proportion with a moderate/marked event at 5 years</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>START-A 50 Gy</td>
<td>32.3 (23.3–43.7)%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>41.6 Gy</td>
<td>31.4 (22.1–43.6)%</td>
<td>1.03 (0.60–1.77)</td>
<td>0.92</td>
</tr>
<tr>
<td>39 Gy</td>
<td>30.8 (21.4–43.0)%</td>
<td>0.96 (0.56–1.66)</td>
<td>0.85</td>
</tr>
<tr>
<td>START-B 50 Gy</td>
<td>29.7 (18.0–46.6)%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>40 Gy</td>
<td>23.6 (14.1–37.9)%</td>
<td>0.94 (0.44–2.00)</td>
<td>0.87</td>
</tr>
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</table>

Swelling in arm or hand

<table>
<thead>
<tr>
<th>Difficulty raising arm</th>
<th>Cumulative proportion with a moderate/marked event at 5 years</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>START-A 50 Gy</td>
<td>41.2 (8.3–23.8)%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>41.6 Gy</td>
<td>18.2 (11.0–29.3)%</td>
<td>1.01 (0.46–2.18)</td>
<td>0.99</td>
</tr>
<tr>
<td>39 Gy</td>
<td>16.1 (9.2–27.3)%</td>
<td>1.15 (0.54–2.47)</td>
<td>0.72</td>
</tr>
<tr>
<td>START-B 50 Gy</td>
<td>9.5 (3.7–23.3)%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>40 Gy</td>
<td>6.0 (2.0–17.4)%</td>
<td>0.55 (0.13–2.36)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Shoulder stiffness

<table>
<thead>
<tr>
<th>Shoulder stiffness</th>
<th>Cumulative proportion with a moderate/marked event at 5 years</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>START-A 50 Gy</td>
<td>18.8 (11.9–29.0)%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>41.6 Gy</td>
<td>9.5 (4.7–19.0)%</td>
<td>0.63 (0.28–1.28)</td>
<td>0.27</td>
</tr>
<tr>
<td>39 Gy</td>
<td>15.4 (8.8–26.1)%</td>
<td>0.63 (0.39–1.80)</td>
<td>0.64</td>
</tr>
<tr>
<td>START-B 50 Gy</td>
<td>18.6 (9.2–35.4)%</td>
<td>0.64 (0.23–1.78)</td>
<td>0.40</td>
</tr>
<tr>
<td>40 Gy</td>
<td>10.1 (4.3–22.6)%</td>
<td>–</td>
<td>–</td>
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</tbody>
</table>

Conclusion: Appropriately dosed hypofractionated lymphatic RT is safe according to patient assessed arm and shoulder symptoms.

No conflict of interest.

Plenary Session (Saturday 28 January 2017)

Practice Changing Trials I

4BA BEST ABSTRACT

Sarcoma care pathways – the patient viewpoint

R. Wilson1, M. Wartenberg2, E. Lecointe3. 1 Sarcoma Patients Euronet, Church Stretton, United Kingdom; 2 Sarcoma Patients Euronet, Bad Nauheim, Germany; 3 Sarcoma Patients Euronet, Rennes, France

Sarcomas are rare cancers of connective tissue. They are a heterogeneous group of some 100 cancers but only account for about 1% of all diagnoses. Treatments are varied but specialist surgery accounts for most of survival. More than 50% of all sarcoma patients are diagnosed with advanced cancer, some at diagnosis, some after a decade or more of otherwise undisturbed survival. Prognosis for this group is poor and attempts to identify targeted and genomic therapies have had few successes, the most notable ones being for GIST.

Sarcoma Patients Euronet (SPAEN) has been approached by several international bodies seeking a patient view on the optimum pathway of care and treatment. Their seek a patient perspective either to complement the views of specialist doctors or to provide a framework for a plan in the absence of specialist viewpoints.

The SPAEN leadership decided to develop a paper to address the pathway issues. The paper was debated by its membership during the annual conference (September 2016; Warsaw). The final paper is available openly and on-demand to any government, regulatory or professional body seeking to improve the services offered to sarcoma patients. In the pathway paper SPAEN has identified a number of areas of primary concern:

- Diagnosis – the importance of specialist pathway supported by second-opinion networks and education
- Specialist surgery – limb tumours account for about 50% of incidence and skills are quite widespread but retroperitoneal tumours are less common and require radical approaches by nominated specialists
- Referral networks – many sarcomas are diagnosed in a non-sarcoma specialty; while GIST is generally well handled by GI specialists SPAEN has more concerns about gynae tumours, while recognising the problems they present

- Patient rehabilitation – this can require specialist skills and is a major factor in patients attaining a good quality of life following primary treatment
- Access to clinical trials – many studies are not available in some countries, for good reasons, but there is virtually no cross-border trial entry; SPAEN wants to see wider access made available
- Advanced disease – in some countries patients diagnosed with lung metastases (the most common distant spread of disease) can be assessed for surgery; in some countries they are not assessed and thoracic surgery is not available
- Second-opinions – patients from the accession countries often seek advice from a specialist in a recognised sarcoma centre in the west; that advice may not be able to be met in the patient’s home country and the funds may not be available to follow that pathway. This leads to: Specialist centres – we believe there should be a minimum of one specialist sarcoma treatment centre, with a full multi-disciplinary team (MDT), in each EU country; the ratio should be 1 centre to between 5000 and 6 million of population. A full MDT is defined.

Conflict of interest: Ownership: The authors are co-founders of SPAEN which is an incorporated body owned in common and regulated in German law. Advisory Board: Roger Wilson is a sarcoma patient, honorary president and unpaid member of the Board of SPAEN. Wartenberg is a member of the Board of SPAEN and receives fees for acting as an executive director; Estelle Lecointe is a GIST patient and an unpaid member of the Board of SPAEN.

5BA BEST ABSTRACT

Impact of chronic neuropathic pain on job retention among cancer survivors: evidence from the French national survey VICAN

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Background: An important economic and social burden has been associated with neuropathic pain but the social impact of chronic neuropathic pain (CNP) in the cancer context has not been specifically studied. Regarding the high prevalence of neuropathic pain among cancer survivors, it is important to focus on consequences of cancer-related chronic pain on return to “normal” life. We assume that CNP is a major long term barrier to return to work for cancer survivors. So we decided to investigate factors associated with job retention, especially CNP, among five year French cancer survivors using data of the French national survey VICAN.

Material and Methods: VICAN is a French national longitudinal survey on life conditions of cancer survivors diagnosed in 2010 for eleven tumour sites and combines clinical, medical and social data collection. Patient questionnaires were administered 2 and 5 years after diagnosis. The patient questionnaire deals with access to healthcare, recovery after treatments and impact of the disease on personal and professional life in the two and five years following diagnosis, respectively (VICAN national surveys 2012 and 2015). Neuropathic characteristic of pain is detected by the seven-item DN4 tool, included in patient questionnaire. To assess the impact of CNP on job retention, univariate and multivariate analyses have been performed including several medical, economic or social characteristics.

Results: In 2010, among the 1139 cancer survivors aged from 18 to 57 years at diagnosis, 962 were employed. The percentage of job retention five years after was 77.4% and was significantly higher among women (80.0% versus 69.9%; p = 0.001). Among the 28.4% cancer survivors who reported CNP 5-years after diagnosis, 67.4% had already reported chronic neuropathic pain three years before. Job retention was significantly lower among survivors who reported CNP five years after cancer diagnosis than among survivors with no chronic neuropathic pain (OR [95% CI], 0.46 [0.337; 0.631]). After controlling on gender, age at diagnosis and adverse cancer evolution, job retention among five-year survivors was significantly associated with education level, working condition and CNP.

Conclusions: Attention must be paid to specific burden of CNP on cancer survivor’s rehabilitation in the context of global underreporting and understatement of pain among this subgroup. In addition of improving pain screening and identification of predominant type of pain, new therapeutic approaches as alternative to common analgesics must be developed to manage adequately CNP and reduce its deleterious effect on cancer survivors’ life conditions.

No conflict of interest.
**Plenary Session (Sunday 29 January 2017)**

**Practice Changing Trials II**

**BEST ABSTRACT**

**Survival of patients with colorectal peritoneal metastases is affected by treatment discrepancies among hospitals of diagnosis: a nationwide population-based study**

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**Background:** In the Netherlands, cytoreductive surgery with HIPEC for peritoneal metastases of colorectal cancer (PMCRC) is performed in high-volume HIPEC centres, whereas PMCRC is diagnosed in all hospitals. This nationwide population-based study assessed whether hospital diagnosis of colorectal synchronous peritoneal metastases or colorectal cancer (PMCRC) affects treatment selection and overall survival (OS).

**Methods:** Between 2005–2015, all patients with synchronous PMCRC without systemic metastases were selected. Treatment was classified as CRS/HIPEC, systemic therapy as single treatment, or supportive care. Hospitals of diagnosis were classified as: (1) non-teaching or academic/teaching hospital, (2) HIPEC centre or referring hospital. Referring hospitals were further classified based on the likelihood of CRS/HIPEC as high-, medium-, or low-probability hospital. Multivariable regression analyses, with different models for hospital categories, were used to assess the influence of hospital of diagnosis on the likelihood of CRS/HIPEC and OS.

**Results:** 2661 patients, diagnosed in 89 hospitals, were included. At individual hospital level, CRS/HIPEC and systemic therapy ranged from 0% to 50% and 6% to 67%, respectively. Hospital of diagnosis was related to the likelihood of CRS/HIPEC: 33% vs. 13% for HIPEC centres vs. referring hospitals (OR 3.66 [2.40–5.58]), and 11% vs. 17% for non-teaching hospitals vs. academic/teaching hospitals (OR 0.60 [0.47–0.77]). Hospital of diagnosis was related to median OS: 14.1 vs. 9.6 months for HIPEC centres vs. referring hospitals (p < 0.001), and 8.7 vs. 11.5 months for non-teaching hospitals vs. academic/teaching hospitals (p < 0.001). Compared to diagnosis in medium-probability referring hospitals, median OS was increased in high-probability referring hospitals (12.6 months, HR 0.82 [0.73–0.91]), and reduced in low-probability referring hospitals (8.1 months, HR 1.12 [1.01–1.24]).

**Conclusion:** This study indicates a lack of uniformity in treatment selection, which influences survival, and potential underuse of CRS/HIPEC for synchronous PMCRC.

**No conflict of interest.**

### Practice Session (Monday 30 January 2017)

**Practice Changing Trials III**

**BEST ABSTRACT**

**American Intergroup 0116 study (Macdonald et al; NEJM; 2001) changed the intended D2 lymph node dissection. The multicenter CRITICS trial (ChemoRadiotherapy after Induction chemotherapy in Cancer of the Stomach) was conducted to compare both treatment strategies with overall survival as primary endpoint. Quality assurance has been given full control in the CRITICS trial is presented.**

**Material and Methods:** The CRITICS trial is an international randomized phase III trial. From 2007–2015, 788 patients with resectable gastric cancer were included. All patients were intended to receive three courses of chemotherapy followed by gastrectomy including a D1+ lymphadenectomy (removal of stations 1–9 and 11 with exception of station 2 and 4s for distal tumors) according to the protocol (surgical compliance) and with a minimum of 15 lymph nodes (surgicopathological compliance). Surgical non-compliance was defined as inadequate removal of intended lymph node stations. Contamination was defined as lymph nodes removed outside the intended level of resection. The Maruyama Index (MI) was determined and used to predict overall survival.

**Results:** For the current analyses 635 patients who underwent gastric resection with curative intent were eligible. Surgicopathological compliance was 73.3% (n = 459) and improved over the years from 55.0% (2007) to 90.0% (2015). Complete surgical compliance occurred in 40.8% (n = 249). Surgical non-compliance occurred mostly in 1 or 2 stations removed (n = 217, 35.6%). Surgical contamination occurred in 58.8% (n = 357). Median MI was 1 (range 0–136) and a MI <5 was associated with an improved survival (P < 0.001).

**Conclusions:** Surgical quality in the CRITICS trial was excellent with a median MI of 1. Surgicopathological compliance improved over the years likely as a result of regular feedback to participating surgeons and pathologists during the study, in combination with centralization of gastric cancer surgery in the Netherlands. Surgical quality control remains very important in multimodal trials with a surgical component.

**No conflict of interest.**

### Proffered Papers (Sunday 29 January 2017)

**Breast Cancer**

**101**

**Efficacy of internet-based cognitive behavioral therapy in improving sexual functioning of breast cancer survivors with a DSM-IV diagnosis of sexual dysfunction: results of a randomized controlled trial**

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**Background:** Breast cancer survival rates have improved as a result of improved screening and more effective treatments. Consequently, more attention is being paid to quality of life after breast cancer including sexual health issues. Sexual dysfunction is a prevalent, long-term complication of breast cancer and its treatment, with 45–77% of women reporting sexual dysfunction after completion of treatment. Face-to-face cognitive behavioral therapy (CBT) is considered to be the gold standard for the treatment of sexual dysfunctions. However, many women consider face-to-face therapy to be too confronting, and it has been suggested that internet-based therapy might be a more acceptable and less threatening approach.
Recent studies have demonstrated the efficacy of internet-based programs in improving sexual functioning in the general population. In the current study, we evaluated the efficacy of an internet-based CBT program in terms of sexual functioning, relationship intimacy (primary outcomes), body image, menopausal symptoms, marital functioning, psychological distress and health-related quality of life (secondary outcomes) in breast cancer survivors with a DSM-IV diagnosis of sexual dysfunction.

**Materials and Methods:** We randomly assigned 169 breast cancer survivors to either the internet-based CBT (n = 84) or a waiting-list control group (n = 85). The CBT consisted of approximately 20 weekly therapist-guided sessions and had a maximum duration of 24 weeks. Self-report questionnaires were completed by the intervention group at baseline (T0), ten weeks after start of therapy (T1), and post-therapy (T2), and at equivalent times for the control group. We used a mixed-effect modeling approach to compare the groups over time.

**Results:** Compared with the control group, the intervention group showed a significant improvement over time in overall sexual functioning (p < 0.03, effect size (ES) T1 = 0.43), which was reflected in an increased interest in sexual desire (p < 0.001, ES T1 = 0.48, ES T2 = 0.72), sexual arousal (p = 0.008, ES T2 = 0.50), and vaginal lubrication (p = 0.01, ES T2 = 0.46). The intervention group reported more improvement over time in sexual pleasure (p = 0.002, ES T1 = 0.33, ES T2 = 0.48), improvement in body image (p < 0.009, ES T2 = 0.45) and fewer menopausal symptoms (p = 0.007, ES T1 = 0.39) than the control group.

**Conclusions:** Internet-based CBT has a clinically relevant, salutary effect on sexual functioning, body image, menopausal symptoms and, to a lesser degree, on relationship intimacy of breast cancer survivors with a DSM-IV diagnosis of sexual dysfunction.

**No conflict of interest.**

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**102**

**Health-related quality of life analysis from the accelerated partial breast irradiation IMRT-Florence phase 3 trial: Impact of age and scores trend over time**


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**Background:** Accelerated partial breast irradiation (APBI) represents a valid option for selected early breast cancer (BC). We present the health-related quality of life (HRQoL) analysis from the APBI IMRT-Florence phase 3 trial (NCT02104485), focusing on the impact of age and the scores trend over time.

**Material and Methods:** Eligible patients were early BC >40 years old for conserving surgery. APBI consisted of 30 Gy in 5 fractions delivered with IMRT technique. Overall 205/520 patients (105 APBI, and 100 WBI) fully completed all the given questionnaires, and were therefore included in the present analysis. Patients were asked to complete the EORTC QLQ-C30, and the BR23 questionnaires at the beginning (T0), at the end (T1), and after 2 years (T2) from radiation. Mean and standard deviations were calculated for all HRQoL domains, all scores were compared between arms using the Mann–Whitney test. The Kruskal–Wallis test was used to compare the scores between age groups. For repeated measures analysis, we used the Friedman test and Wilcoxon signed rank test, by applying the Bonferroni adjustment (level of statistical significance, p = 0.017).

**Results:** We evaluated the impact of age in each arm, considering three age groups (<50, 51–70, >70 years). As regard the QLQ-C30, in APBI arm we found a significant difference on global health status (GHS) (p = 0.0001), physical functioning (p = 0.0001), and fatigue (p = 0.002) between the three age groups, with better scores among younger patients. No significant difference between the three age groups emerged in the WBI arm. Concerning the QLQ-BR23 module, we found that the younger women in APBI arm showed a better sexual functioning (p = 0.008).

**References**


**No conflict of interest.**
Optimal duration of extended letrozole treatment after 5 years of adjuvant endocrine therapy; results of the randomized phase III IDEAL trial (BOOG 2006–05)

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Despite the success of adjuvant endocrine therapy in early breast cancer, approximately 50% of recurrences occur after the initial 5 years of therapy. Earlier studies showed that endocrine therapy extension after 5 years of tamoxifen with either tamoxifen or aromatase inhibitors (Al) up to 10 years leads to an improved clinical outcome. However, Als are currently standard care in the initial 5 years of therapy, and the benefit of extended use beyond 5 years of AI based therapy is still debated. The randomized phase III IDEAL trial was designed to study the optimal duration of extended adjuvant endocrine therapy after the initial 5 years of any endocrine therapy. Between April 2007 and November 2011, 1824 postmenopausal, HR-positive early breast cancer patients were included by 74 hospitals in the Netherlands. Enrolled patients were older than 50 years and were free of any endocrine therapy (88% AI based). Completed this treatment no longer than 2 years before randomization, and did not have a recurrence at inclusion. The included patients were randomly allocated to either 2.5 or 5 years of letrozole (daily 2.5 mg). Primary outcome was disease free survival (DFS), secondary endpoints were overall survival (OS), distant disease free interval (DDFI), secondary primary breast cancer and safety. Since the randomizations arms diverged after 2.5 years, and by allowing a margin of 10%, a secondary analysis was performed in which patients were only included when being on treatment and event-free at 2.25 years. Of the 1824 included patients, 73 were retrospectively ineligible and excluded. The median follow-up was 6.4 years. From randomization to the end of follow-up, 147 DFS events had occurred in 2.5-year group versus 141 events in the 5-year group (hazard ratio (HR) 0.95, 95% CI 0.76–1.20, \( p = 0.68 \)). For the secondary endpoints, the HRs were 1.11 for OS (95% CI 0.82–1.48, \( p = 0.50 \)) and 1.08 for DDFI (95% CI 0.79–1.49, \( p = 0.62 \)). For second primary breast cancers, 27 (3.1%) events were recorded in the 2.5-year group and 10 (1.1%) in the 5-year group (HR 0.37, 95% CI 0.18–0.76, \( p = 0.007 \)). The secondary analysis starting at 2.25 years included 1291 patients, and showed similar results with only a borderline significant benefit on second primary breast cancer (HR 0.4, \( p = 0.059 \)). No significant difference in the proportion of grade 3/4 events was observed (2.5 yr: 9.8%, 5 yr: 9.7%, \( X^2 = 0.52 \)). No significant differences were observed between treatment extension with either 2.5 or 5 years of letrozole for DFS, OS and DDFI. However, a reduction in second primary breast malignancies was observed in the group treated with 5 years of letrozole, with an absolute risk reduction of 2.2%. In conclusion, this study with a median follow-up of 6.4 years after the initial 5 years of endocrine therapy did not show a benefit of extending AI based adjuvant endocrine therapy beyond a total of 7.5 years. No conflict of interest.

Promising alternative for classic randomized controlled trials: first experience with the cohort multiple randomized controlled trial design in the oncologic setting

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Introduction: The randomized controlled trial (RCT) is the gold standard for evaluation of effectiveness of new interventions, however, RCTs in the oncology setting are often complicated by logistic challenges with multiple interventions in need of testing and patient’s and doctor’s preferences for interventions. The cohort multiple randomized controlled trial (cmRCT), which is a new design for pragmatic trials, was implemented at the University Medical Center Utrecht (UMCU) in the Netherlands.

Methods: The ‘Utrecht cohort for Multiple BReast cancer interVention studies and Long-term evaluAtion’ (UMBRELLA), a prospective cohort designed according to the cmRCT design, was initiated as a subproject of Radiation Oncology of the UMCU. All breast cancer patients undergoing radiotherapy were eligible for participation and asked for informed consent. Informed consent consists of consent for standard outcome measurements and a second consent for treatment allocation (i.e., randomization) when experimental interventions become available to be tested in a RCT. Clinical data on tumor characteristics, treatment, imaging, toxicity, recurrence and survival was collected. Patients filled out validated questionnaires on patient reported outcomes (PROMs) such as quality of life (QoL), pain, fatigue, anxiety and depression, physical activity and cosmetic satisfaction. For each intervention to be randomly tested against standard care, a subcohort of patients who are eligible for the intervention, are identified if they signed consent for treatment allocation. From this, a random sample of patients will be offered the intervention; which they can accept or refuse. Other patients from the subcohort are randomly allocated to the control group and receive standard care without further notification. Routinely collected PROMs of those offered the intervention are compared with the control group.

Results: Since October 2013, 1408 (90% participation rate) patients have been enrolled in UMBRELLA, and of these, 87% (n = 1222) gave consent for randomization. PROMs return rates ranged from 80% at baseline to 62% after 24 months of follow-up. In September 2015, within the cmRCT design was initiated: the FIT trial. The FIT trial assesses the impact of exercise programs on QoL in breast cancer survivors with low levels of physical activity. A subcohort of 130 UMBRELLA participants was selected and all patients were randomized, 65 (50%) patients were allocated to the FIT intervention.

Conclusion: The high participation rates, broad informed consent for randomisation rates, PROMs return rates of UMBRELLA and the initiation of the FIT trial indicate that this innovative design is practically feasible and acceptable to patients.

No conflict of interest.

Hypo- vs normofractionated radiation therapy of early stage breast cancer in the randomized DBCG HYPO trial

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Background: Based on poor results using hypofractionated adjuvant radiotherapy (RT) of early breast cancer (BC) 50 Gy/25 fr. has been Danish Breast Cancer Group (DBCG) standard since 1982. Results from the UK and Canada stimulated a renewed interest in hypofractionation, and the non-inferiority DBCG HYPO trial was initiated. The hypothesis was that 40 Gy/15 fr (2.67 Gy/fr), 3 weeks) did not result in more grade 2–3 breast induction than 50 Gy/25 fr (2.0 Gy/fr, 5 weeks) 3 years post RT.

Material and Methods: 1883 patients >40 years operated with breast conservation for early pT1–2 pN0–1 (muc) BC (n = 1629) or DCIS (n = 253) were enrolled 2009–14 irrespective of breast size, systemic therapy and boost, and randomized 50 Gy/25 fr vs. 40 Gy/15 fr. Strata were institution, breast size (≤600 ml vs. >600 ml), systemic therapy and boost. The primary endpoint was grade 2–3 induction 3 years post RT, secondary endpoints were other normal tissue responses, genetic risk profile for RT-induced fibrosis and recurrences. ClinicalTrial NCT0099818.

Results: 949 pts (50.4%) were assigned to the 50 Gy group and 934 (49.6%) to the 40 Gy group. Median age was 58 years range (39–63), 1323 pts (70.3%) had 3 years follow up. The analysis was intention to treat. Results are actuarial 3 year rates using morbidity in 1801 pts 1 yr post RT as baseline. The 3-y rate of grade 2–3 induction was 12.2% ±1%. Grade 2–3 induction was seen in the 50 Gy group in 91 of 655 pts with the rate 14.2% ±1.4%, and in the 40 Gy group in 85 of 688 pts, the rate being 10.1% ±1%, representing a HR 1.27 (95% CI 0.97–1.66), \( p = 0.08 \). 873 pts (46%) had small breasts with a 3-yr rate of grade 2–3 induction of 9.8% ±1% compared to 14.3% ±1% among 973 pts with large breasts.
HR 1.56, (95% CI 1.18–2.05), p = 0.001. Among the 683 pts (36%) treated with chemotherapy (CT) the rate of grade 2–3 induration was 12.4% ±1%, whilst in the 1200 pts with no CT the rate was 11.8%±2%. HR 0.98 (95% CI 0.74–1.30), p = 0.90. In 438 pts (23%) treated with sequential loco-regional recurrence was 0.3% ± 1%. Moderate hypofractionated whole breast irradiation in early node-negative BC or DCIS does not result in more grade 2–3 induration compared to normofractionated therapy. Large breast size is an independent risk factor for developing induration.

**No conflict of interest.**

**Poster Session (Saturday 28 January 2017)**

**Breast Cancer**

### BRCA 1 status and its association with family history

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**Objective:** To determine the status BRCA 1 in cancer patients of Pakistan. An observational study was conducted Sir Ganga Ram Hospital, Lahore. The duration of study was one year from June 2014 to June 2015. A total of 100 patients were selected in the study who were confirmed cases of breast cancer. The selection was done by various clinical, laboratory investigations and with a family history of breast cancer. Peripheral blood films were prepared after collecting blood samples in EDTA tube. Subsequent to DNA extraction, mutational analysis of BRCA1 exons 2, 5, 6, 16, 20 and 22 was carried out using single strand conformation polymorphism (SSCP) assay while protein truncation test (PTT) was used to examine mutations in exon 11. All BRCA1 sequence variants were confirmed by DNA sequencing.

**Results:** Forty one patients were diagnosed with early onset breast cancer, 39 patients had moderate family history. At the time of diagnosis, the median age of enrolled patients was 36 years (range 24–65 years). Of 100 patients, analyzed by SSCP assay, mobility shift was detected in exon 6, 16 and 20 of three patients, whereas ten patient were tested positive for mutation in exon 11 by PTT assays. All patients with BRCA1 mutations were further confirmed by DNA sequencing analysis. In exon 16 c.4837A>G was confirmed, which is a common polymorphism reported in several populations including Asians. Moreover, mutations in exon 6 (c.271T>G), exon 20 (c.5231 delG) and exon 11 (c.1123T>G) were reported first time in the Pakistani population.

**Conclusion:** Several BRCA1 mutations were observed in Pakistani breast cancer patients with moderate family history. Therefore, mutation-based genetic counselling for patients with moderate family history can facilitate management, if one first or second degree relative or early onset disease is apparent.

**No conflict of interest.**

### Survival outcomes in Egyptian elderly patients with breast cancer: single institute experience

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**Background:** Data of breast cancer (BC) in elderly are limited. Safety concerns during the treatment of those patients is always an issue in presence of multiple medical and social factors. The aim of this study is to evaluate the clinico-pathological characteristics of BC and their effect on the survival of Egyptian women aged ≥65 years.

**Material and Methods:** Data of 1295 BC patients was collected between 2007 and 2012 at Oncology Department of Ain Shams University, Egypt. Survival outcome was described using Kaplan–Meier curves and the association of clinico-pathological characteristics with OS and DFS was assessed.

**Results:** Of the 1295 patients, 162 patients were elderly. In elderly cohort; Median age was 68 years (SD ± 5.06, Range 65–88). About 75.3% of the tumors were IDC and 5.6% were ILC. About 18.5% and 51.9% of the patients presented in early and advanced stages respectively. Positive axillary lymph nodes (ALN) were seen in 57.4%. ER, PR and HER2neu expression was seen in 88.5%, 59.3%, and 12.3% respectively and 10.5% were TNBC. Adjuvant chemotherapy (CT), neo-adjuvant CT, adjuvant radiotherapy (RT) and adjuvant hormonal therapy (HT) has been received in 61.7%, 5.6%, 45.4% and 50.6% respectively. Mean DFS was 31.4 months (SD = 24.18, 95% CI = 24.8–38.3) and the mean OS (calculated from the date of diagnosis till the date of last follow up as we do not have updated mortality records) was 34.5 months (SD = 24.94, 95% CI = 28.5–40.3). About 35.8% relapsed. About 41.4%, 10.3% and 8.6% of the relapsed patients received 1st, 2nd and 3rd lines of CT respectively. Positive ER was seen in (79.9)% of elderly versus 64% in non-elderly (p = 0.00). Percentage of patients received adjuvant CT was 77.2% in elderly versus 85.1% in non-elderly (p = 0.022).

**Conclusion:** BC in elderly has to be treated with much caution to avoid under or overtreatment and more clinical trials should be directed toward this aim.

**No conflict of interest.**
160

POSTER

Direct linear correlation between serum vascular endothelial growth factor (VEGF) and Ki-67 (MIB-1 rate) in women with pT1-2 breast cancer

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Background: Several prognostic and predictive factor are available for patients with breast cancer (BC), including the expression of the hormone receptors, HER2 (luminal vs. non luminal subtypes) and the cell proliferation marker Ki-67. Because neangiogenesis, tumor growth and risk of metastases are strictly interdependent, the role of the vascular endothelial growth factor (VEGF), which is regulator of vascular growth and function, is crucial. Circulating VEGF measurement can be a clinically useful indicator for diagnostic and prognostic evaluation in patients with several solid tumors, including ovarian cancer, hepatocellular carcinoma, and BC. Elevated serum VEGF are currently considered a negative prognostic factor. The aim of this study was to evaluate the relationship between VEGF serum levels and the expression of Ki-6 in patients with BC, hypothesizing that they have the same prognostic value.

Materials and Methods: Fifty-nine women (median age 62, range 35–77 years) with pT1-2 pN0 BC who underwent curative surgery and final histological examination were prospectively enrolled in the study. In all patients a commercially available quantitative enzyme-linked immunosorbent sandwich (ELISA) VEGF assay and the Ki-67 expression (evaluated by MIB-1 immunohistochemistry as % of positivity) were available. All the measurements were performed in twice.

Results: A very wide variation of values, both as regards the VEGF (median 58, range 5–296 pg/mL) and the MIB-1 (median 12%, range 1–50%) was observed. There was no correlation (p=NS) between the age of the patients and both VEGF (R = 0.049) and MIB-1 (R = 0.071). A strong direct linear relationship between VEGF and MIB1 (R = 0.69, p < 0.0001, α = 4.804, β = 0.016, regression line equation: y = 4.8041644114118 + 0.0158784932092385) was found.

Conclusions: According to the results of this study, VEGF and MIB-1 should be considered interdependent markers in patients with BC, and thus they have similar prognostic value.

No conflict of interest.

161

POSTER

MDR-1 C3435T transition and breast cancer risk: A meta-analysis in Asian population and a bioinformatics approach

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Background and Aim: The MDR-1 gene encodes a protein which acts as a transmembrane efflux pump for numerous exogenous and endogenous toxins. Polymorphisms in this gene might influence the function of protein, thereby inducing the susceptibility to various cancers, including breast cancer. The aim of this study was to investigate the association of MDR-1 C3435T transition with breast cancer risk in Asian population by meta-analysis which followed by a bioinformatics approach.

Materials and Methods: For meta-analysis purpose, we performed a comprehensive search in PubMed, Google Scholar, and ScienceDirect databases. After screening the studies, a total of 4 eligible studies involving 1419 cases and 1439 controls were included in our meta-analysis. Some bioinformatics tools were applied to investigate the effects of C3435T transition on the structure of protein and mRNA.

Results: The results of meta-analysis revealed that there are a significant association between MDR-1 C3435T polymorphism and breast cancer risk within Asian population in allelic (OR = 1.535, 95% CI 1.107–2.128, p = 0.010), co-dominant (OR = 1.912, 95% CI 1.221–1.872, p < 0.001), and recessive (OR = 1.422, 95% CI 1.181–1.712, p = 0.001) models. We don’t find any publication bias in meta-analysis (P Egger >0.05). But, our bioinformatics analysis revealed that the C3435T transition has no effects on protein and mRNA structure (Distance: 0.0128, P = 0.8009).

Conclusion: The results suggest that the MDR-1 C3435T transition might be a genetic risk factor for breast cancer in Asian population. Bioinformatics results suggest that the C3435T transition has no effects on mRNA and protein, and it may influence other aspects such as mRNA splicing and codon preference.

No conflict of interest.

162

POSTER

A randomized controlled lifestyle intervention in BRCA mutation carriers

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Background: The lifetime cumulative risk (penetrance) of breast cancer (BC) associated with BRCA mutations is of the order of 50%, and a sizeable proportion of carriers does not develop the disease. Therefore, the penetrance of the genetic trait may be regulated through other genetic or environmental factors, including dietary, metabolic, and growth factors. We hypothesized that IGF-I and other markers of insulin resistance (IRm) that are both risk and prognostic factors for sporadic BC might be relevant also for hereditary BC, due to a deleterious mutation of BRCA genes. Abdominal obesity, high body weight and high energy intake (usually associated with higher bio-availability of growth factors) are associated with BC risk in BRCA mutation carriers. A multinational case-only study on 3000 young BC women suggested that patients with BRCA mutation had higher consumption of milk. Milk directly stimulates insulin production and release, and is associated with higher levels of IGF-I. In a case-control analysis on 308 high genetic risk women, we showed that high serum levels of IGF-I are associated with a significantly increased penetrance. Consistently, mechanistic studies hypothesize a functional interaction between the BRCA genes and the IGF-I system.

Materials and Methods: We have designed a study with 600 BRCA mutation carriers (with or without a previous diagnosis of BC) to test: (1) whether a lifestyle intervention significantly reduce IGF-I and IRm (randomized trial); (2) whether carriers with a previous diagnosis of BC have higher IRm than carriers without BC (case-control study); (3) whether IRm and their change over time affect subsequent BC incidence and prognosis (cohort follow-up).

Results: Currently, we have randomized 191 BRCA mutated women in a control group (91) or in a lifestyle intervention group (94) to reduce IGF-I and IRm levels. All women received the WCRF Decalogue for the prevention of cancer. Intervention women were invited to participate into 6 full days of activities along the subsequent 6 months (6 kitchen courses, 6 physical activity sessions and 6 conferences). They were recommended to reduce calorie intake, protein intake down to 10–12% of total calorie and their change over time affect subsequent BC incidence and prognosis.

Control women remained with the baseline recommendations. Preliminary results suggest that the women included in the intervention group showed a significant decrease of weight, waist circumference, total cholesterol, LDL cholesterol, triglycerides, and a borderline significant reduction of IGF-I (p = 0.05). The women included in the control group did not significantly reduce any IRm.

Conclusions: These very preliminary results suggest that the lifestyle intervention successfully reduce IRm in BRCA mutation carriers.

No conflict of interest.

163

POSTER

Local hyperthermia for inflammatory breast cancer

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Background: The prognosis for inflammatory locally advanced breast cancer (LABC) patients continues to be poor. According to the literature the overall 5-year survival rate of these patients ranges from 12–65% with a median of 32–54 months. The results of the application of local hyperthermia in the treatment of inflammatory breast cancer and its own data at these patients were presented.

Material and Methods: From 2006 to 2008 in combination with chemotherapy (radiotherapy) applied to 14 patients with inflammatory...
breast cancer in MRRC. Age of patients ranged from 37 to 72 years (mean 53 years). IIIB stage was in 11 patients, IV stage in 3. Chemotherapy in combination with local hyperthermia in the amount of 5–6 courses conducted by the schemes CAP or FEC. Effects of local hyperthermia was subjected to only the primary tumors in 15–45 minutes after chemotherapy. Local hyperthermia was performed on hyperthermic machine “Yakhta-4” (334 MHz) by using external applicators. During HT the temperature control inside the tumor was performed using 2–3 thermoresistor probes. Temperatures in the center of the tumor ranged between 42.5 and 44.5°C, and at the periphery of the tumor – between 41.4°C and 41.7°C. The total duration of a sitting of hyperthermia was 70–90 min.

Results: An objective response was observed in 12 (86%) patients and all 4 primary unresectable tumors regarded as resectable. Mastectomy with or without radiotherapy was performed in 10 patients, others in order to continue palliative chemotherapy and/or radiation therapy, according to the pre- or postoperative radiotherapy performed in 10 patients, others in order to continue palliative chemotherapy and/or radiation therapy, according to the pre- or postoperative radiotherapy performed in 10 patients, others in order to continue palliative chemotherapy and/or radiation therapy, according to the pre- or postoperative radiotherapy performed in 10 patients, others in order to continue palliative chemotherapy and/or radiation therapy, according to the pre-

Conclusions: The study results indicate promising applications for inflammatory breast cancer as a neoadjuvant in operable cases and palliative treatment for inoperable patients.

No conflict of interest.

164
Evaluation of prognostic and predictive value of novel markers (NF-xB and ODC) alone and in combination with other markers for patients with breast cancer

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Background: NF-xB and ODC expression was shown to have prognostic value for breast cancer patients mediated by role in tumor chemoresistance mechanisms. But, these mechanisms are depended of more comprehensive molecular profile, so deeper understanding what markers are included in chemoresistance formation is needed to promote personalization of cancer treatment.

Material and Methods: 132 patients with invasive ductal carcinoma were included in the study. Expression of molecular markers was determined by immunohistochemistry on FFPE tumor tissue. To identify the correlation between factors the Pearson coefficient was defined, and verified by $r^2$ test. To study the prognostic value of investigated factors the Cox's regression model and Kaplan–Meier method with log-rank test were performed.

Results: Analysis of clinical, morphological and molecular features of tumors showed the inverse correlation of NF-xB and ODC expression with ER (r = -0.206, p = 0.009), PR (r = -0.200, p = 0.011), Bcl-2 (r = -0.203, p = 0.010) and E-cadherin (r = -0.196, p = 0.012); and direct correlation with Nottingham prognostic index (NPI): r = 0.206, p = 0.009) and Her2/neu status (r = 0.193, p = 0.013). In addition, it has been found increasing correlation of NF-xB expression (r = 0.213, p = 0.07) in the direction: Luminal A (ER+PR+/Her2−) → Luminal B (ER+PR+/Her2+) → Her2/neu enriched (ER-/PR-/Her2+) subtype. It was shown the direct correlation of ODC expression level with Grade (r = 0.147, p = 0.047), p53 (r = 0.225, p = 0.005), Ki-67 (r = 0.192, p = 0.014) and E-cadherin (r = 0.154, p = 0.040). High ODC expression was also shown as strong predictor to chemoresistance (low level of pathomorphosis: (r = 0.338, p = 0.001).

Statistical analysis of prognostic value shown that Ki-67, Grade, NPI, stage, Basal-like and Her2/neu enriched subtypes were negative predictors for progression-free (PFS) and overall survival (OS), while ER, PR, Bcl2 and Luminal subtypes – positive. Moreover, NF-xB and ODC expression were negative predictors (but not significant) and their prognostic value greatly enhanced when their coexpression with apoptotic markers (Bcl-2 and p53) was analyzed. Thus, NF-xB+p53/Bcl2- profile was found to have the worst prognosis (3-year PFS 55.6% vs 60.5% for other profiles, OS 68.7% vs 97.0%).

Conclusions: According to our results the highest level of NF-xB detected in Basal-like and Her2/neu enriched subtypes of BC. These subtypes as shown in literature and in our study are associated with poor prognosis. These data and negative prognostic value of NF-xB+p53+/Bcl2− expression profile indicate poor prognosis of BC patients with activated NF-xB and suggest the important role of NF-xB in expression of apoptotic markers. Considering predictive value of ODC expression, we can conclude that ODC and NF-xB may become important markers to individualize treatment strategy and to predict the outcome of BC patients.

No conflict of interest.

165
Is Indian breast cancer biology different from its western counterpart? A study of clinical & pathological correlation of biomolecular subtyping of breast cancer in Northern India

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Background: Breast cancer can be considered a complex disease demonstrating heterogeneity at clinical and histopathological levels. Breast cancer in the Indian population has been believed to be biologically different from those of the west. Little is known whether the difference is actually reflected in molecular sub-typing of the population. We attempt to study the clinical & pathological aspects of breast cancer and its correlation with biomolecular sub-typing with comparison to the western population.

Materials and Methods: This was a prospective and retrospective study. All patients of surgical oncology treated from the period of August 2014 to August 2016 were included in the prospective group. Patients have been previously treated in department having follow up data and tissue blocks available for analysis consists of the retrospective group. Clinical and histopathological data was recorded.

Results: A total of 355 patients were analysed. Average age of patients with disease was 45.3 yrs. The premenopausal group consists of 52% of patients. 99% of patients had more than one child. Mostly patients presented in locally advanced stage. The response rate to chemotherapy was low with only 9% patients having complete response and almost one fourth of patients having progressive disease on chemotherapy. Among the classification Triple negative group was most common (43%) with almost 60% patients being hormone negative. This subgroup was significantly higher in premenopausal patients (p = 0.016). Also premenopausal patients presented with later stage with significantly higher in locally advanced and metastatic patients as compared to postmenopausal patients (p = 0.0068).

Conclusion: As compared to the western population the breast cancer in India presents in younger, premenopausal, multiparous and breast feeding women. Most common presentation was in locally advanced stage with low response rates to neoadjuvant chemotherapy. Molecular subgrouping reveals that about 80% of the patients are hormone negative. 43% of patients were triple negative. It appears to be that breast cancer in India is a different subset from the western world in having different molecular signatures that translates into distinct clinical and histopathological subgroup.

No conflict of interest.

166
Triple negative breast cancer in Indian population: An analysis from a tertiary cancer center in India

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Introduction: Triple negative breast cancer is defined as breast cancer which does not express the estrogen receptor, progesterone receptor or human epidermal growth factor receptor 2 receptor. This subset is supposed to have aggressive biological behaviour, translating into poor clinical and pathological features like younger age, advanced disease and higher grade. Our study is to analyse the triple negative population at our centre and identify subgroups within the population.

Materials and Methods: This was a prospective and retrospective study. All patients diagnosed as triple negative breast cancer on immunohistochemistry and treated in the department of surgical oncology from the period of August 2014 to August 2016 were included in the prospective group. The follow up data and tissue blocks of patients previously treated in the department were analysed and these patients formed the retrospective group. Clinical and histopathological data was recorded.
Results: Total 193 patients were analysed in the study. Mean age was 42.49 yrs. Almost two third of the patients were premenopausal with all of them having at least one child. All the patients had breast fed their children. 45% of total patients presented in locally advanced stage with 41% in early and 14% in advanced stage. Nodal positivity rate was seen in 54% of the patients. The median age was 49 yrs. The response rate to chemotherapy was low with almost 70% of patients not responding to anthracycline based chemotherapy. On further subgroup analysis, premenopausal triple negative patients presented in a more later stage as compared to post-menopausal patients (p = 0.008). Also the premenopausal patients had a significantly higher rate of nodal positivity than post-menopausal patients (64% vs 36% p = 0.048). These patients had significantly poorer response rate to chemotherapy than their postmenopausal counterparts (47.7% vs 85.5%, p = 0.02).

Conclusion: In our study we found that the triple negative population was young and predominantly premenopausal. All of them had breast fed their children. 60% patients presented with advanced stage. Nodal positivity in patients that were operated was high. Response to anthracycline based chemotherapy in patients was quite good and only 14% did not receive adjuvant endocrine or targeted therapy and situation has become more complex after the discovery of genomic tests. So, the need to enhance the understanding of the disease process and treatment response the hunt for suitable tumor marker is still on.

No conflict of interest.
correlated with histopathological findings using ultrasound-guided Trucut needle biopsy. The statistical analysis was made through SPSS version 20.0 (SPSS, Chicago, IL). Chi-square test was used for comparing BI-RADS classification and pathologic results.

Results: The mean age of our patients was 56.8±12.3 years (range 25–85); 30% of them were younger than 50 years old. BI-RADS 3 was found in 5 (5.1%) women, BI-RADS 4 and BI-RADS 5 were found in 15 (15.5%) and 77 (79.4%) women, respectively. According to the histopathological findings 4 (4.1%) of patients had benign lesions and 93 (95.9%) had malignant lesions [infiltrative ductal carcinoma (85/97), infiltrative lobular carcinoma (4/97), lobular carcinoma in situ (2/97) and other lesions (2/97)]. Malignant lesions were predominant on the age-groups of 50–69years (50/97). Only one patient who was classified as BI-RADS 3 had ductal carcinoma in situ and all cases with BI-RADS 4 and 5 resulted in malignant masses. We have found a statistically significant correlation between the BI-RADS findings by ultrasonography and the histopathology diagnosis p < 0.005.

Conclusions: We illustrated that BI-RADS classifications and histopathologic results revealed significant correlation. However, BI-RADS 3 breast lesions should be work-up with ultrasound-guided Trucut needle biopsy.

References

No conflict of interest.

170 POSTER
Treatment and prognosis of leptomeningeal disease secondary to metastatic breast cancer: a single-centre experience
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Background: Leptomeningeal disease (LMD) is an uncommon complica­tion of advanced breast cancer, sometimes occurring in association with parenchymal brain metastases or via direct spread from skull or spinal bone metastases. The prognosis is poor, with median overall survival (OS) of 5–7 months previously reported. Radiotherapy (RT), systemic and intra­thecal (IT) chemotherapy are accepted treatment modalities, but efficacy data are limited. This study was designed to determine potential predictors of survival in this patient group.

Methods and Materials: Breast cancer patients with LMD diagnosed by MRI in a 10-year period (2004–2014) were identified from electronic patient records. Baseline demographics, histopathologic sub-type and receptors, presenting symptoms, sites of LMD, treatment, concomitant bony and brain metastases and dates of initial and metastatic breast cancer diagnoses, disease progression and death were collected. Progression-free survival (PFS) and OS estimates were calculated using Kaplan–Meier method with planned sub-group analysis by treatment modality. Cox regression was employed to identify significant prognostic variables.

Results: We identified 162 eligible patients; all female, median age at LMD diagnosis was 52.5 years (range 23–80). Ninety patients (49.5%) were ER positive/HER2 negative; 48 (29.8%) were ER negative. 27 (16.8%) were triple negative. HER2 status was unknown in 17 (9.3%). Skull or spinal bone metastases were present in 134 patients (73.6%), 92 (50.6%) had concomitant brain metastases: 67 (36.8%) had both, 23 (12.6%) had neither. Initial management of LMD was whole or partial brain RT in 62 (34.1%), systemic therapy in 45 (24.7%); most commonly capecitabine and supportive care only in 37 (20.3%). A further 18 (6.8%) had RT to the base of skull or spine. Fourteen patients (7.7%) underwent IT chemotherapy of whom two also received IT trastuzumab. Twenty-six patients had 2nd line treatment for LMD (RT in 15, systemic therapy in 7, both in 3, IT chemotherapy in 1).

From diagnosis of LMD, the median PFS was 3.9 months (95% CI 3.2–5.0) and median OS was 5.4 months (95% CI 4.2–6.6). Patients treated with systemic therapy had the longest OS (median 8.8 months, 95% CI 5.5–11.1), compared to RT (6.1 months, 95% CI 4.2–7.9 months); IT therapy (2.9 months, 95% CI 1.2–5.8) and supportive care (1.7 months, 95% CI 0.9–3.0). One patient who received IT trastuzumab remains well on treatment at 2 years. On multivariable analysis triple negative histology, concomitant brain metastases, and LMD involving both the brain and spinal cord were associated with poor OS.

Conclusions: Breast cancer patients with triple negative LMD, concomitant brain metastases or LMD affecting both the spine and brain have the poorest prognosis. Clinical trials to identify more effective treatments in these patients are urgently needed.

No conflict of interest.

171 POSTER
Nottingham Prognostic index (NPI) – a simple predictive tool for operable breast cancer – utility in non screened cohort
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BACKGROUND: Nottingham prognostic index (NPI) is a simple clinicop­oncological prognostic tool for prognostication in breast cancer patients. We aim to evaluate the utility of NPI in present cohort and its relationship with survival.

Methods: This series comprised of 421 symptomatic consecutive patients diagnosed with primary breast cancer between June 2011 and June 2014 and operated at Tata Medical Center, Kolkata. A total of 358 cases were assembled for analysis; rest were not included due to technical reasons, lack of relevant data or loss of follow up. Kaplan–Meier test was applied for survival analysis.

Result: Mean age and tumor size were 54 yrs (IQR 28, 70) and 3 cm (0.3, 10) respectively. 7 patients (2%) were in excellent (E) group, 36 (10.1%) in good (G), 181 (50.5%) in intermediate (I) & 134 (37.4%) in poor (P) risk group as per NPI scores classification. Compared to original NPI cohort, present group patients had more high grade tumor (90% vs. 84%, p=0.08), size >1.5 cm (97% vs. 77%, p<0.001), >2 nodes positive (25% vs 8%, p<0.001) and in high risk NPI group (37% vs 17%, p<0.01).

80% of patients received chemotherapy compared to 20% in original cohort (p<0.001). Chemotherapy administered for 20% in E, 30% in G, 56% in I, and 85% in poor risk group. Median follow up was 32 months (0–60). No recurrence found in excellent risk group, 1 (1.8%) in G, 16 (5.5%) in I and 29 (15.34%) in P risk group. No deaths in E and G groups, 13 (4.5%) in I and 13 (7.4%) in P. On Kaplan–Meier analysis, disease free survival was significantly associated with NPI risk category (p=0.08).

Although there were more deaths in poor risk group, overall survival was not significantly associated with NPI risk group (p=0.08).NPI is a useful tool in predicting the outcome of patients, it was helpful to guide decision making for different treatment options, and in prognosticating early outcome

No conflict of interest.

172 POSTER
Biological features of triple negative BRCA-related breast cancer
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Background: The incidence of triple negative breast cancer among the BRCA gene mutation carriers, according to literature, constitutes 70–75%. However, the lower survival rate among BRCA carriers is still very controversial. The objective of this retrospective trial is to determine if there are any differences in the distant relapse free survival and overall survival in patients with BRCA mutation associated and non-BRCA associated triple negative breast cancer.

Materials and Methods: The trial included 44 women with triple negative breast cancer who underwent genetic tests for BRCA1/2 mutations in National Cancer Research Centre of Uzbekistan during the period from 2009–2012. Differences in groups were analyzed by Chi Square Test, and using also the Cox hazard regression model.

Results: From 44 tested women 54.5% (24/44) were BRCA carriers: of them 62.5% (15/24) – positive for BRCA1 mutation, 29.2% (7/24) – had BRCA2 mutation, and in 8.3% (2/24) were identified to have mutations of both genes. Age median constituted 41 years (27–73). Follow-up median made up 2.8 years (range 0.8–7.0). Those patients who had not mutation associated triple negative breast cancer showed remarkably lower DRFS (p = 0.03); HR = 7.17, CI 1.15–21.5) and OS (p < 0.05; HR = 7.55, CI 1.22–46.0), than in patients who had BRCA related triple negative breast cancer.

Conclusion: Data shows 54.5% prevalence of BRCA mutations in triple negative breast cancer. However, comparison of overall prognosis in BRCA-carriers and non-carriers is significantly different for the first 3 years following the diagnosing. Introductory results we get in our trial present a big scientific and intrigue, and push us to study whether biological features of triple negative breast cancer in patients with BRCA-mutations differs in comparison with other forms.

No conflict of interest.
173 Low cause-specific mortality in women treated for ductal carcinoma in situ of the breast

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Background: Ductal carcinoma in situ (DCIS) is considered a non-invasive breast disease, with consequently no risk of disseminated disease and death due to breast cancer. Further, whole breast irradiation – indicated after breast conservation – is alleged to be associated with increased cardiac disease and death. In this study we analyzed cause-specific mortality after a median of 10 years in women treated for DCIS, compared with the expected mortality in the general population.

Material and Methods: We compared observed cause-specific mortality among a nationwide cohort of 9,799 women treated by surgery +/- radiotherapy for DCIS with expected mortality rates in the general female population by calculating standardized mortality ratios (SMRs).

Results: Among 9,799 women treated for DCIS between 1989 to 2004 in the Netherlands, 1,429 deaths occurred over a median follow-up of 10 years, of which 368 deaths were due to cardiovascular disease (4% of total population) and 244 deaths due to breast cancer (3%). Overall, the study population had a significantly lower risk of dying of all causes combined compared to the general population (SMR 0.9, 95% confidence interval [CI] 0.87–0.96). DCIS patients experienced lower risk of dying due to diseases of the circulatory, respiratory and digestive system (SMR 0.8 [95% CI 0.69–0.85], 0.7 [95% CI 0.60–0.89] and 0.7 [95% CI 0.55–0.98]), mental and behavioural disorders (SMR 0.7, 95% CI 0.52–0.90) and endocrine, nutritional and metabolic diseases (SMR 0.7, 95% CI 0.49–0.94). With regard to cancer deaths, DCIS patients had higher risk of breast cancer death (SMR 3.3, 95% CI 2.95–3.74), but lower risk of mortality from lung and urogenital cancer (SMR 0.7 [95% CI 0.58–0.94] and 0.6 [95% CI 0.45–0.83]). At 15 years, the cumulative breast cancer-specific mortality was 3.9%. The SMR for breast cancer specific mortality rises with increasing age (95% CI 15.65–33.11 to 1.9 [95% CI 1.11–3.06] for women aged <40 years and >75 years, respectively). Patients who did develop subsequent invasive breast cancer had much higher excess breast cancer-specific mortality than women who did not develop invasive breast cancer (SMR 26.6 [95% CI 22.08–31.74] versus SMR 2.0 [95% CI 1.71–2.34]).

Conclusions: DCIS patients had lower risk of dying of all causes combined compared to the general population and seem to represent a generally healthy subgroup. The absolute risk of breast cancer death was low at 3.9% at 15 years. The risk of dying from breast cancer among women treated for DCIS alone was only slightly higher than that in the general population. These results suggest that a history of primary DCIS has no negative effect on overall survival.

No conflict of interest.

174 Investigation of the role of VEGF-A +936C>T and −634G>C as prognostic and risk factors in breast cancer patients

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Background: The single nucleotide polymorphisms (SNPs) of the VEGF-A, +936C>T and −634G>C, have been shown to be important prognostic and predictive factors for breast cancer patients. The aim of the current study was to evaluate the role of these SNPs as a prognostic and risk factors in the Bulgarian population.

Material and Methods: An approval from the ethical committee of the Medical University of Sofia (MU-Sofia) was obtained to conduct a prospective case control study of patients with breast cancer managed at the MU-Sofia between 1996 and 2015. Peripheral blood DNA of 140 patients from MU-Sofia Breast Cancer Biobank was assessed for VEGF-A +936C>T and 634 G>C variants using TaqMan® Real-Time PCR assay (ThermoFisher) and analyzed relative to 140 control patients. All patients were included in the analysis of these variants as risk factors for developing breast cancer. Only patients who had ≥2 years follow up were included in the overall survival (OS) analysis.

A 2×2 contingency table was used to evaluate for odds ratio (OR) and significance of associations. Cox regression model was used to estimate impact of VEGF-A +936C>T and −634G>C on OS.

Results: The allelic frequencies for +936C>T and −634G>C were 0.16 and 0.34, respectively. Our results were comparable to the frequencies of the variants in the Single Nucleotide Polymorphism Database of National Center for Biotechnology Information (0.13 and 0.33, respectively). There was a statistically insignificant trend, of the association of +936C>T and −634G>C with the disease with OR of 0.86 (CI: 0.54–1.37, p = 0.55) and 1.35 (CI: 0.95–1.91; p = 0.09), respectively. There was a statistically significant correlation between +936C>T and the histology of the tumor (p = 0.038) and between −634G>C and bilateral disease (p = 0.038). Patients were followed up until 1st of August 2016. There was no significant association with OS.

Conclusions: The VEGF-A variant +936C>T showed a trend of protective effect and the −634G>C showed a trend of increased risk for breast cancer development. Both SNPs did not prove as prognostic for the OS. The significance of the association of −634G>C with bilateral tumors could improve decision making, when prophylactic mastectomy is considered. There are studies which find association of presence of +936C>T with better response to anti VEGF target treatment in patients with triple negative breast cancer. This could improve survival for 6 patients in our study.

No conflict of interest.

175 Burden of early and advanced breast cancer in the Netherlands

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Background: The aim of this study was to estimate the total economic and health related burden due to breast cancer in women in the Netherlands.

Material and Methods: Data from the Dutch National Cancer Registry from between 1990 and 2014 were used to obtain prevalence and European Standardized incidence- and survival rates. Additionally, an extensive literature search was performed to further build and validate the analysis. Results are reported for overall, early (stage 0-IIa) and advanced breast cancer (stage IIb-IV).

Results: Since 1990, the overall incidence of breast cancer increased from 102 up to 141 per 100,000. This increase was driven by an increase of 44% in early breast cancer (88 to 128 per 100,000), as the incidence of advanced breast cancer was constant over time at 14 per 100,000. In 2014, 15,600 were diagnosed with breast cancer, of whom 1,600 were diagnosed with advanced breast cancer. The 5-year prevalence of breast cancer was 72,807. Although the ten-year overall survival rate increased from 65% to 77% between 1990 and 2014, the ten-year overall survival for advanced breast cancer is still only 30%. Each year breast cancer is still responsible for 3161 deaths, 26,000 life years lost and 90,000 DALYs in the Netherlands. The total economic burden of breast cancer was €1.7 billion in 2014. The majority of these costs were due to healthcare costs (€768 million), followed by productivity losses due to morbidity (€260 million) and mortality (€243 million).

Conclusion: This study provides a comprehensive assessment of the burden of breast cancer and subsequent trends over time in the Netherlands. The results emphasize that the burden of disease due to breast cancer is significant and show large differences in the prevalence and survival of early and advanced breast cancer in the Netherlands.

176 Ethnic disparities in breast cancer survival in New Zealand: Why do Māori fare poorly?

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Introduction: Ethnic disparities in cancer survival are well known among many populations for a variety of cancers. Underlying reasons for these disparities are complex and poorly understood, but include patient, tumour and healthcare system factors. We investigated on the breast cancer...
survival disparity between Indigenous Māori and European women in New Zealand and quantified the relative contributions of patient, tumour and healthcare system factors towards this survival disparity.

Materials and Methods: All women with newly diagnosed breast cancer in the Waikato, New Zealand between 1999 and 2012 were identified from the Waikato Breast Cancer Register. Cancer specific survival between Māori and NZ European women was compared using Kaplan–Meier survival curves while contributions of different factors towards the survival disparity were quantified with Cox proportional hazard modelling.

Results: Of the total of 2791 women included in this study, 2260 (80.1%) were NZ European and 419 (15%) were Māori. Māori had a significantly higher age adjusted cancer specific mortality (hazard ratio [HR] = 2.02, 95% confidence interval [CI], 1.59–2.58) with significantly lower 5-year (76.1% vs. 88.6%, p < 0.001) and 10-year (69.9% vs. 79.9%, p < 0.001) crude cancer-specific survival rates compared with NZ European women. Stage at diagnosis explained approximately 40% of the survival disparity, while screening, treatment and patient factors (i.e. comorbidity, obesity and smoking) contributed by approximately 15% each towardsthe survival disparity between Māori and NZ European women. The final model accounted for almost all of the cancer survival disparity between Māori and NZ European women (HR = 1.07, 95% CI, 0.80–1.44).

Conclusions: Māori women experience an age-adjusted risk of death from breast cancer, which is more than twice that for NZ European women. Lower screening coverage, delay in diagnosis, inferior quality of treatment and greater patient comorbidity appear to be important factors contributing to survival disparity between Māori and NZ European women.

No conflict of interest.

177 Phase 1b/2 study to evaluate eribulin mesylate in combination with pembrolizumab in patients with metastatic triple-negative breast cancer

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Background: Eribulin mesylate (ERI) is approved for the treatment of (1) patients (pts) with advanced/metastatic breast cancer (MBC) who have received ≥1 [European Union] or ≥2 [United States] prior chemotherapy regimens for metastatic disease, including an anthracycline and taxane, and failing to the adjuvant/neoadjuvant setting; and (2) pts with unresectable/metastatic liposarcoma who have received a prior anthracycline regimen. Pembrolizumab (PEM) is approved for the treatment of (1) pts with unresectable/metastatic melanoma and disease progression following ipilimumab and, if BRAF mutation positive, a BRAF inhibitor and (2) pts with advanced non-small cell lung cancer with tumors expressing PD-L1. PEM is also being evaluated for the treatment of metastatic triple-negative breast cancer (mTNBC) and other tumor types. Here, we report an interim analysis from an open-label, single-arm, multicenter, phase 1b/2 study to evaluate the safety and efficacy of the ERI and PEM combination in pts with mTNBC previously treated in the metastatic setting.

Materials and Methods: A total of 95 pts (aged ≥18yrs, ECOG PS 0 or 1) with mTNBC previously treated with <2 prior lines of chemotherapy for metastatic disease will be enrolled. Phase 1b included a safety run-in cohort in which ≥6 pts received intravenous (IV) ERI 1.4 mg/m² on day (d) 1 and d8 and IV PEM 200 mg on d1 of a 21-d cycle. Dose-limiting toxicities (DLT) of the combination regimen were assessed in the first cycle to determine the recommended phase 2 dose (RP2D). In phase 2, pts were enrolled in 2 cohorts according to receipt of prior chemotherapy in the metastatic setting (0 vs 1–2 prior lines). Primary endpoints were safety and tolerability (phase 1b) and objective response rate (phase 2); secondary endpoints included progression-free survival, overall survival, and duration of response.

Results: We report an interim analysis of the first 39 enrolled pts (n = 7, phase 1b; n = 32, phase 2). No DLTs were observed in phase 1b. The RP2D was defined as ERI 1.4 mg/m² on d1 and d8 and PEM 200 mg on d1 of a 21-d cycle. As of data cut-off (May 16, 2016), the most frequent adverse events (AEs; all grades) were fatigue (69%), nausea (51%), alopecia (36%), neutropenia (36%), and peripheral neuropathy (28%). The most frequent AEs of grade 3 or 4 were neutropenia (31%) and fatigue (8%). Serious AEs (all nonfatal) occurred in 36% of pts; AEs leading to dose adjustment were observed in 56% of pts. Objective responses, including a complete response, by investigator assessment were observed during this interim analysis, and will be presented at the meeting.

Conclusions: The combination of ERI and PEM represents a novel treatment regimen in pts with mTNBC. AEs observed with the combination were comparable to those observed with either treatment as monotherapy. Clinical Trials.gov: NCT02513472

Conflict of interest: Ownership: Claudio Savulsky hold stock with Eisai. Gursel Aktan holds stock with Merck. Vassiliki Karananta holds stock with Merck. Advisory Board: None for all authors. Board of Directors: None for all authors. Research Support: Sara Tolaney has done contracted research for Lilly, Genentech, Pfizer, Merck, Novartis, Exelixis, Eisai, & AZ. Other Substantive Relationships: Claudio Savulsky is an employee of Eisai; Gursel Aktan is an employee of Merck; Dongyuan Xing is an employee of Eisai; Ana Almonte is an employee of Eisai; Vassiliki Karananta is an employee of Merck.

178 New biomarker of tumor progression of breast cancer – survivin gene expression in the primary tumor and circulating tumor cells

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Background: Breast cancer is a leading cause of morbidity and mortality of the female population from malignant tumors. Distant metastases are the main cause of death of patients, a substrate for the development of which are circulating tumor cells (CTCs). However, the search for these cells alone is not sufficient to provide full information about the nature and course of tumor in a single patient. Determination of the expression of tumor-genes responsible for the different processes of tumor progression allows a more complete picture. Such genes include the gene survivin (BIRC5) family of inhibitors of apoptosis (IAP).

Material and Methods: Using real-time PCR we investigated the expression of survivin gene in 36 samples of primary breast cancer of the breast, 10 samples of benign tumors – fibroadenoma of the breast, as well as 36 samples of peripheral blood of patients with breast cancer at various stages of tumor and stage specific treatment, and 10 healthy people as controls.

Results: In primary breast carcinoma we determined a high expression of survivin gene in all 36 samples with the average value (M±m) 1.58±0.31 (min 1.19; max 4.41). The highest figures were found in tumors of medium and high grade (G II–III) with lympohonous invasion (LVSI). In 2 of 3 samples of benign tumor expression of survivin was not found, and one was 0.015. In CTCs, isolated from peripheral blood of breast cancer patients, all 36 samples as determined by the gene expression of survivin with an average value (M±m) 1.10±0.19 (min 0.36; max 3.79). The level of expression of the control samples did not exceed 0.003. It should be noted that the maximum volume of expression was observed in samples of tumor patients with stage N+, and especially M1, on TNM classification. Reliable, depending on the expression level of survivin in tumor size is not set. In patients, receiving chemotherapy average expression of survivin gene was observed, but it never approached the indicators of control.

Conclusions: Determination of expression of the survivin gene in primary tumor and in CTCs may be one of the most promising markers of tumor progression and for monitoring of breast cancer therapy. No conflict of interest.

Expression of ErbB-2 (Her-2/neu) and survivin gene (BIRC5) in tumor infiltrating lymphocytes (TILs) in breast cancer

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Background: It is now known that the presence of is an indirect indication of the active anti-tumor immunity and combined with improved prognosis in patients, breast cancer (breast cancer) suffering from resectable cancer. According to the literature, patients with a high content of TILs holding one chemotherapy alone was associated with a 5-year disease-free survival rate of 91%. Adding Anila-her-2 directional drug trastuzumab in this group did not improve outcomes. On the other hand, it was observed no significant decrease in 5-year disease-free survival to 80%. The explanation of this phenomenon yet. Perhaps this is due to antigen-presenting mechanism of lymphocytes themselves. To study the expression of the gene ErbB-2 (Her-2/neu) and survivin (BIRC5) in lymphocytes infiltrating breast carcinoma tissue, and in peripheral blood lymphocytes for patients suffering from breast cancer.

Material and Methods: After homogenization of frozen tumor specimen isolated lymphocytes (CD8 +) by separation. In the same way, the lymphocytes isolated from the peripheral blood. Using real-time PCR Gene expression was investigated on tumor ErbB-2 and lymphocytes (CD8 +) isolated 16 samples of primary invasive ductal breast carcinomas and in 26 samples of peripheral blood of patients suffering from breast cancer.

Results: B-lymphocytes isolated from all carcinoma samples were determined by gene expression BIRC5 and ErbB-2 with a mean value (M±m)
Poster Session, Saturday 28 January 2017

180

POSTER

Quality of life in elderly patients with breast cancer after mastectomy evaluated using the short form of the Medical Outcomes Study questionnaire (MOS-SF-36)

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Background: Breast cancer (BC) is a common malignancy among women, and the second or third leading cause of cancer-related death in Western countries. BC common in the elderly, because the risk of getting BC increase with the age. BC and its treatment can impact the quality of life (QoL) of women in several ways, including potential psychological and physical dysfunctions, because in the mind of each the patient, breast surgery remains a destroying surgery. The first effort of physicians to assess the consequences of cancer treatment was suggested by Karnofsky in 1948. Since then, many other assessment tools have been proposed, including the Medical Outcomes Study (MOS) questionnaire. The aim of this study was to evaluate the short-term postoperative health-related QoL between elderly (>65 years) and younger patients (<65 years) who underwent mastectomy for BC using the MOS questionnaire.

Patients and Methods: We reviewed the medical records of 117 women with advanced BC who required mastectomy. Unfortunately, only 31 (26.5%) patients accepted the short-form (36 items) of the MOS questionnaire (SF-MOS-36) administration (the day before discharge after surgery) and completely asked to the items related to their temporary psychosocial distress and functional limitation after mastectomy. There were 12 (38.7%) elderly and 19 (61.3%) younger patients, with an overall median age of 61 years (range 46–86 years). In the SF-MOS-36 questionnaire, 8 groups of items are designed to obtain information about bodily pain, emotional role functioning, general health perceptions, mental health, physical functioning, physical role functioning, social role functioning, and vitality. Because the data obtained had a non-Gaussian distribution, the non-parametric Mann–Whitney U test was used to evaluate the statistical significance between groups. A p-value <0.05 was considered significant.

Results: The results are reported in the Table. In general, the healthy-related QoL perceived by young and elderly patients assessed by analyzing the results of the SF-MOS-36 questionnaire was similar. However, the scores related to social role functioning and vitality were significantly different between groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Younger patients (&lt;65 years)</th>
<th>Elderly (&gt;65 years)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>19</td>
<td>12</td>
<td>–</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>54 (46–65)</td>
<td>71 (66–86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>67±21</td>
<td>73±35</td>
<td>0.67</td>
</tr>
<tr>
<td>Emotional role functioning</td>
<td>64±19</td>
<td>74±32</td>
<td>0.28</td>
</tr>
<tr>
<td>General health perceptions</td>
<td>63±13</td>
<td>59±14</td>
<td>0.42</td>
</tr>
<tr>
<td>Mental health</td>
<td>71±17</td>
<td>68±19</td>
<td>0.65</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>73±16</td>
<td>79±12</td>
<td>0.27</td>
</tr>
<tr>
<td>Physical role functioning</td>
<td>63±20</td>
<td>67±21</td>
<td>0.60</td>
</tr>
<tr>
<td>Social role functioning</td>
<td>64±21</td>
<td>50±12</td>
<td>0.04</td>
</tr>
<tr>
<td>Vitality</td>
<td>66±12</td>
<td>49±15</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusion: Older patients with BC who underwent mastectomy seem to be more susceptible than younger against social problems and their vitality after surgery. However, these preliminary results need to be confirmed by studies on a larger sample of patients.

No conflict of interest.

181

POSTER

Proliferative markers in predicting recurrence risk of breast cancer

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Background: Oncotype DX® (ODX) is a validated clinical genomic tool that needs to be efficiently utilized especially in areas of limited resources. Proliferative genes highly weights in calculating Recurrence score (RS). Ki67 is a nuclear protein highly expressed in the S phase and not in G0 phase. Assessment of tumor proliferative index by Ki67 immunohistochemistry and standard pathological grade may represent a relatively inexpensive screening approach to identify patients with a low risk of recurrence.

Methods: We retrospectively studied 205 patients with Early stage, node negative, hormone receptor (HR) positive, HER2 negative status (ODX candidates) treated at a community oncology practice. Fisher’s exact test was used to test the association of baseline characteristics with Ki67 and mitotic score. Log-rank test was used for survival analysis. Proliferation score was calculated by combining tumor grade, mitotic score and Ki67 (1–3 and each added).

Results: Ki67 was significantly associated with tumor grade (p<0.0001), ODX (p=0.032) and with mitotic score (p<0.001) but was not associated with age or T stage. Patients with Ki67<20% had a 95%±2% ten-year freedom from progression, p=0.024 after stratified by tumor grade [table 1]. Ninety percent of low/intermediate Ki67 (<20%) patients did not receive chemotherapy. There was significant association of proliferation score and FFP (p=0.014) [Table 1].

Table 1. Association of Ki67, Mitotic score and proliferation score with Freedom from progression at 10 years

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Freedom from progression (at 10 yrs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ki67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20%</td>
<td>167</td>
<td>0.95±0.02</td>
<td></td>
</tr>
<tr>
<td>&gt;20%</td>
<td>29</td>
<td>0.62±0.14</td>
<td></td>
</tr>
<tr>
<td>Mitotic Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/intermediate</td>
<td>185</td>
<td>0.93±0.02</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>20</td>
<td>0.61±0.16</td>
<td></td>
</tr>
<tr>
<td>Proliferation score 3−4 (low)</td>
<td>119</td>
<td>0.96±0.02</td>
<td></td>
</tr>
<tr>
<td>5−6 (intermediate)</td>
<td>37</td>
<td>0.91±0.05</td>
<td></td>
</tr>
<tr>
<td>7−9 (high)</td>
<td>40</td>
<td>0.75±0.10</td>
<td></td>
</tr>
</tbody>
</table>

*p-value based on log-rank test, ^p-value based on Likelihood ratio test, after stratified by tumor grade.

Conclusion: Low Ki67 by itself or when combined with pathological data is predictive of excellent outcomes and genomic testing may unlikely to re-categorize these patients. The limitations of discrepancies with lack of standardization of Ki67 staining and retrospective nature of the study while important should be tested in an expanded and prospective setting.

No conflict of interest.

182

POSTER

Gremlin 1 expression correlates with prognostic features and survival in breast carcinoma

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Background: Breast carcinoma affects 1 in 8 women in the UK. If treated early, 5 year survival is 88–99%, dropping for those with metastatic disease

RESULTS: The results are reported in the Table. In general, the healthy-related QoL perceived by young and elderly patients assessed by analyzing the results of the SF-MOS-36 questionnaire was similar. However, the scores related to social role functioning and vitality were significantly different between groups.

Conclusion: Older patients with BC who underwent mastectomy seem to be more susceptible than younger against social problems and their vitality after surgery. However, these preliminary results need to be confirmed by studies on a larger sample of patients.

No conflict of interest.
Gremlin (GREM1) is a multi-functional protein, primarily a bone morphogenetic protein (BMP) antagonist. Over expression of GREM1 has been characterised in various human tumours. It seems to promote epithelial-to-mesenchymal transition (EMT) by inhibiting BMP2, BMP4 and BMP7 and activates vascular endothelial growth factor receptor-2 (VEGFR2), mediating angiogenesis. GREM1 therefore, may promote invasive and metastatic properties via these interactions. We profiled expression of GREM1 and BMPs in breast carcinoma, evaluating association with prognostic features and survival.

Material and Methods: 82 breast carcinoma samples were compared to 24 normal breast tissue samples. Immunohistochemistry (IHC) and qPCR evaluated GREM1 expression in the two cohorts.

Public patient sample data on KMPlotted evaluated prognostic value of the genes GREM1, BMP2, BMP4 and BMP7. It splits breast cancer samples into two groups according to expression of the proposed gene and cohorts are compared by Kaplan-Meier survival plot (significant if \( p < 0.005 \)). The gene expression omnibus (GEO) profiles database was used to compare expression of these genes across different tissues or cell lines. Comparisons used two tailed T test, Mann-Whitney, or Pearson co-efficient. Significance at \( p < 0.005 \).

Results: IHC showed GREM1 in mammary epithelial cell cytoplasm but no significant difference in transcript level on qPCR for breast carcinoma vs. background tissue. GREM1 expression was lower in poor prognosis patients (\( p = 0.032 \) ) and HER2 positive (\( p = 0.043 \)). GEOdata however showed high GREM1 expression in breast carcinoma tissue with poor prognostic biomarkers (Table 1).

Table 1. GREM1 has positive correlation with HER2 and negative correlation with ERα

<table>
<thead>
<tr>
<th></th>
<th>GREM1 vs. HER2 (n = 327)</th>
<th>ERα (n = 327)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson co-efficient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value 0.00852</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0122</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

KMplot associates high GREM1 expression with poor survival rates compared to low GREM1 expression (\( P = 0.0054 \)). This is also seen in grade 3 and ER negative tumours. Both low BMP2 and high BMP4 expression associated with poor survival (\( p = 0.018 \) and \( p = 0.038 \) respectively). This was emphasised for BMP4 if the tumour was ER negative (\( p = 0.012 \)) or HER2 positive (\( p = 0.043 \)). There was no significant expression or survival differences for BMP7.

Conclusions: This study reflects variable expression and potentially significant and the \( p \)-value was calculated to be 0.0389 by McNemar test. It was not able to find a primary was found on further examination (False Negatives). It was not able to find the primary site in 13 cases and in these cases no primary was found even on subsequent examination. It was able to identify an additional site of metastases in 5 out of 30 cases: liver (1), mediastinal lymph nodes (1), supravacular lymph node (1), pleural deposit (1), the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of our study was 85.7%, 81.25%, 80%, 86.6% and 83.3% respectively. Above findings were found to be statistically significant and the \( p \)-value was calculated to be 0.0389 by McNemar test.

Conclusions: Our study found PET/CT to be a very useful modality in evaluation of patients with carcinoma of unknown primary and suggest it be included in the diagnostic algorithm at an early stage.

No conflict of interest.

183

First findings: Cooperation of two different cell membrane proteins in breast cancer

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Background: Sphingosine-1-phosphate (S1P) is a bioactive sphingolipid. Potassium channels are pore-forming transmembrane proteins that regulate a number of biological processes (by controlling potassium flow across cell membranes). These special structures in the cell membrane regulate essential cellular processes, such as proliferation, migration, cytoskeletal structures, angiogenesis, vascular stability, and morphogenesis. Given common features, they can interact with each other in the cancer’s progression. Thus, in our work, we aim to observe the effects of single and combined silencing to determine their possible interaction on cells.

Material and Methods: In this study, the potential role of S1P receptors and potassium channels on the viability, proliferation, adhesion and lateral motility of breast cancer cells (with different characteristics) was evaluated. To demonstrate this association, the receptors and channels in weakly invasive MCF-7, strongly invasive MDA-MB-231 cells were silenced with precise, small interfering RNAs (siRNAs). After the transfection process, identification of cells at the 24th, 48th, and 72nd hours was performed.

Results: We determined that a decrease in viability, proliferation, and lateral motility lead to increased adhesiveness in both cell types when the receptors and channels are silenced together.

Conclusions: Effective results can be obtained in the cancer process when sphingosine receptors and potassium channels are simultaneously silenced in breast cancer cells regardless of whether the cells are weakly invasive or strongly invasive. This information is provided in our initial findings. Due to these results, they should open new horizons for other researchers. There is a distinct need for more detailed work to clarify our results.

This study was supported by Scientific Research Project Commission, Eskişehir Osmangazi University (Project Number: 201511023).

No conflict of interest.

184

Role of PET CT in detection of primary in carcinoma of unknown origin

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Aim: The aim of this study was to assess the role of PET/CT in detection of to be included carcinomas of unknown primary (CUP), compare it with conventional imaging modalities and find its role in detection of additional site of metastases.

Methods: Thirty patients with CUP [cervical lymph node (12), liver (8), pancreas (7), axillary lymph node (1) and peritoneal deposit (1)] underwent a whole-body FDG-PET/CT study after being unsuccessfully investigated with complete relevant history, general and systemic examination, laboratory tests and conventional diagnostic procedures. The positive suspicious findings on PET/CT were further evaluated and the patients were followed up for a period of 3 months.

Results: PET/CT was able to find a primary in 12/30 cases (40%): lung (4), pancreas (3), tongue (2), oropharynx (1), liver (1), breast (1). In 3 cases it localized an area to be the likely site of primary but no malignancy was found on further investigation (False Positives). In 2 cases it was not able to find a primary but was found on further examination (False Negatives). It was not able to find the primary site in 13 cases and in these cases no primary was found even on subsequent examination. It was able to identify an additional site of metastases in 5 out of 30 cases: liver (1), mediastinal lymph nodes (1), supravacular lymph node (1), thigh (1), pleural deposit (1). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of our study was 85.7%, 81.25%, 80%, 86.6% and 83.3% respectively. Above findings were found to be statistically significant and the \( p \)-value was calculated to be 0.0389 by McNemar test.

Conclusions: Our study found PET/CT to be a very useful modality in evaluation of patients with carcinoma of unknown primary and suggest it to be included in the diagnostic algorithm at an early stage.

No conflict of interest.

185

Breast cancer subtypes in an oncology centre in Nigeria: a retrospective review of 240 cases from Lagos

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Background: Breast cancer is a heterogeneous disease with several biologic subtypes. It is presently the most common cancer among Nigerian women. As conventional clinical factors such as tumor grade, size, lymph node involvement, and surgical margins are no longer sufficient as sole prognostic factors in the treatment, it is important to consider breast cancer subtypes in treatment decision making. Four main breast cancer subtypes have been identified based on the estrogen receptor (ER), progesterone receptor (PR), and HER2. These subtypes include luminal types A and B, basal-like and HER2-enriched. The study aims to analyze the epidemiological and pathological characteristics of breast cancer in an Oncology centre.

Material and Methods: This is a retrospective study of 240 breast cancer subtypes in the Department of Radiotherapy, Lagos University Teaching Hospital (LUTH) from January 2012 to December 2015. Case files were retrieved through the record department and the information required was gathered with the aid of a data extraction form for patients with pathological characterization of tumour.

Results: A total of 240 Breast cancer subtypes were recorded during the study period. The mean age of Breast cancer patient is 46.44 ± 10.6. The median age is 45.0 years with an age range of 25–80 years. The peak age incidence for females was 40–49 years accounting for 38.75% of all female presentations. The male to female ratio was 1:59. 136 (57.6%) of the patients were premenopausal. 43.5% had grade III tumours.
No conflict of interest.

186

Sphingosine-1-phosphate, sphingosine-1-phosphate receptors (S1P1/S1P3) and cell behaviors in breast cancer cells

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Introduction: S1P is a bioactive lipid that binds to a family of specific GPCRs (S1P1–S1P5) to induce cellular responses such as growth, survival, and migration of mammalian cells. S1P1, S1P2 and S1P3 receptors are expressed almost everywhere. In contrast, S1P4 is expressed in the lung and lymphoid tissue, while S1P5 is found in the brain and skin. S1P1 and S1P3 signaling encourages migration, while S1P2 signaling blocks migration. S1P1 and S1P3 signaling also induces cell proliferation; S1P2 signaling inhibits cell proliferation; S1P1 and S1P3 signaling positively regulates cell motility and invasion, while S1P2 signaling negatively regulates cell motility and invasion.

The role of S1P and its receptors in various types of cancers have been researched; however, their contribution to breast cancer metastasis has not been elucidated yet. The interaction between metastasis and S1P and its receptor will be examined using breast cancer cells. MCF-7 and MDA-MB-231 are breast cells with different characteristics. MCF-7 cells are estrogen sensitive and weakly invasive; MDA-MB-231 cells are estrogen insensitive and strongly invasive. Because of their different characteristics, MCF-7 and MDA-MB-231 cells are chosen as models to study normal breast cancer and metastatic processes.

Materials and Methods: First, S1P was administered to cells. Then, MCF-7 and MDA-MB-231 cells were incubated with siRNA that targeted single and both S1P1 and S1P3. The potential role of S1P1 and its receptors on the viability, proliferation, adhesion and lateral motility of breast cancer cells (with different characteristics) were assessed. Experiments were set up separately for MCF-7 and MDA-MB-231. One-way Anova was used to determine statistical differences between treatment groups.

Results: In MCF-7 and MDA-MB-231 cells, after S1P was administered, cell viability was reduced at all time points examined, by suppression of S1P1 and S1P3 either alone or together. While there was no significant change in the proliferation of MCF-7 cells, proliferation of MDA-MB-231 cells was significantly reduced in the S1P1- and S1P3-silenced group compared to control group. While S1P1- and S1P3-silenced MCF-7 cells were less adherent, adhesion of MDA-MB-231 cells was increased in the S1P1- and S1P3-suppressed groups. Lateral motility of both MCF-7 and MDA-MB-231 cells was statistically reduced in S1P1-suppressed, S1P3-suppressed, and S1P1- and S1P3-suppressed groups at every time point.

Conclusions: S1P1 and its receptors have critical roles in cancer progression and metastasis. The most significant result in our study is that at any given time, it is more effective to silence both receptors at once rather than separately. Interactions between these molecules contribute to the decline in the breast cancer survival ratio and drug resistance.

No conflict of interest.

187

BRCA1/2 mutation in breast cancer: biological aspects, patterns of care and impact on outcome in a monoinstitutional cohort

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Background: BRCA1/2 mutations are involved in breast cancer (BC) susceptibility and accounts for 3% of breast tumors: it is unclear whether mutated countries which had impacted outcome that could justify tailored treatment schedules. The aim of our study is to define the biological aspects and clinical management of a series of BC according to BRCA status.

Material and Methods: We retrospectively reviewed a cohort of BC patients who consecutively underwent BRCA testing due to high individual or familial BC risk (age at diagnosis <50 years, contralateral BC, personal or family history of male BC/BRCA mutation/ovarian cancer). We assessed the clinicopathological features and patterns of care of BRCA-mutated BC compared to a non-BRCA mutated population. Factors influencing local relapse (LR), distant metastasis-free survival (DMFS) and disease specific survival (DSS) were analyzed.

Results: Median followup from surgery was 87.5 months (18.3–409.9). 88 patients were included, accounting for 115 breast tumors (58.8%). 75 (47.8%) were synchronous, 24 metachronous tumors). BRCA mutation type 1 and 2 were found in 33 (38.3%) and 16 (18.6%) patients, accounting for 66/115 tumors (57.4%). Surgery consisted of mastectomy (n = 48; 41.7%) or breast conserving surgery (n = 67; 58.3%). Tumor stage was pTis (n = 3; 2.5%), pT1 (n = 86; 74.8%) and pT2 (n = 26; 22.6%), while nodal status was N0, N1 and N2 in 78 (67.8%), 29 (25.2%) and 8 (7.0%) cases, respectively. Estrogen receptor (ER) and progesterone receptor (PgR) expression was absent in 44 (38.2%) and 33 (28.6%) tumors; HER2 determination, available in 75 cases, showed HER2 over-expression in 12 (10.4%) cases. Tumor nuclear grade (G) was scored G1 (n = 10; 8.7%), G2 (n = 40; 34.8%) and G3 (n = 57; 49.5%); ki-67 was >20% in 61 (53.0%) cases. Adjuvant chemotherapy was administered in 67 cases (55.8%); while 55 (47.8%) patients received endocrine therapy (RT) was performed in 73 (63.5%) cases. BRCA mutation was correlated to younger mean age at diagnosis (p = 0.035), nodal involvement (p = 0.030), higher G (p = 0.0022) and ki-67 (p = 0.014), ER (p = 0.00042) and PgR negative status (p = 0.00091), and use of adjuvant chemotherapy (p = 0.00038). At multivariated logistic regression the use of adjuvant chemotherapy was related to only negative ER (p = 0.0014), higher G (p = 0.00029), and positive nodal status (p = 0.00034). No correlation was found between BRCA and occurrence of metachronous tumors. LR, DMFS, and DSS were 9.3%, 91.8% and 96.6%, respectively. At multivariated analysis no prognostic factor influenced LR, while only nodal involvement impacted on DMFS (p = 0.015) and DSS (p = 0.03).

Conclusion: In our experience, despite higher biological aggressiveness and younger age at presentation, BRCA status was not significantly associated with worse outcome in BC patients treated accordingly to current clinical practice.

No conflict of interest.

188

Advanced breast cancer; clinicopathological data and predictors of estrogen receptor positivity prior to biopsy, National Cancer Institute (NCI) pooled data experience

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Background and Objective: Prior literature assessed biomarkers, ER, PR and HER-2/neu status as well as different gene profiles, multigene assays and genetic polymorphisms with response to hormone therapy. We aimed to identify clinicopathologic characteristics affecting breast cancer estrogen status and identify factors predictive of ER positivity and hence hormonal treatment response.

Methods: A retrospective review of breast cancer patients referred to NCI, Cairo University between 2012 and 2014. Clinical and pathologic data were collected. Pearson’s Chi (x2) square and Logistic regression model were used for statistical analysis.

Results: 153 patient were identified. Median age was 53 years (Range; 27–86). Thirty-six (23.5%) cases were T3N1M0. Ninety-six cases were ER negative. Eighty-one cases were PR negative. Her-2/neu were positive in 31 cases. Advanced nodal (N) stage (p = 0.03) and ER positivity (p = 0.015) were more prevalent in old BC patients (>45 years) vs young cohort. We evaluated predictors of positive ER prior to breast biopsy in 69 cases with full clinical data. Sixty-one (88.4%) cases were PS = 1. Median number of off-spring was 3. Fifty-nine (85.5%) cases had negative family history for breast cancer. Univariate analysis revealed that advanced age (p = 0.035), lower number of off-spring (p = 0.043), menopausal women (p = 0.042), absence of peau d’orange (p = 0.015), low grade tumor (p = 0.006) and advanced T stage (p = 0.005) are significant predictors of ER positivity. On multivariate analysis, absence of peau d’orange (p = 0.019), low grade tumor (p = 0.004), advanced T stage (p = 0.054) were the significant predictors of ER positivity.

Conclusions: Absence of peau d’orange, low grade tumor and non-advanced T stage are predictors of ER positive breast cancer cases in whom neoadjuvant hormonal treatment should be considered. No conflict of interest.
**189 POSTER**

The therapeutic possibility of intrathecal administration of trastuzumab for the carcinomatous meningitis of HER2-positive metastatic breast cancer: the low penetration of trastuzumab into the cerebrospinal fluid via intravenous administration

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**Background:** Case reports or pooled analyses of outcomes of intrathecally administered trastuzumab to treat carcinomatous meningitis of HER2-positive metastatic breast cancer (HMBC) have not yielded clinical evidence of a response and the safety of the procedure remains unknown. Whether trastuzumab can penetrate the cerebrospinal fluid (CSF) or pass through the blood-brain barrier has also not been established.

**Materials and Methods:** Seven patients with carcinomatous meningitis resulting from HMBC were treated with intrathecal trastuzumab at Tokyo Metropolitan Komagome Hospital. Carcinomatous meningitis was diagnosed using MRI, and patients without cancer cells according to CSF cytology were included. Patients were administered methotrexate (MTX), cytarabine (Ara-C), and trastuzumab (10−30 mg/body) into the intrathecal space through the Ommaya reservoir. We then measured serum and CSF concentrations of trastuzumab and then six, 24, and 48 h after systemic administration. Once a 200-fold immuno-tolerant assay was done, the concentration of systemic trastuzumab administration, we delivered trastuzumab into the intrathecal space and measured concentrations in the CSF 12 h later. The Research Ethics Committee of Komagome Hospital approved the study.

**Results:** Six patients received trastuzumab combined with Ara-C and MTX, and one received trastuzumab alone into the intrathecal space. The median total dose of trastuzumab was 210 (range 118−450) mg. Meningeal symptoms or Kornovsky performance status at the time of diagnosis improved in all patients after intrathecal administration. The number of cancerous cells in the CSF of three patients decreased or diminished to zero. The median carcinomatous meningitis-progression-free survival was 10 (range 2−24) months. One patient developed the adverse event of grade 3 convulsions, but was able to continue treatment. Grade 1−2 nausea comprised most of the other adverse events. Serum concentrations of trastuzumab before and six, 24, and 48 h after administration were 4.119, 220.39, 160.72, and 139.40 μg/mL, respectively. The concentration of trastuzumab in the CSF at 12 h was 0.01 μg/mL at 24 and 48 h, respectively. The concentration of trastuzumab in the CSF at 12 h was 500-fold higher (12.21 mg/mL) after intrathecal, than systemic administration.

**Conclusions:** These findings indicate that trastuzumab does not penetrate the CSF when compared to the systemic administration. Intrathecal administration of trastuzumab cannot be recommended in CSF of patients with carcinomatous meningitis.
The numbers of Fopx3+ cells ranged from 0 to 28 (median 3)/HPF, and the difference in individuals ranged from 0 to 21 (median 3)/HPF. Differences in tumor size, node status, or in the expression rate of PgR in individuals did not impact the number of Fopx3+ cells. However, the number of Fopx3+ cells in tumors that were NG3 were increased compared with tumors in the same host that were NG1 or 2.

**Conclusions:** The number of Fopx3+ cells showed no relationship with tumor size, lymph node status, or the expression rate of the PgR in simultaneous bilateral ER+ and HER2+ breast cancer patients. High NG of the tumor may possibly be involved with enhancement of the recruitment of Tregs.

**No conflict of interest.**

193 POSTER

**Evaluation of Her-2/neu receptor status and its association with age, menopausal status, histopathological features and ER/PR status in operable carcinoma of the breast**

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**Background:** Breast cancer is the most common specific cancer in females responsible for over 33% of the cancer burden in them. Although breast cancer is now being increasingly diagnosed and there are a number of treatment modalities available yet the ultimate prognosis depends on the extent of disease at the time of presentation.

**Objectives:**
- To determine the frequency of HER-2/ neu receptor positivity in patients of carcinoma breast.
- To study the association of HER-2/neu receptor status with age, menopausal status, histopathological features (histological subtype, tumor size, tumour grade, number of lymph nodes involved) and ER/PR status.

**Materials and Methods:** The study was a hospital based prospective study conducted in Department of Surgery, SMS Medical College, Jaipur, from March 2015 to March 2016. Study includes 50 female patients with breast cancer admitted through surgical outpatient department. Triple assessment (Clinical, Radiological examination, FNAC/Trucut biopsy) was done to confirm the diagnosis. Patients were operated according to the clinical stage of disease. Operative procedures done were Breast conservation surgery/Modified radical mastectomy/Radical mastectomy and the specimen was sent to pathology lab for detailed histopathological examination including histological subtype, tumour size, tumour grade and number of lymph nodes involved and immunohistochemical examination for ER/PR status and HER-2/neu receptor status.

**Results:** In this study of 50 cases of operable breast cancers in which HER-2/neu protein was detected by immunohistochemistry, HER-2/neu over-expression was seen in 14 (28%) cases. A statistically significant association was established between HER-2/neu protein over-expression and large tumor size (p-value <0.05), high histologic grade (p-value <0.05) and high lymph node metastasis (p-value <0.05). HER-2/neu receptor positivity was not significantly associated with age (p-value >0.05), menopausal status, histological subtype and status of oestrogen and progesterone receptors.

**Conclusion:** HER-2/neu status in breast cancer is important because it provides valuable prognostic, predictive and therapeutic information. Thus, HER-2/neu status should be incorporated into a clinical decision, along with other prognostic factors, regarding whether to give any adjuvant systemic therapy. So, HER-2/neu testing should be routinely performed in patients with a new diagnosis of invasive breast cancer along with ER/PR study of the affected tissue.

**No conflict of interest.**

195 POSTER

**Which one is the best for breast cancer; tamoxifen plus hyperthermia or tamoxifen plus radiotherapy?**

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**Background:** Resistance to Tamoxifen denotes a major drawback to the treatment of hormone-dependent breast cancer. Therapeutic hyperthermia is a procedure that involves heating tissues to a higher temperature level. Tamoxifen can be used in combination with Hyperthermia and Radiotherapy. We aimed to find the best combination for 2 types of breast cancer.

**Objectives and Material:** The anti-neoplastic activity of Tamoxifen in combination with Hyperthermia and Radiotherapy in T47D human breast cancer cell line and 4T1 balb/c metastatic breast cancer cell line was assessed by the standard 3-(4,5 dimethyl-2-thiazolyl)-2,5 diphenyl-2H-tetrazolium bromide (MTT) method. In order to approve the inhibitory effect, we used Acridine Orange/Propidium iodide fluorescent staining. As Hyperthermia treatment, we exposed the cells to 43±0.2°C for 30 minutes in a regular incubator, and after 2 hours cells were irradiated into 4 Gy Gamma irradiation as Radiotherapy. We applied Hyperthermia before and after Radiotherapy, with the time interval of 2 hours, to detect the differences. Then the viability rates of cells were determined after 24 hours. All data are expressed as the mean ± standard deviation. P-values of less than 0.05 were considered to be statistically significant.

**Results:** The findings indicated that adding hyperthermia before Radiotherapy showed 88.5±2.38% viability in T47D cells versus 79.4±3.6% viability in 4T1 cells; while applying it after Radiotherapy showed 87.4±5.12% viability in T47D cells versus 83.6±1.9% viability in 4T1 cells after 24 hours.

**Conclusions:** It was concluded that in ER+ breast cancer applying hyperthermia after radiotherapy is more efficient, while in Triple-negative breast cancer it is vice versa.

**No conflict of interest.**

196 POSTER

**Accuracy of ultrasound scan guided node biopsy in pre-operative diagnosis of metastatic axillary lymphadenopathy in breast cancer**

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**Background:** Preoperative diagnosis of metastatic axillary lymphadenopathy is important in management of breast cancer patients. Ultrasound scan (US) is an essential part of triple assessment of these patients with fine needle aspiration cytology (FNAC) and/or core biopsy (CB) of suspicious lymph nodes. The aim of this study is to establish the accuracy of preoperative US and US guided node biopsy diagnosis of metastatic disease and the underlying prevalence of axillary lymph node metastases.

**Material and Methods:** A retrospective analysis of all patient diagnosed with breast cancer who underwent preoperatively US axillary assessment followed by axillary surgery between April 2015 till March 2016. All
ultrasonics and preoperative FNA or CB were correlated with final history of sentinel lymph node biopsy (SLN) or axillary lymph node clearance (ALND).

Results: In total 292 patient were eligible (163 symptomatic invasive cancer, 129 screen detected). Following axillary surgery 95/292 patients had nodal metastatic involvement on final histology (32.5% prevalence). 68/163 of the symptomatic group had proven metastatic disease on final histology with 41.7% prevalence versus 27/129 (21.5%) of the screen detected group with 20.9% prevalence. Sensitivity of US diagnosis of symptomatic group was 73.5% and US guided sampling of 55.9% versus the screen group of 44.4% and 37% respectively.

Conclusions: Our results meet and exceed the Royal College of Radiology guidelines (targets of 50% or above) for both US assessment and US guided biopsy for symptomatic group. Screening group results were lower than the symptomatic group which merits further research in this group.

No conflict of interest.

197

POSTER

Does combination of neoadjuvant chemotherapy and therapeutic mammoplasty reduces the need for mastectomy?

M. El Gamal 1, N. Thanvi 2.

Background: Neo-adjuvant chemotherapy (NAC) in breast cancer patient has the advantage of achieving tumour shrinkage to allow less radical breast surgery. The establishment of modern oncoplastic breast surgery methods in addition to neoadjuvant chemotherapy may have the synergistic effect of allowing more breast conserving surgery (BCS) and hence a reduction in mastectomy rate.

Material and Methods: Retrospective study of patients who underwent NAC and therapeutic mammoplasty (TM) over a 12 month period starting from April 2015. MRI assessment pre and post chemotherapy in all cases. Correlation to NAC response and MRI size to the final histology was performed.

Results: 105 patients had a mastectomy during this period. 9 patients with average age of 50 for whom mastectomy was, initially, the only available option converted to BCS following NAC, 9/105 (9%). Mean size 42.6 mm on MRI (range 19–106 mm) prior to NAC versus mean final histology size 15 mm (range 4–40 mm). Mean weight of excised TM Issue 59 g (range 30–205 g). 8/9 patients had complete excision and only one patient needed further excision to clear margins. None had converted to mastectomy.

Conclusion: A combination of NAC and TM help to reduce the need for mastectomy in a selected group of patients with a reduction of mastectomy rate by 9%.

No conflict of interest.

199

POSTER DISCUSSION

A decision aid for curatively treated breast cancer patients to effectively individualize the aftercare, improve shared decision making, and reduce costs

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Background: Thanks to the improved survival of breast cancer patients, an increasing number of breast cancer patients require some form of aftercare. Earlier, we showed that individualizing aftercare is more cost-effective than delivering aftercare at regular standard intervals. We hypothesized that offering patients adequate information about the pros and cons of aftercare, using a decision aid, would result in less intensive aftercare, and thus in lower costs, by improving shared decision making processes. The aim of this study was therefore to evaluate the effect of the decision aid on perceived shared decision making, patient-reported choice evaluation, and on costs.

Material and Methods: A prospective before-and-after pilot study, including 50 patients in the control group (usual care) and 50 patients in the experimental group (use of decision aid during consultation with an oncology nurse) was conducted. The patients filled out a short survey at three different measurement points; one week before the consultation to measure background information, directly after the consultation to measure the outcomes: shared decision making perceptions (SDM-Q-9), patients-reported choice evaluation (uncertainty-satisfaction, choice information and choice control) and the choice of aftercare trajectory. Three months after the consultation patient-reported choice evaluation was evaluated again.

After three months, medical costs were also assessed from patient files. MANOVA, Mann-Whitney U test, ANOVA and Chi-square tests were performed to analyse the data.

Results: Patients that used the decision aid scored higher although statistically non-significantly on shared decision making (M=48.8, SD=5.9) than patients that did not (M=45.5, SD=10.7) (U=541.5, P=0.33). There were no significant differences on choice evaluation. Furthermore, patients that used the decision aid were more likely to choose a less intensive aftercare trajectory than patients in the control group (χ²=3.84, df=1, P=0.05), resulting in lower medical costs although not statistically significantly in the experimental group (M=48.15, SD=21.15) compared to the control group (M=136.03; SD=21.15) (F=3.09, P=0.09). However, using the decision aid during a consultation significantly increased the length of this consultation (t=−5.47, df=7.27, P<0.001).

Conclusions: The current study is the first test to study an aftercare decision aid for breast cancer patients. This pilot study shows positive effects of the decision aid; stimulating shared decision making and leading to less intensive aftercare trajectory choices and subsequently lowering medical costs.

No conflict of interest.

200

POSTER

18FDG PET-CT–SUV correlation with molecular subtypes in locally advanced/recurrent breast carcinoma


Background: 18FDG PET-CT–SUV correlation with molecular subtypes in locally advanced/recurrent breast carcinoma.

Materials and Methods: Retrospective study of patients who underwent mastectomy during this period. 105 patients had a mastectomy during this period. 9 patients with average age of 50 for whom mastectomy was, initially, the only available option converted to BCS following NAC, 9/105 (9%). Mean size 42.6 mm on MRI (range 19–106 mm) prior to NAC versus mean final histology size 15 mm (range 4–40 mm). Mean weight of excised TM Issue 59 g (range 30–205 g). 8/9 patients had complete excision and only one patient needed further excision to clear margins. None had converted to mastectomy.

Conclusion: A combination of NAC and TM help to reduce the need for mastectomy in a selected group of patients with a reduction of mastectomy rate by 9%.

No conflict of interest.

201

POSTER

A study of lymphangiogenesis and vascularity in triple negative breast cancer patients in India

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Background: A triple negative breast cancer (TNBC) is carries an unfavourable prognosis as compared to non TNBC breast cancers and further lacks the benefit of standard targeted therapies. Lymph node metastasis is the most important prognostic marker in breast cancer and lymphatic microvessel density (LMVD) along with lymphatic vessel invasion (LVI) can serve as a proxy prognostic marker to lymph node involvement. Tumor vascularity is the key factor responsible for tumor growth and metastasis which can serve as a prognostic marker. Color Doppler ultrasonography parameters of vascularity can be measured by resistivity index (RI), pulsatility index (PI) and maximum flow velocity (Vmax). The study of lymphangiogenesis and vascularity in TNBC in Indian patients has not been done till now.

After three months, medical costs were also assessed from patient files. MANOVA, Mann-Whitney U test, ANOVA and Chi-square tests were performed to analyse the data.

Results: Patients that used the decision aid scored higher although statistically non-significantly on shared decision making (M=48.8, SD=5.9) than patients that did not (M=45.5, SD=10.7) (U=541.5, P=0.33). There were no significant differences on choice evaluation. Furthermore, patients that used the decision aid were more likely to choose a less intensive aftercare trajectory than patients in the control group (χ²=3.84, df=1, P=0.05), resulting in lower medical costs although not statistically significantly in the experimental group (M=48.15, SD=21.15) compared to the control group (M=136.03; SD=21.15) (F=3.09, P=0.09). However, using the decision aid during a consultation significantly increased the length of this consultation (t=−5.47, df=7.27, P<0.001).

Conclusions: The current study is the first test to study an aftercare decision aid for breast cancer patients. This pilot study shows positive effects of the decision aid; stimulating shared decision making and leading to less intensive aftercare trajectory choices and subsequently lowering medical costs.

No conflict of interest.
Materials and Methods: Fifty histopathologically proven early and locally advanced invasive breast cancer patients were included in the study. Assessment of vascularity was done using Colour Doppler. Post mastectomy specimen (as primary surgery or post neo adjuvant chemotherapy) was analysed for detailed histopathologic evaluation and also for assessment of ER, PR, Her2 and D2-40 endothelial marker by immunohistochemistry. The clinico-pathological parameters, LMVD, LVI and color Doppler parameters were assessed in TNBC group and compared with non TNBC group.

Results: The mean age was 44.40 ± 10.37 years. Compared with non-TNBC cases, TNBC presented with younger age (below 35 years, p < 0.001), higher histological grade (p < 0.001), RI (p = 0.02) and PI (p = 0.03); however, there was no difference observed in tumor size, clinical lymph node involvement, Vmax and stage between the TNBC and non-TNBC groups. Intratumoral and peritumoral LMVD in TNBC tissue was significantly increased (p < 0.001) compared to non TNBC tissues. LVI was seen in 76.2% of the TNBC cases compared to 22.9% of non-TNBC cases (p < 0.001).

Conclusion: The result of present study supports increased vascularity and lymphangiogenesis in TNBC as compared to non TNBC. This could give a possible explanation for poorer prognosis in this subgroup of patients.

No conflict of interest.

202 POSTER Comparative study of Doppler, MAGS, and CD31 assay as vascularity index in advanced breast carcinoma

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Introduction: Assessment of angiogenesis in solid tumors has always been a subject of high priority research. Angiogenesis index calculated in breast cancer as a part of pre treatment workup can prove to be of therapeutic and prognostic significance.

Materials and Methods: This was a prospective study undertaken in 25 advanced breast cancer patients over a period of 2 years. The angiogenesis was assessed in the cohort by means of immunocytochemistry, microsopic angiogenesis grading score (MAGS) and color Doppler Study. The results were compared with the presence of metastasis, occurrence of recurrence and the response following chemotherapy.

Results: Assessment of micro vessel density done with MAGS and CD31 assay correlated with the Doppler assessment (p < 0.001). High MVD was associated with higher percentage of metastasis (p < 0.001), and higher chances of local recurrence (p < 0.02). The MVD assessed using CD31 assay showed a statistical significance for the presence of metastasis (%^\text{2} < 0.05, d.f = 2). While the results obtained with MAGS also showed similar finding (%^\text{2} < 0.05, d.f = 2). Both the results are statistically significant. Recurrences were more in cases with high pre chemotherapy vascularity. However this did not show a significant result when the assessment was done with MAGS (%^\text{2} < 0.05, d.f = 2). While when comparing the local recurrence with MVD assessed using CD31 assay the results were statistically significant (%^\text{2} < 0.05, d.f = 2).

Conclusions: The study has validated the role of angiogenesis assessment, in breast cancer, in which the pre chemotherapy Microvesssel density was associated with poorer patient’s prognosis. This also suggests the role of high vascularity as an important step in tumor dissemination. Poorer response to chemotherapy predicted higher possibility of local recurrence. The assessment of MVD also correlated with the non invasive assessment done by color Doppler ultrasound which suggests that the modality can be an adjunctive tool for the angiogenesis assessment.

No conflict of interest.

203 POSTER Cooperative signaling of FHIT and p53 modulates celecoxib-induced growth inhibition through Akt and MDM2 signaling crosstalk in MCF-7 breast cancer cells

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Background: Cyclooxygenase-2 (COX-2) is an indispensable pathway in the pathogenesis and progression of breast tumors. Previous reports have suggested COX-2 signaling interaction with a number of tumor suppressors, such as FHIT and p53 in inflammatory processes. Meanwhile, growing evidence has substantiated the growth inhibitory effect of celecoxib in breast cancer cells, although the underlying molecular mechanisms have not been fully defined. Herein, we investigated the effect of celecoxib on FHIT expression and pursued FHIT signaling interplay with p53, Akt, and MDM2 pathways in MCF-7 breast cancer cells.

Materials and Methods: Cell viability was assessed using MTT assay. Protein expression was measured using Western Blot in a time-course study (15 min to 6 h). FHIT and p53 expression was studied by RNAI.

Results: MTT results indicated that celecoxib could exert growth inhibition in parental cells. Abrogation of p53 pathway attenuated anti-proliferative activity of celecoxib. Knock-down FHIT expression completely abolished celecoxib cytotoxicity. Western blotting analyses revealed that celecoxib augmented both FHIT and p53 expression, independently of COX-2 inhibition, whereas decreased p-Akt and MDM2 expression compared to control (P values <0.01). While p53 ablation had no effect on FHIT and MDM2 expression, it caused constitutive Akt activation. Silencing FHIT expression not only remarkably reduced sensitivity of the cells to celecoxib, but also notably enhanced MDM2 expression (P value <0.05). Of note, celecoxib could no longer increase p53 in the absence of FHIT functionality (P value <0.01).

Conclusion: Our data illustrate an intricate, time-dependent regulatory crosstalk among these pathways and provide insight into the signaling convergence of FHIT and p53, as possible COX-2-independent molecular targets of celecoxib, contributing to growth inhibition in breast cancer cells. Furthermore, our findings designate FHIT as a novel participating target of celecoxib, contributing to growth inhibition in breast cancer cells. FHIT-FHIT signaling interplay governing the growth inhibitory effect of celecoxib, underscoring the therapeutic role of selective COX-2 inhibitors in breast cancer.

No conflict of interest.

204 POSTER To evaluate P-glycoprotein expression in relation to molecular subtypes and predicting response to neoadjuvant chemotherapy in breast cancer – a study from a tertiary care center in India

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Background: Neoadjuvant chemotherapy is an integral part in management of breast cancer. Chemoresistance is an important factor determining the response of tumor to neoadjuvant chemotherapy (NACT). P-glycoprotein (P-gp) expression-mediated drug efflux is one of the mechanisms responsible for multi-drug resistance. Our study was aimed to determine the role of P-gp expression as a predictor of response to NACT in locally advanced breast cancer (LABC) patients and relation with clinicopathological characteristics.

Methods: Between August 2013 and July 2014, n=49 patients with LABC were enrolled after ethical approval. Clinicopathological data of each patient was recorded. Trucut biopsy was taken from the breast tissue before starting NACT and repeated post 3 completed NACT cycles for studying the P-gp expression in breast tissue using CD243/Glycoprotein P Monoclonal Antibody on immunohistochemistry. Response to adriamycin-based regimen was assessed using WHO criteria before and after NACT. Statistical analysis was done using SPSS 17.0 software.

Results: Increased number of patients stained positive for P-gp after receiving chemotherapy especially in patients showing stage III and stage IV disease (p = 0.02). With relation to molecular subtypes, P-gp was increased more in post NACT period in Her2neu and triple negative LABC (p = 0.01). With relation to response higher expression was significantly associated with stable or progressive disease (p = 0.01).

Conclusion: Detection of P-gp expression status before initiation of chemotherapy can be used as a predictive marker for NACT response in different biological subtypes and will also aid in avoiding the toxic side effects of NACT in non-responders.

No conflict of interest.

205 POSTER DISCUSSION Are community detected cancers more biologically similar to screen detected or interval breast cancers and how is this reflected in survival?

K. Elders1, C. Nickson1, H. Farrugia2, B. Mann3. 1Royal Women's Hospital, Breast Surgery, Melbourne, Australia; 2University of Melbourne, Faculty of Medicine- Dentistry and Health Sciences, Melbourne, Australia; 3Victorian Cancer Registry, Director, Melbourne, Australia

Background: In populations with breast screening programs, interval cancers are of higher grade, and more likely to involve the nodes...
Abnormalities in miRNAome contribute to epithelial–mesenchymal transition of breast cancer cells

V. Halytskyi, 1 Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Molecular Immunology Department, Kiev, Ukraine

Background: Epithelial–mesenchymal transition (EMT) is a transdifferentiation process in which epithelial cells downregulate epithelial gene expression signature, lose cell polarity, junctions with each other as well as interactions with the basement membrane and acquire mesenchymal traits incl. stem cell properties, enhanced motility, invasiveness and elevated resistance to anoikis (detachment-induced apoptosis). EMT is necessary for cancer resistance, progression as well as metastasis and, therefore, plays central role in acquisition of the malignant phenotype. This research aims to identify in what way the shifts in expression of non-coding RNAs, especially miRNAs, can contribute to the EMT of breast cancer cells.

Material and Methods: miRNA targets within gene transcripts were predicted in silico using the TargetScan software.

Results: MiRNAs miR-10, miR-18, miR-25, miR-181, miR-206, miR-221/222 and miR-373 hyperexpression of which is essential for breast cancer cells, can target transcript of CDH1 gene encoding E-cadherin. Overexpressed miRNAs miR-18, miR-19, miR-21, miR-23, miR-27, miR-79, miR-155, miR-181, miR-206, miR-210, miR-221/222 and miR-375 can also silence other genes responsible for cell-cell adhesion – JAM-A/JAM-C, CLDN1 (claudin 1), TPJ1/2 (tight junction proteins ZO-1 and ZO-2), OCLN (occludin), PECAM1 (p-selectin), CADM1 (nectin-like molecule 2), CTNNAL (alpha-catenin) and CTNNB1 (p120-catenin), CGN (cingulin). In addition, hyperexpressed miRNAs can suppress genes encoding PALS1/PATJ, DLG and PAR3 – main components of, respectively, CRB, SCRIB and PAR complexes responsible for the establishment of epithelial cell polarity. Transcripts of SNA1 (Snail), SNA2 (Slug), ZEB1/2, TWIST1, KLFG, TF3/SIX1, FOXC2 and LEF1 genes carry targets of miRNAs miR-15/16, miR-22, miR-31, miR-34, miR-101, miR-124, miR-125, miR-137, miR-140, miR-143, miR-145, miR-148/152, miR-199, miR-200, miR-203, miR-204 and miR-205. Down-regulation of these miRNAs is characteristic to the breast cancer cells and allows reactivation and hyperexpression of above genes encoding the key transcription factors responsible for the EMT. Moreover, targets of down-regulated miRNAs are revealed in transcripts of VIM, FN1, COL1A2 and CDH11 genes encoding fibronectin, N- and OB-cadherin, expression of which is the sign of EMT.

Conclusions: Shifts in miRNA expression profile can contribute to loss of E-cadherin and silencing of other epithelial junction and polarity genes as well as to activation of mesenchymal genes in breast cancer cells undergoing, as a result, the EMT phenotype and stem-like properties. These abnormalities affect also contact inhibition and facilitate cell detachment, surviving, movement and invasiveness, underlying the tumor progression and metastasis.

No conflict of interest.

207

RAPID SINGLE-CELL COPY-NUMBER ABERRATION ANALYSIS USING HIGH-THROUGHPUT SEQUENCING

T. Graier1, M. Auer1, E. Heitzer1, P. Ulz2, S. Perakis2, M.R. Speicher1, J.B. G detailed text here...
Results: Of 356 eligible patients, 218 (61%) were included in the analyses. Patient experienced continuity was statistically significantly higher in the smaller BCU as compared to the larger (76.3 and 67.1 points respectively of 100 points possible, p < 0.0001). Corresponding results were shown for patients scoring above cut-off score of 75 points for "high continuity" (86.6% at the smaller BCU and 73.7% at the larger BCU, p < 0.0001). However, no clinically significant differences were found regarding medical quality and lead times.

Regarding the association between experienced continuity and HRQoL, differences were found in HRQoL between the two groups of patients; high experienced continuity and low experienced continuity. High experienced continuity was associated with higher levels in all measured HRQoL scales. The differences in HRQoL score between the two groups were clinically significant (n difference more than four) regarding global HRQoL (9.3), emotional functioning (11.8), cognitive functioning (7.3), role functioning (5.8) and fatigue (11.2). The differences were also statistically significant, regarding global HRQoL (p = 0.03), emotional functioning (p = 0.005) and fatigue (p = 0.02).

Conclusion: The higher continuity of care at the smaller unit was compatible with good medical quality and approved lead times. High experienced continuity and HRQoL were strongly associated. Prospective stuctural data is often required, but can be difficult to obtain. Variations in functional data is often required, but can be difficult to obtain. Variations in population frequency, and familial segregation data are used and/or the amount of evidence needed to classify a variant.

Background: In recent years, analysis for hereditary cancer has expanded beyond well-known, high-risk genes such as BRCA1 and BRCA2, to multi-gene panels. One gene in which mutations are frequently identified is CHEK2. Mutations in CHEK2 have been linked to an increased risk of several cancers, primarily breast and colorectal cancer, but these risks are not well defined. Advising patients on variants of unknown significance, which are inconclusive with regard to predicting cancer risk, is challenging for clinicians. Clinical laboratories must constantly work to classify these variants based on evolving data. Recommendations for interpreting genetic variants are well established, but may not completely apply for moderately penetrant genes, like CHEK2. For these genes, population frequency data. Discussions regarding evidence and resolving classification discrepancies are in progress.

Results: Of the CHEK2 variants in common between both labs (n=28), classifications were concordant for 67.9% (n=19), including two alterations with only confidence discrepancies, i.e. pathogenic versus likely pathogenic or likely benign versus polymorphism. Classification discrepancies (n=9, 32.1%) were primarily due to differences in how phenotype, general population frequency, and familial segregation data are used and/or the amount of evidence needed to classify a variant.

Conclusions: In this comparison, 32.1% of classifications were discrepant based on differences in classification criteria and available data at each lab. We are currently working to resolve these discrepancies by sharing data and supporting evidence. Our study highlights the challenges of interpreting variants in moderate risk cancer genes, and the importance of data sharing and collaboration between laboratories to reduce classification discrepancies, improve variant interpretation, and provide clearer information for clinicians and patients. This work was supported by grants NV15-28830A, NV15-27895A and NV16-29995A.

Conflict of interest: Other Substantive Relationships: Espenschied, Richardson, Panos Smith, Dolinsky, and Gau are full-time employees of Ambry Genetics, a diagnostic laboratory which provides hereditary cancer genetic testing.

Early phase clinical trials conducted in North America are more likely to exclude breast cancer patients based on organ function and comorbidities compared to other countries: Analysis of 484 studies V. Mariotti1, M. Gonzalez Velez2, N. Duma3, R. Parrondo3, S. Kothadia1, B. Gladney1, R. Panchal1, J. Liu1, K. Patel1, R. Undamatalia1, S. Rutgers, NIMS, Internal Medicine, Newark, USA; 2Mayo Clinic, Hematology Oncology, Rochester, USA

Background: Exclusion criteria used in Early phase clinical trials (EPCT) help to achieve accurate results and protect volunteers from potential risks associated with treatments. Such exclusions, however, can impair the comparability of EPCT results. The aim of this study is to analyze and compare the most common exclusion criteria used in breast cancer (BC) EPCT in North America (NA) with the ones used internationally.

Material and Methods: ClinicalTrials.gov was queried on 12/01/2015. We reviewed the exclusion criteria of 484 BC EPCT including; age, organ function and comorbidities. Logistic regressions were used to assess association between exclusion criteria and EPCT location/funding.

Results: Among the 484 EPCT, 273 (56.4%) were conducted in North America (NA), 55 (11.4%) in Europe (EU) and 156 (32%) in other countries. 241 (49.8%) EPCT were funded by industry, while 243 (50.2%) were investigator initiated or internally funded. NA EPCT were less likely to be industry funded compared to EPCT conducted elsewhere (NA 33.3% vs. EU 60% vs. international/other countries 75%). 149 (67.7%) EPCT excluded patients (pts) <18 years old, 56 (11.6%) pts with diabetes mellitus, 122 (25.2%) pts with arrhythmias, 233 (48.1%) pts with heart failure, 231 (47.7%) pts with coronary artery disease, 139 (28.7%) pts with HIV, 92 (19%) pts with hepatitis, 235 (48.6%) pts with previous or synchronous cancer history, and 347 (71.7%) pts with brain metastasis. On univariate analysis, trials conducted in NA were more likely to exclude pts with brain metastasis (OR 0.63, 95% CI 0.42−0.93, p < 0.05), hemoglobin 12 g/dL or lower (OR 0.6, 95% CI 0.41−0.87, p < 0.05), platelets 150 × 10^9 cells/L or lower (OR 0.3, 95% CI 0.20−0.43, p < 0.05), white blood cells (WBC) 4500 cells/μL or lower (OR 0.34, 95% CI 0.18−0.63), heart failure (OR 0.47, CI 0.32−0.66, p < 0.05), arrhythmias (OR 0.54, CI 0.35−0.83, p < 0.05), coronary artery disease (CAD) (OR 0.43, 95% CI 0.29−0.62, p < 0.05), HIV (OR 0.37, 95% CI 0.24−0.57, p < 0.05) or hepatitis (OR 0.56, 95% CI 0.35−0.91, p < 0.05). EPCT funded by the industry were more likely to include pts with platelets 150 × 10^9 cells/L or lower (OR 5.9, 95% CI 4.8−7.7, p < 0.05), WBC 4500 cells/μL or lower (OR 4.8, 95% CI 2.5−9.3, p < 0.05), CAD (OR 1.5, 95% CI 1.2−2.1, p < 0.05), HIV (OR 2.9, 95% CI 1.2−7.7, p < 0.05) and previous or synchronous cancer history (OR 1.7, 95% CI 1.1−2.4, p < 0.05) compared to EPCT funded by investigators or institutions.

Conclusions: EPCT conducted in NA are more likely to exclude BC pts based on organ function and comorbidities, and EPCT funded by industry are more likely to include pts with organ dysfunction or with comorbidities. Our findings highlight that careful evaluation of exclusion criteria in EPCT is needed, as the results might not be applicable to the real-world BC patient population.

No conflict of interest.
**Methods:** In the present study, we compared the RNA-sequencing transcriptions of a collection of breast cancer cell lines to transcriptions obtained from hundreds of tumours using The Cancer Genome Atlas. Tumour purity was accounted for by analysis of stromal and immune scores using the ESTIMATE algorithm so that differences likely resulting from non-tumour cells could be accounted for.

**Results:** We found the transcriptional characteristics of breast cancer cell lines to mirror those of the tumours. We identified basal and luminal cell lines that are most transcriptionally similar to their respective breast cancer cells in situ. Hence, extra precautions should be taken when modelling extracellular proteins in vitro. The specific differences discovered emphasize the importance of choosing an appropriate model for each research question.

**No conflict of interest.**

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210 **POSTER**

Vaccine targeting HIF1A in triple negative breast cancer

A. Sispensala1, 1 Save Alife Foundation, Research, Kampala, Uganda

**Objective:** The high rates of relapse in triple negative breast cancer (TNBC) are thought to be due to the presence of increased levels of cancer stem cells (CSC), which have been shown to be resistant to standard therapies. It has been demonstrated that hypoxia-inducible factor 1 (HIF1A) can induce the expression of numerous gene products associated with stemness and epithelial–mesenchymal transition in breast cancer cells and has been shown to be hyperactivated in TNBC.

**Method:** In this study, we aimed to target HIF1A with a therapeutic immune response through active immunization. HIF1A is a tumor-associated antigen.

**Result:** We have determined that both the magnitude and incidence of HIF1A-specific IgG is significantly elevated in TNBC compared to volunteer donors. We identified epitopes derived from HIF1A that selectively elicited IFN-gamma secretion with little to no IL-10 secretion in human peripheral blood mononuclear cells and T cell lines generated with these epitopes responded to recombinant HIF1A protein. Furthermore, these epitopes are highly homologous between mouse and man. To evaluate therapeutic efficacy, we immunized MMTV-neu (HER2+ model) and C3(1)Tag (TNBC model) mice with a plasmid-based vaccine containing an extended sequence of the identified epitopes. Tumor growth was inhibited over 80% (p < 0.001) in the TNBC model; however, growth was inhibited only by 40% (p < 0.001) in the HER2+ model. We determined the majority of the tumor cells from the TNBC model expressed the mouse stem cell marker, Sca-1, whereas only a minority of the cells derived from the HER2+ model expressed the marker.

**Conclusion:** Finally, we detected a 52% decrease in tumor Sca-1 expression after HIF1A-specific vaccination in the TNBC model (p = 0.004). Targeting HIF1A via active immunization may be an effective way to prevent disease relapse in patients with TNBC.

**No conflict of interest.**

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211 **POSTER**

Dosimetric advantage of Deep Inspiration Breath Hold in left breast radiotherapy: comparative analysis with free breathing

A.S. Rolão1, S. Germaino1, F. Mascalhena1, T. Almeida1, C. Miguel1, C. Machado1, A. Rocha1, 1Hospital da Luz, Radiotherapy, Lisboa, Portugal

**Background:** Previous studies have demonstrated that deep inspiration breath hold (DIBH), using 3D optical surface imaging (3D OSI), allows reproducible positioning and breathing amplitude for breast cancer patients. Radiotherapy (RT), while simultaneously avoiding exposure to extra-dose volume (CTV), and planning target volume (PTV) were contoured in both CTS, according to the RTOG guidelines for breast cancer. Different CTV to PTV margins were used for FB and DIBH due to better positioning reproducibility and less intra-fraction motion of DIBH.

**Material and Methods:** Two treatment plans were generated for each patient: DIBH and FB. The prescription dose was 40.05 Gy. DVH were obtained for OAR for all plans. Conformity and Homogeneity indexes (CI and HI) were also determined. The dose differences were evaluated using the paired t-test. p < 0.05 (two-tailed) was considered statistically significant.

**Results:** Table 1 lists the average values and standard deviation (SD) of dosimetric parameters for OAR, obtained from DVH, for DIBH and FB.

**Conclusion:** The average of mean heart doses is 1.3 Gy (0.39–2.96 Gy) for DIBH and 3.0 Gy (0.6–6.11 Gy) for FB (p = 0.001). The average of maximum doses to LADCA is 17.9 Gy (2.8–38.5 Gy) for DIBH, and 32.0 Gy (7.1–38.8 Gy) for FB (p < 0.001).

Table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DIBH Average SD</th>
<th>FB Average SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omax (Heart)/Gy</td>
<td>21.2 ± 10.76</td>
<td>35.9 ± 8.6</td>
</tr>
<tr>
<td>Dmean (Heart)/Gy</td>
<td>1.3 ± 0.71</td>
<td>3.0 ± 1.7</td>
</tr>
<tr>
<td>Dmax (LADCA)/Gy</td>
<td>17.9 ± 12.29</td>
<td>32.0 ± 10.0</td>
</tr>
<tr>
<td>Dmax (Liver)/Gy</td>
<td>17.7 ± 10.93</td>
<td>35.3 ± 8.6</td>
</tr>
<tr>
<td>Dmean (Liver)/Gy</td>
<td>1.6 ± 0.84</td>
<td>4.5 ± 2.4</td>
</tr>
<tr>
<td>V25 (Left Lung)/%</td>
<td>8.0 ± 1.97</td>
<td>11.5 ± 3.2</td>
</tr>
<tr>
<td>V16 (Left Lung)/%</td>
<td>10.8 ± 2.40</td>
<td>14.7 ± 3.7</td>
</tr>
<tr>
<td>V8 (Left Lung)/%</td>
<td>14.5 ± 2.99</td>
<td>18.6 ± 4.3</td>
</tr>
<tr>
<td>V4 (Left Lung)/%</td>
<td>19.6 ± 4.01</td>
<td>23.6 ± 5.2</td>
</tr>
<tr>
<td>Dmean (Left Lung)/Gy</td>
<td>4.7 ± 0.80</td>
<td>6.1 ± 1.3</td>
</tr>
<tr>
<td>V4 (Right Lung)/%</td>
<td>0.0 ± 0.07</td>
<td>0.0 ± 0.2</td>
</tr>
<tr>
<td>Dmean (ContBreast)/Gy</td>
<td>0.3 ± 0.21</td>
<td>0.4 ± 0.4</td>
</tr>
<tr>
<td>D2% (ContBreast)/Gy</td>
<td>2.0 ± 1.80</td>
<td>2.7 ± 4.2</td>
</tr>
</tbody>
</table>

These results corroborate that DIBH allows a significant reduction of dose received by cardiac structures and right and left lungs. Regarding the contralateral breast, no significant difference was found between DIBH and FB.

We provided evidence of dosimetric advantage of DIBH over FB in left breast cancer RT.

**No conflict of interest.**

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212 **POSTER**

Initial experience of a single cancer care centre in treating left breast cancer using first Helical Tomotherapy-H in India

N. Hanumanthappa1, A.B.S. Kumar2, S. Ramamurthy1, 1Health Care Global Hospitals, Radiation Oncology, Bangalore, India

**Background:** Adjuvant radiotherapy is now established standard of treatment post breast conserving surgery and in high risk cases post mastectomy. However, studies have found a link between radiation therapy for breast cancer and a higher risk of heart and lung problems, especially if the cancer is in the left breast, the same side as the heart. Early breast cancer patients are living longer and therefore it’s important to keep the dose to heart and lungs to minimum and at the same time not compromising on the target coverage to prevent local recurrence. The first ever Tomotherapy-H system in India became operational in Feb 2016 in our hospital, Health care global enterprises, a tertiary level cancer care centre active and we undertook prospective collection of Dosimetric data for first 10 patients with left sided breast cancer treated on Tomotherapy-H.

**Materials and Methods:** We treated 10 patients with left breast cancer using helical Tomotherapy-H technique in our centre between February 2016 and June 2016. The treatment planning objectives were to cover 95% of the PTV using a 95% isodose (V95 >95%), with a minimum of 90% isodose covering 100% of PTV (V100 >90), no more than 10% of PTV to receive 110% (V110 <10%) of the prescribed dose. The heart and lungs were contoured as organs at risk (OAR) and doses received were recorded.

**Results:** Seven out of ten patients had undergone breast conserving surgery and three had modified radical mastectomy. Three patients had chemotherapy prior to commencement of RT. All chemotherapy
IMRT vs. VMAT for breast cancer treatment using a Monte Carlo algorithm

Poster Session, Saturday 28 January 2017 Abstracts S27

IMRT vs. VMAT for breast cancer treatment using a Monte Carlo algorithm

J. Sanchez Mazon1, M.A. Mendigueru Santiago1, F. Saez Hernandez1, C. Arguelles Rodriguez1, A. Perez Ochoa1, J.M. Lopez Vega1, Mompia Clinic, Radiation Oncology, Mompia, Spain

Background: There have been significant advances in the delivery of radiotherapy over the past few decades. Newer radiation techniques, e.g., intensity modulated radiotherapy (IMRT), have been developed. IMRT techniques employ variable intensity across multiple radiation beams. More recently, there has been some interest in arc-based or rotational techniques to overcome some of the limitations associated with fixed field IMRT, e.g., volumetric modulated arc therapy (VMAT). VMAT is a radiation technique that can achieve highly conformal dose distributions with improved target volume control and sparing of normal tissues compared with conventional radiotherapy techniques. The main aim of this work is to compare two different VMAT techniques with the IMRT technique in breast cancer.

Material and Methods: We have calculated three different treatment techniques in 10 patients with breast cancer: IMRT, VMAT1 and VMAT2. We have used Monaco Treatment Planning System from Elekta and Monte Carlo algorithm. VMAT1 is a VMAT technique describing two half arcs (180° each) around the breast, one of them clockwise and the other one counterclockwise direction. VMAT2 consists of two partial arcs, starting in the same point as VMAT1 but 40 degrees of amplitude each. The IMRT technique has been calculated with 4 step and shoot static fields. All techniques were calculated to deliver 50 Gy (2 Gy per day) to the whole breast. In the three cases, we have compared the PTV coverage (V95), PTV high doses (V107) and the OAR sparing (isoluminal lung, contralateral lung, heart and contralateral breast).

Results: PTV coverage, V95, were similar between the three plans and no statistically significant discrepancies were found, although dose conformity and homogeneity are better using VMAT. Significant differences were found in PTV high doses (V107), with IMRT delivering about 4% more dosage than VMAT techniques. In terms of OAR sparing, doses in lung (both ipsilateral and contralateral) and in contralateral breast were similar in the three plans. However, differences in heart doses were statistically significant between IMRT and VMAT1, with an increase of about 3% using VMAT1 technique. Comparing both VMAT techniques, we find similar PTV coverage. However, statistically significant differences were found in the heart and contralateral breast doses. VMAT1 increases the dose in about 6% in contralateral breast and 3% in heart, compared to VMAT2.

Conclusions: The data suggests that VMAT and fixed field IMRT will produce largely equivalent target volume coverage. However, dose conformity and homogeneity are better using VMAT. The absolute difference in dosimetric parameters reported as statistically significant is relatively small and may not be clinically significant. So, we cannot assure that VMAT is better than IMRT in the case of breast cancer.

No conflict of interest.

IMRT vs. VMAT for breast cancer treatment using a Monte Carlo algorithm

J. Sanchez Mazon1, M.A. Mendigueru Santiago1, F. Saez Hernandez1, C. Arguelles Rodriguez1, A. Perez Ochoa1, J.M. Lopez Vega1, Mompia Clinic, Radiation Oncology, Mompia, Spain

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No conflict of interest.

Outcomes of breast cancer patients older than 80 years treated with adjuvant radiotherapy

R. Barrientos1, M. Freilinghuesen2, M. Burotto1, Clínica IRAM, Radioterapia, Santiago, Chile; 1Hospital Clínico Regional de Concepción, Radiation Oncology, Concepción, Chile; 2Clínica Alemana de Santiago, Medical Oncology, Santiago, Chile

Background: The main purpose was to estimate the overall survival of patients older than 80 years, diagnosed by Stage I−III breast cancer that were treated by surgery and adjuvant radiotherapy with curative intent. Clinical and pathologic factors that influence survival were estimated.

Material and Methods: We analyzed 85 breast cancer patients older than 80 years that received surgery and adjuvant radiotherapy with curative intent. Overall survival was defined as the time from the date histopathological diagnosis until the last date of follow-up (official death certificate). Survival was analyzed by Kaplan–Meier method. A log rank test was used to compare survival of different clinical and pathological factors. Significance level was determined at p-value <0.05.

Table 1. Significant clinical/pathological factors for survival

<table>
<thead>
<tr>
<th>Clinical tumor stage</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
<th>Number of events</th>
<th>5-year survival</th>
<th>Log-rank test (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT1</td>
<td>8</td>
<td>9</td>
<td>1</td>
<td>80</td>
<td>0.003</td>
</tr>
<tr>
<td>cT2</td>
<td>8</td>
<td>9</td>
<td>0</td>
<td>NR</td>
<td>0.007</td>
</tr>
<tr>
<td>cT3</td>
<td>36</td>
<td>42</td>
<td>6</td>
<td>69</td>
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<tr>
<td>cT4d</td>
<td>28</td>
<td>33</td>
<td>4</td>
<td>NR</td>
<td>0.0006</td>
</tr>
<tr>
<td>Overall</td>
<td>84</td>
<td>100</td>
<td>13</td>
<td>80</td>
<td>0.0006</td>
</tr>
<tr>
<td>Clinical Nodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>58</td>
<td>69</td>
<td>11</td>
<td>80</td>
<td>0.006</td>
</tr>
<tr>
<td>Negative</td>
<td>29</td>
<td>34</td>
<td>8</td>
<td>75</td>
<td>0.05</td>
</tr>
<tr>
<td>Overall</td>
<td>85</td>
<td>100</td>
<td>19</td>
<td></td>
<td></td>
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<tr>
<td>Regional lymph node irradiation</td>
<td></td>
<td></td>
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<tr>
<td>Local irradiation</td>
<td>53</td>
<td>62</td>
<td>7</td>
<td>74</td>
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<td>Intergroup irradiation</td>
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<td>Overall</td>
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<td>Pathologic tumor stage</td>
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<tr>
<td>pT1</td>
<td>40</td>
<td>48</td>
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<td>77</td>
<td>0.003</td>
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<td>pT2</td>
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<td>Overall</td>
<td>57</td>
<td>68</td>
<td>13</td>
<td>60</td>
<td>NR</td>
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*Significant estimated by Kaplan–Meier. Comparison between subset of factors by Log-Rank (Mantel–Cox) test.*

NR, not reached.
POSTER

214

The role of post-mastectomy radiotherapy (PMRT) and prognostic factors of locoregional recurrence

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Background: The purpose of the study was to evaluate the outcome of patients with breast cancer undergoing or not by postmastectomy radiotherapy (PMRT) and to investigate the clinicopathological prognostic factors of locoregional recurrence (LRR).

Methods and Materials: We retrospectively reviewed data of patients underwent total mastectomy and sentinel lymph node examination at a single institution. Patients were staged according to AJCC/UICC 7th Edition. According to consensus in literature PMRT was limited to the chest wall (CW-PMRT) in stage pT3 N1 or extended to the lymphatic drainages of apex axilla and supracavitular nodes (CWLD-PMRT) in stage pT4 N2-3. Patients underwent salvage mastectomy after a previous conservative surgery and RT or with of systemic disease at diagnosis were excluded from the study.

Radiotherapy treatment was performed with linear accelerator and 3DCRT technique using X photons of 6 and/or 15 MV energy. Two tangential beam technique was used for CW-PMRT whereas an half beam technique with the addiction of 1-2 anterior-posterior (AP-PA) beam was used for CWLD-PMRT. The prescription dose was 50 Gy delivered in 25 fractions adding a boost of 20 Gy and 14-16 Gy for positive and close (<2 mm) surgical margins, respectively. Neoadjuvant chemotherapy (CT), adjuvant CT, Trastuzumab, Tamoxifen and hormone therapy were prescribed according to international guidelines. Radiotherapy was deferred after the completion of adjuvant CT. Univariante and multivariate analyses were performed using SPSS 22 (SPSS Inc., Chicago, IL, USA) technology.

Results: Between January 2004 and June 2013 a total of 912 patients underwent total mastectomy; of whom 269 (29.5%) underwent PMRT and 643 (70.5%) did not. Among PMRT group 77 underwent CW-PMRT and 566 CWLD-PMRT. Median follow up was 40 months (range, 3–118). No significant difference in terms of LRR was found between the no-PMRT and PMRT groups (p = 0.175, HR = 1.613; 95%CI = 0.808–3.219). The uni- and multivariate analysis of LRR for patients not undergone to PMRT showed a significant correlation with the presence of ECE (p = 0.049), Mib-1 >30% (p = 0.048) and triple negative status (p = 0.001). On the contrary, the triple negative status resulted as the only variable significantly correlated to LRR (p < 0.0001) in the PMRT group whereas ECE and Mib-1 >30% lost the significance. Finally, no significant difference was shown between CWLD and CW-PMRT (p = 0.078; HR = 0.375; 95% CI = 0.126–1.116).

Conclusions: Based on our data, we strongly confirm the positive impact of PMRT in local advance disease and recommend to carefully consider it in presence of ECE and Mib-1 >30% regardless T and N stage. CW irradiation might be a valid option in selected intermediate disease (p.i.e. less than 3 positive lymph nodes). Future “well designed” prospective studies are needed to properly validate our results.

No conflict of interest.

POSTER

214A

Breast irradiation using personalised thermoplastic mask for immobilisation: Pros and cons

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Background: The goal of radiotherapy is to achieve a high therapeutic ratio by increasing tumour control via adequate CTV dosimetry and decreasing normal tissue toxicity through better protection of the organs at risk. To attain this goal, solutions are often required for treatment optimisation, such as the use of immobilising devices for setup error reduction. There is a scarcity of literature data regarding thermoplastic masks for breast immobilisation when no prone breast board is available. Thus, the aim of the current study was to assess the advantages and drawbacks of thermoplastic masks used for patients with large breasts undergoing radiotherapy.

Materials and Methods: Patients with large breasts presenting with invasive left-sided breast carcinomas were treated post-segmentectomy in our radiotherapy department. Personalised thermoplastic masks were prepared to assist with immobilisation during fractionated radiotherapy. In order to evaluate the pros and cons of thermoplastic masks in late breast patients, all those irradiated with the mask while other 7 were used as control. Dose prescriptions were identical for the two patient groups: 50 Gy in 25 fractions to the whole breast CTV and boost dose to the tumour bed of 60 Gy in 25 fractions. The two main aspects assessed in our study were: (1) the reduction of setup errors with the immobilising mask; (2) the acute effects with/without the mask.

Results: For an accurate determination of the setup errors, EPID images were fused with the DRR images for each patient. Weekly positioning errors were determined for the two patient groups along the X and Y axes. The results indicated a clear advantage of the thermoplastic mask, which has reduced the errors to one third of the no-mask scenario. Furthermore, while the setup errors over the first two treatment weeks in both groups ranged between 1 and 2 mm, after the third week of treatment the errors in the no-mask group started to increase up to 4 mm. The immobilised group presented no changes. These errors could pose long-term risks to the heart. A shortcoming of the thermoplastic mask is the increase in the skin dose which resulted in grade 3 radiodermatitis, which however, resolved in 3 months post-irradiation.

Conclusions: The use of breast masks considerably increases the reproducibility of patient positioning and limits the setup errors. This is an important outcome, since positioning errors are often a challenge when treating large-breasted patients, given the fact that after 15–20 dose fractions the inflammatory processes can change the shape and the volume of the breast. The error reductions allowed an accurate D95% dose delivery, while the heart was adequately protected. A drawback of this irradiation technique is the increase in the skin dose, a consequence that can be managed with suitable medical care.

No conflict of interest.

POSTER

215

Hyperfractionated radiotherapy after conservative surgery in breast cancer patients: a phase II-II trial (MARA-1)

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Background: The aim of this study is to evaluate late toxicity after hyperfractionated radiotherapy (MARA-1 protocol) in early stage breast carcinoma as compared to a control group (CG) treated with standard fractionation.

Material and Methods: MARA-1 is a prospective phase I-II study on hyperfractionated IMRT. In the CG the whole breast received 50.4 Gy in 28 fractions (fx) with a sequential boost on the tumour bed of 10 Gy in 4 fx with 3D technique. In MARA-1 an IMRT technique was used and prescribed dose to the breast was 40 Gy in 16 fx with a concomitant boost of 4 Gy.
Primary objective was to evaluate late toxicity and secondary objectives were acute toxicity, survival and local control. Radiation Therapy Oncology Group/ European Organization for Research and Treatment Cancer criteria were used to assess late toxicity.

Results: A total of 174 patients were included in MARA-1 group and 130 patients in CG. The median follow-up was 52 months (range: 3–115). Five year actuarial cumulative incidence of G3 late skin toxicity was 1.5% in CG while no G3 toxicity was observed in MARA-1 and for G3 late subcutaneous toxicity was 0.6% and 0.3%, respectively. At multivariate analysis, tobacco smoking and larger PTV volume were associated with an increased risk of late G1 skin toxicity (HR: 2.15, 95% CI: 1.38–3.34 and HR: 1.12, 95% CI: 1.07–1.18, respectively), whereas patients with a larger PTV also showed an increased risk of G1 and G2 late subcutaneous toxicity (HR: 1.14, 95% CI: 1.08–1.20 and HR: 1.14, 95% CI: 1.01–1.28, respectively). Even the use of accelerated-hypofractionated regimen increased the risk of late G1 and G2 subcutaneous toxicity (HR: 2.35, 95% CI: 1.61–3.41 and HR: 3.07, 95% CI: 1.11–8.53, respectively).

Conclusions: Higher incidence of subcutaneous side effects was recorded in patients undergoing hypofractionated-accelerated radiotherapy. This increase was limited to G1-G2 toxicity. Further trials with prolonged follow up are needed to better define patients subgroups more prone to develop late toxicity when treated with hypofractionated regimens.

215A POSTER
Study of the breast dose coverage using auto-flash margin option in Monaco
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Background: Typically, when a target is superficial or lies in the build-up region just beneath the patient surface (like a breast), it is difficult to sufficiently cover the target with the prescribed dose due to the rapid fall off dose at the surface. Select Auto Flash option in Monaco, automatically opens the jaws, when needed to cover the virtual target when it is near the surface of the patient, so the prescribed dose is better achieved to superficial targets.

Material and Methods: For 10 patients with breast cancer, IMRT plans were generated in Monaco (IMRT treatment planning system, Elekta-CMS) with the implemented Monte Carlo dose calculation algorithm. For each patient two different plans were calculated: without using auto flash margin (plan1) and using 2 cm auto flash margin. All techniques were calculated to deliver 50Gy (2Gy per day) to the whole breast. In the three cases, we have compared the PTV coverage (V95). PTV high doses (V107) and the OAR sparing (ipsilateral lung, contralateral lung, heart and contralateral breast). The prescription was 50 Gy in 25 fractions.

Results: We find statistically significant discrepancies in PTV coverage. V95. Using Auto Flash margin increases the PTV coverage about 4%. However, PTV high doses (V107) increase too, in about 3% when we use Auto-Flash margin.

In terms of OAR sparing, doses in lung (both ipsilateral and contralateral) heart and in contralateral breast were similar in both cases.

Conclusions: The data suggests that using Auto Flash margin we get better PTV coverage. High doses (V107) increase when we use Auto Flash margin, however it is an acceptable increase. No statistically significant discrepancies were found in terms of OAR sparing.

216 POSTER DISCUSSION
Effect of radiotherapy for breast cancer on the prognosis of a subsequent myocardial infarction
N.B. Boekel1, L.Y. Boekel2, J.N. Jacobse1, M. Schaapveld1, J.Sanchez Amazon 1, M.A. Mendiguren Santiago2.

Background: Radiotherapy for breast cancer increases the risk of subsequent myocardial infarction (MI), it is unclear whether it also influences the outcome of these MI. We assessed the prognosis of MI in patients previously treated with radiotherapy for breast cancer.

Material and Methods: We selected patients diagnosed with a MI following radiotherapy from our hospital-based cohort of stage I-IIA breast cancer patients aged <71 years, treated between 1970–2009, and extracted detailed oncologic information. Cardiovascular disease (CVD) information and cause of death were acquired through questionnaires to general practitioners and cardiologists.

Radiotherapy for breast cancer often leads to exposure of the heart to radiation. As the highest dose is usually caused by internal mammary chain (IMC) irradiation, patients were compared based on yes/no IMC treatment (IMC+/-). Statistical analyses comprised estimation of cumulative incidences of cardiac death, death due to MI and CVD following MI (heart failure [HF] and valvular heart disease [VHD]). Death due to other causes was used as competing risk. Similar outcomes were evaluated for IMC irradiation using Cox proportional hazard regression models adjusted for possible confounders (including chemotherapy regimen, CVD risk factors, CVD history, and year of MI diagnosis).

Results: A total of 398 patients were included (62% IMC+, 38% IMC-) with a median age of 67 years at MI diagnosis. Median time between breast cancer diagnosis and MI was 15 years. Compared to IMC-, IMC+ patients more often died on the day of MI (20.0% vs. 11.1%, p=0.02). The 10-year cumulative incidence of cardiac death was 34.5% among IMC+ patients (95%confidence interval [CI] 28.5–40.6) compared to 23.6% (95% CI 16.8–31.0) among IMC- patients (p = 0.04). Other cumulative incidences were higher among IMC+ patients as well, although not significantly so (death due to MI 26.8% [95% CI 21.2–32.4] vs. 17.7% [95% CI 15.4–28.9] among IMC+ and IMC- patients, respectively and VHD 16.9% [95% CI 12.4–22.0] vs. 9.1% [95% CI 4.9–14.9] among IMC+ and IMC- patients, respectively).

After considering above-mentioned possible confounders, IMC irradiation was associated with a higher risk of cardiac death compared to IMC patients (hazard ratio [HR] = 1.68, 95% CI 1.11–2.53). The risk of death due to MI (HR = 1.29, 95% CI 0.82–2.03) and risk of VHD after MI (HR = 1.68, 95% CI 0.89–3.19) were nonsignificantly increased after IMC irradiation. IMC irradiation was not associated with an increased risk of HF following MI (HR = 1.06, 95% CI 0.64–1.75). At ECO2017 comparisons with the general population will also be presented.

Conclusion: Radiotherapy to the IMC appears to increase the risk of cardiac death following MI. Although further research is needed, our results suggest that radiotherapy may not only increase the risk of MI, but IMC irradiation also worsens MI prognosis.

216A POSTER
Optimal contouring and planning algorithm for surface dose in the treatment of chest wall radiation
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Background and Aim: Chest wall irradiation with adequate surface dosing is one of a major component of curative breast cancer management. Tomotherapy is an effective and often used IMRT option. Chest wall dosimetric parameters during breathing can be managed using the patient’s breathing plan, which is usually segmented with variables (x, y, z where x being the direction of the beam and y and z being the dorsoventral directions). The lung is the largest organ in the cranioventral direction (3–5 mm), and increases with deep breathing. Respiratory rate for adult is 12–18/min. We aimed to investigate the effects of breathing motion on PTV delineation related factors on the surface dose in the treatment of chest wall irradiation using tomotherapy.

Method: CT scan of random phantom were taken. PTV ~3mm, PTV 0 and PTV +5mm bolus was generated on chest wall. A one frx of 200 Gy to 95% of PTVs were planned with tomotherapy. A board system mimicking dornoventral breathing movements was generated. Board was set to 3 and 5 mm dornoventral movements with 0, 0.2 and 0.3 Hertz (no breaths, 12 and 18 and 30 breaths/min) speed. Mosfelt dosimeter was used to perform measurements. Probes were placed to 4 different locations using lasers as a guide.

Results: When PTV was generated with a subtraction of 3 mm from body contour, plan showed a mean surface dose of 182 Gy at predetermined 4 different positions. Mean Mosfet measurements of these points were 159.5 Gy with a difference of 12.3% when the board was immobile and were 150.5 Gy to 157 Gy with a difference of 13.7% to 17.3% with motion. PTV was generated as body contour, predicted mean skin dose of 200 Gy while mean Mosfet measurement was 188.8 Gy with a difference of 5.7% when the board was immobile. When measurements repeated while the board was mobile with 0.3 Hertz and 5 mm movement, the difference increased to 10%. Differences between measurements and planning results were min 5.7% and max 10%. When static measurement and
planning were done with a 5 mm bolus, skin dose was 207 cGy on plan and measured 210 cGy with Mosfet, a difference of 1.4%. Differences between mosfet measurements and planning were min +0.6% and max +2.9% when the system was mobile.

Conclusion: PTV, adjacent to external body contour causes surface dose deficiency up to 10%. PTV with a 5 mm bolus results an excess dose of 0.5% to 2.9%. Bolus can be used while treating chest wall with tomotherapy in sometime during radiotherapy. These results have to be confirmed in vivo.

No conflict of interest.

217 POSTER 
Mesh versus acellular dermal matrix in immediate implant based breast reconstruction - a prospective randomized trial

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Background: Comparative studies on the use of meshes and acellular dermal matrices (ADM) in implant-based breast reconstruction (IBBR) have not yet been performed.

Methods: This prospective, randomized, controlled, multicenter pilot study was performed at four Austrian breast cancer centers. Fifty patients with oncologic or prophylactic indication for mastectomy and IBBR were randomized to immediate IBBR with either an ADM (Protexa®) or a titanized mesh (TILLOOP®). Complications, failed reconstruction, cosmetic outcome, patients’ quality of life and the thickness of the overlying tissue were recorded immediately postoperatively and 3 and 6 months after surgery.

Results: 48 patients participated in the study (Protexa® group: 23; TILLOOP® Bra group: 25 patients). The overall complication rate was 31.25% with similar rates in both groups (Protexa® group 9 vs. 6 in TILLOOP® Bra group; p = 0.188). There was a higher incidence of severe complications leading to failed reconstructions with implant loss in the Protexa® group than in the TILLOOP® Bra group (7 vs. 2; p = 0.0001).

An inverted T-incision technique led to significantly more complications and reconstructive failure with Protexa® (p = 0.037, p = 0.012, respectively). There were no significant differences in patients’ satisfaction with cosmetic results (p = 0.632), but surgeons and external specialists graded significantly better outcomes with TILLOOP® Bra (p = 0.034, p = 0.032).

Conclusion: This pilot study showed use of TILLOOP® Bra or Protexa® in IBBR is feasible leading to good cosmetic outcomes and high patient satisfaction. To validate the higher failure rates in the Protexa® group, data from a larger trial are required.

No conflict of interest.

218 POSTER 
Volume displacement techniques for filling partial mastectomy defects

A. Moustafa, Benha University Hospitals, General Surgery, Benha, Egypt

Background: This prospective comparative study was designed to compare between different volume displacement oncoplastic techniques in management of breast cancer as regarding oncological safety and better cosmetic outcome.

Patients and Methods: The study comprised 42 female patients with mean age of 40.1±6.5. All patients underwent full clinical examination, preoperative mammography and core-cut biopsy. The patients were randomized into 3 equal groups: Local tissue rearrangement, Mastopexy approaches & therapeutic reduction mammaplasty to fill the defect of partial mastectomy. Surgical margins were assessed by frozen section analysis (FSA). Follow-up for cosmetic results and post-operative complications for one year was planned.

Results: Overall complication rates for oncoplastic reconstruction range from 15–30% in skin/flap necrosis, nipple and nipple areola complex necrosis, seroma, hematoma, infection, wound dehiscence and fat necrosis. Intraoperative FSA decreases the incidence of positive margins, need for completion mastectomy and local recurrence. Oncoplastic breast reconstruction results in better aesthetic outcomes and higher patient satisfaction relative to partial mastectomy without filling the glandular defect.

Conclusion: Oncoplastic breast reconstruction at the time of partial mastectomy, either through local tissue rearrangement or mastopexy/reduction mammaplasty technique, is an extremely valuable tool in comprehensive oncologic treatment. These techniques leave patients with minimal breast deformities following proper treatment, without compromising oncologic safety. These are procedures that all reconstructive breast surgeons should be familiar with and offer their patients at the time of breast conserving surgery for breast cancer.

No conflict of interest.

219 POSTER 
Frozen section analysis versus imprint cytology for assessment of safety margins in breast conservation surgery

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Background: This cross-sectional comparative randomized study was designed to evaluate the accuracy of intraoperative lumpectomy margins assessment in patients with early-stage breast cancer treated with Breast-conserving therapy; frozen section analysis versus imprint cytology.

Patients and Methods: The study comprised 40 female patients with mean age of 47.1±5.5. The patients were randomized into 2 equal groups: frozen section group & imprint group. After adequate margins had been achieved, additional 5 mm normal breast tissues were removed all around the wound site and subjected to paraffin section examination.

Results: There was a non-significant difference in both groups as regards the need of intraoperative resection. The mean patients’ waiting time was significantly longer in frozen section group (105.4±17.4 minutes) compared to that recorded in imprint group (85.1±16.2 minutes). On paraffin section examination, there was a significant higher rate of positive margin in frozen section group. The accuracy rate of frozen section analysis and imprint cytology to define positive margin was 85% & 100% respectively.

Conclusion: Both techniques were effective in reducing the need of a second operation for margin control. However, imprint cytology; in addition to saving tissue for paraffin histo-pathologic examination, has the advantages of being more accurate to ensure clear margins with significant decrease in the operative time.

No conflict of interest.

220 POSTER 
Value of intra-operative ultrasound in localization of breast masses during breast conserving surgery

A. Moustafa, Benha University Hospitals, General Surgery, Benha, Egypt

Background: This prospective, controlled study was designed to evaluate the use of Intraoperative Ultrasound (IOUS) in localization of breast lesions during breast conserving surgery and correlate with pathological results for adequate negative margins.

Patients and Methods: The study comprised 60 female patients. 30 patients as case study: patients undergo breast conserving surgeries with IOUS guidance and 30 patients as control: patients undergo breast conserving surgeries without IOUS guidance. Pathological microscopic examination of the specimen will be conducted to ensure adequate negative margins.

Results: Use of IOUS significantly improve the surgical outcome of breast conserving surgery via better localization, good assessment of the safety margins and a satisfactory cosmetic results via minimizing rate of re-excision.

Conclusion: Intra Operative Ultrasound is an essential adjunct to surgery that should be experienced to obtain safety and cosmesis.

No conflict of interest.

221 POSTER 
Oncoplastic breast surgery is oncologically safe in locally advanced breast cancer after neoadjuvant chemotherapy, an Egyptian experience

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Background: Oncoplastic surgery (OPS) has emerged as a new approach for extending breast conserving surgery (BCS) possibilities, reducing both mastectomy and re-excision rates, while avoiding breast deformities. Evidence for OPS comes from Western literature. These techniques is emerging and our experience in Egypt has been gradually increasing. Our aim was to extend the applicability of OPS into more advanced tumours following neoadjuvant chemotherapy. This is the first study of OPS in developing country.

Methods: This is a prospective feasibility cohort study of oncoplastic breast surgery after neoadjuvant chemotherapy that was carried at the National Cancer Institute – Cairo University and included 40 patients. We aimed to look at long term oncologic safety and cosmetic outcomes. The primary
outcome was the local recurrence rate. Secondary outcomes included survival and margins obtained as well as cosmetic outcomes. Survival analysis was performed with Kaplan–Meier curves. Cosmetic outcomes were assessed using a modified Breast Q questionnaire (EORTC 10801).

**Results:** 40 patients with locally advanced breast cancer diagnosed between September 2012 and January 2015 at NCI – Cairo University were included. All were treated primarily with neoadjuvant chemotherapy (Anthracycline-based). The median follow-up period was 42 (Range 24–60) months. 27.5% showed complete pathological response. 62.5% of patients had a negative OLS procedure, 10% had a level II procedure, and 27.5% had a volume replacement procedure. The median margin of resection with level I was 10 mm, level II 25 mm and volume replacement was 15 mm. Statistically significant difference between the procedures was observed when level I and II were compared to each other in terms of margins obtained (p = 0.028). It was also observed when the three different categories were compared to each other (p = 0.035). Three patients (7.5%) had local recurrence and needed mastectomy; at 11, 13 and 16 months respectively. One (2.5%) developed distant bone metastasis. The disease-free survival (DFS) for the whole cohort was 90.2%. The overall survival (OS) was 100%. The DFS for patients with level I surgery was 85.4% while for those with level II and volume replacement it was 100% (p = 0.2). The DFS with a median resection margin less than 20 mm was 86.3%, and with more than 20 mm, was 100% (p = 0.2). The cosmetic outcomes ranged between excellent result (70%), very good (15%), good (10%) and poor results (5%) on a scale that was used for the purpose of the study.

**Discussion:** Oncoplastic breast surgery didn’t compromise oncologic safety in the patients included in the study. The local recurrence rate, the DFS and OS were all within acceptable ranges. It allowed wider margins which could be associated with better oncologic outcomes. It gave better cosmetic outcome and higher patient satisfaction. No conflict of interest.

224 POSTER
Feasibility of Port-a-cath insertion through external jugular vein cut down in cancer patients
M. Sakkary1, 1National Cancer Institute, Surgery, Cairo, Egypt

**Background:** Long-term central venous access with totally implantable port is frequently needed for administration of cancer chemotherapy. Most frequently, long-term central venous access has been obtained via blind percutaneous cannulation of subclavian and internal jugular veins or via internal jugular vein cutdown. In order to avoid potential complications associated with the subclavian or internal jugular approaches, a simple and safe method for central venous access through an external jugular vein (EJV) cutdown will be described and evaluated.

**Patients and Methods:** This is a prospective study involving 62 breast cancer patients submitted to breast surgery and scheduled for adjuvant chemotherapy, in the period from November 2015 to May 2016, at the National Cancer Institute, Cairo, Egypt. They were taken to the operating room with the intention of placing port-a-cath through the EJV cut down as an alternative way to subclavian or internal jugular vein routes. The patients were monitored for immediate postoperative complications. All patients data were entered in a prospectively prepared data sheet.

**Results:** Successful cannulation and placement of the Port-a-cath was possible in 57 cases with success rate of 92%. In the other 5 failed cases, the procedure was completed through the internal jugular vein of the same side. No significant intraoperative or postoperative complications reported except for one case of retraction of the vein from around the catheter and bleeding and another case of subcutaneous hematoma. These were immediately controlled and managed. No life threatening events occurred even if the catheterization was not successful.

**Conclusions:** EJV cut down is a simple, easy, and safe way for central venous access and port-a-cath insertion for administration of cancer chemotherapy avoiding the possible life threatening complications of central venous access. No conflict of interest.
NICE guidelines: BCS is an operation that both minimises local recurrence and achieves a good aesthetic outcome.

Association of Breast Surgery (ABS) guidelines: Minimum standard >95% of patients should have three or fewer operations. Target ~ 100% of patients should have <3 operations.

Methods: All the patients who had breast conserving surgery from 1st February 2016 until 31st May 2016 were included in this audit. Data collection was performed prospectively as a part of National Margins Audit (NMA).

Results: Positive margins were present in 11.1% (n = 7) patients. Further excision of margins was required in 5 patients only (7.9%) as in 2 patients the involved margin was posterior and excision reached the muscle. Only one further procedure was required to clear margin in all cases. 35 radial cavity shaves were taken in 25 patients, most had one shave only, two shaves were in 8 patients and only one patient had 3 shaves taken. Average thickness of a radial shave was 12.1 mm (1−30 mm). Anterior and posterior cavity shaves were taken in 5 patients.

Conclusion: This audit confirmed that our department is performing breast-conserving surgery as per standard set by ABS.

No conflict of interest.

225 POSTER
Breast cancer in young women in Algeria
N. Caid, 1 EHS en Latte contre le Cancer, Department of Medicine, Blida, Algeria

Background: Breast cancer in young women is increasing. The objective of this work is to analyze the epidemiological, clinical, biological, therapeutic and prognostic characteristics of breast cancer in young women with age lower than or equal to 35 years.

Patients and Methods: This is a retrospective study of 215 patients aged lower than or equal to 35 years, in whom a diagnosis of breast cancer was made between January 2011 and December 2015. To give: nulligece, notion of taking oral contraceptive, history of breast cancer in the family, reason for consultation, classification, presence or absence of distant metastases, the following parameters were evaluated: histology of tumor, SBR, carcinoma in situ, vascular emboli, receptor hormone and HER2/new number of metastases lymph nodes.

Results: The mean age was 32 years, 25% patients had a family history of breast cancer. The pauciparity and nulliparity were predominant 58.6%, concept of oral contraceptive 52%. The self-examination of a nodule was predominant 93%. The predominant histological type was the invasive ductal carcinoma with a grade SBR II and III in 94% of cases, carcinoma in situ 34.6%. The expression of hormone receptors in 70.2% of cases, ductal carcinoma with a grade SBR II and III in 94% of cases, carcinoma predominant 95%. The predominant histological type was the invasive ductal carcinoma with a grade SBR II and III in 94% of cases, carcinoma in situ 34.6%. The expression of hormone receptors in 70.2% of cases.

Conclusion: The incidence of breast cancer in young women in Algeria patients is high. In our context, it is distinguished by a delayed diagnosis, explaining the advanced stage at diagnosis. The biological characteristics are often more aggressive.

No conflict of interest.

226 POSTER
Breast conservation surgery without frozen section study control for intra operative margin status – a prospective study
M.I. Mohammed Ilyas1, 1 Kauvery-HCG Cancer Centre, Surgical Oncology, Chennai, India

Background: Breast conservation surgery is the “gold” standard surgical treatment in Early Breast cancer. The various factors which determine the successful outcome after a Breast conservation surgery can be divided into patient factors, Tumour factors and Surgeon’s factors. Of the most important surgeon’s factor is the “margin status” after the primary tumour excision.

Aim: To assess the margin status after primary breast tumour excision without frozen control in the final histopathological report.

Materials and Methods: 102 consequent patients of carcinoma breast who underwent Breast Conservation surgery without frozen section study control were assessed for the final margin status and followed prospectively for a minimum period of 24 months. All the patients completed Adjuvant Radiotherapy and relevant other adjuvant therapies.

Results: See the table.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Margin status</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>More than 1 cm</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>1 to 0.5 cm</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>0.5 to 0.1 cm</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>Less than 0.1 cm</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Piece meal excision</td>
<td>Nil</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>102</td>
</tr>
</tbody>
</table>

Re Surgeries: Total ~ 4; Re-Excision ~ 3; Total Mastectomy ~ 1.

Conclusion: Breast conservation surgery without frozen section study control is a reality with lesser margin of error if proper pre-operative imaging and work up has been done. The results of this study are comparable to the studies comparing margin status with frozen section study control and final pathological margins.

Discussion: There is a huge difference in the incidence of Breast Conservation Surgery between India and their European and US counterparts. Though there are less number of reasons for the same but the most important reason behind is the non-availability of the proper expertise and armamentarium including frozen section study control for margins assessment during tumour excision. This study shows that the margin of error is less even when we perform a Breast conservation surgery without frozen section study control and the re-excision rates for a margin positivity or close margin is same as in a Breast conservation surgery with frozen section study control.

No conflict of interest.

227 POSTER
Oncoplasty in breast conservation surgery: cosmesis and oncological safety – a prospective study
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Background: Breast Conservation is the treatment of choice for Early Breast Cancer. The MILAN and NSABP trials’ results suggest that it is oncologically safe and is also cosmetically superior. Oncoplasty has come as a great help for breast conservation with increased cosmesis but with no oncological compromise.

Aims of the study:
• Oncological safety and cosmetic outcomes in breast conservation following large volume resections using oncoplastic techniques.
• The role of oncoplastic techniques in improving breast conservation rates in our clinical practice

Materials and Methods:
• 50 patients
• Period of study – 36 months
• Large volume resections
• Undergo immediate partial breast reconstruction with Lattisimus dorsi flap
• Oncological safety – margin status
• Cosmetic outcome – photographs (1 month, 3 months, 6 months & 1 year)

Photographs were assessed by three independent observers not involved in the study
• Questionnaire to evaluate her personal experience after the reconstruction.

Cosmetic Assessment (Subjective)
• LENT–SOMA SCORE (Late Effects of Normal Tissues – Subjective, Objective, Management, Analytic – Score 1-poor to 5-excellent)
• Score ≥3 was considered as acceptable cosmesis
• t test, Kappa test – Inter observer Variability

Results:
• The age range was 20 to 65 years (mean 39.4)
• Tumour size:
  - pT1 – 08 (16%) patients
  - pT2 – 37 (74%) patients
  - pT3 – 05 (10%) patients
• Operating time – 110 to 210 minutes (mean 153.9)
• Blood loss – 75 to 350 ml (mean 134.2)
• Volume of resection – 30 to 300 cc (mean 123.4 cc)
• Skin island used for volume replacement – 4 cm × 5 cm to 14 cm × 6 cm (mean of 8.9 cm × 5.08 cm)
• Margin positivity or close margins – nil

Complications:
• Major wound complications – 3
• Minor wound complications – 5
Feasibility of extended sentinel lymph node biopsy after neoadjuvant chemotherapy in node-positive breast cancer patients

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Background: The use of sentinel lymph node biopsy (SLNB) following neoadjuvant chemotherapy (NAC) for patients with cN1 disease has been controversial, because after NAC, SLNB has a lower detection rate and a higher false-negative rate (FNR) compared with SLNB done before NAC in previous studies. The ACOSOG Z1071 trial and the SENTINA trial, to determine the FNR for SLN surgery following NAC in women initially presenting with breast cancer, reported that the use of dual-agent mapping and recovery of more than 2SLNs were associated with a lower likelihood of FNR. However, the problem is the difficulty of the examination of at least 3 SLNs. The pilot study was designed to assess the feasibility of accuracy of SLNB after NAC, by using 2 mapping agents, the combination of radionuclide labeled colloid and indocyanine green (ICG)-fluorescence. ICG-fluorescence is the most suitable means of decreasing the FNR because this method has a high SLN identification rate and can be used for more than 3SLNs.

Material and Methods: We enrolled women who had histologically proven clinical stage T1 through T2, N0 through N1, M0 primary invasive breast cancer. Patients with cN1 breast cancer, triple-negative breast cancer or HER2-positive breast cancer selected to receive NAC. The protocol required that at least 4SLNs be resected by combination of radionuclide labeled colloid and ICG-fluorescence. SLNs were ordered by the count using gamma probe and the fluorescence intensity by Photo Dynamic Eye (PDE). We reviewed women presenting with pathologically confirmed node positive disease, classified patients as receiving NAC or not, and investigated which lymph node were metastasis-positive in radionuclide labeled colloid and ICG-fluorescence. Patients with cN1 breast cancer before NAC were required to undergo SNB followed by axillary lymph node dissection.

Results: From May 2011 to October 2015, of the 59 patients with breast cancer, 12 patients were pN1 after NAC (3 patients cN0 before NAC, and 9 patients cN1 before NAC) and 47 patients who didn’t receive NAC were cN0 and pN1. Comparing in the patients receiving NAC, in the patients not receiving NAC, more lymph node metastasis were detected in the first or second lymph node. In the patients receiving NAC, the residual node-positive was detected 4 of 12 patients by radionuclide labeled method. In these patients, we confirmed that we prevented residual node-positive remained, by recovery of more SLNs in the means of the combination of radionuclide labeled colloid and ICG-fluorescence.

Conclusions: The order of node-positive is not consistent with the count using gamma probe and the PDE between patients receiving NAC and patients not receiving NAC. We pointed out that we prevented residual node-positive remained significantly, by recovery of more than 4SLNs in the means of the combination of radionuclide labeled colloid and ICG-fluorescence.

No conflict of interest.

Local adipodermal flap in decreasing fluid drainage and seroma formation after axillary lymph node dissection in breast cancer patients

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Background: Prolonged and excessive drainage of serous fluid and seroma formation after axillary lymph node dissection in breast cancer especially in old obese patients with subaxillary excess fat and redundant skin. Several approaches have been investigated to minimize seroma formation and decrease drained fluid. Here, a new technique is described with the same intent of minimizing seroma and remove subaxillary redundant skin.

Materials and Methods: Between December 2015 and June 2016, thirty six patients with breast carcinoma, scheduled for modified radical mastectomy, were randomly divided into 2 groups; the study group (18) and the control group (18). In the study group; after completing modified radical mastectomy, a broadly based adipodermal flap taken by de-epithelializing the lateral part of mastectomy skin flap, rotated and fixed deep in the axilla to the serratus muscle, thus obliterating the axillary space. In the control group; the wound was closed in the conventional method at the edges. Closed suction drains were used in both groups. Patients, tumor characteristics and operative related factors were recorded. The amount and color of drained fluid were recorded daily. The drains were removed when the amount become less than 50 cc. The total amount and duration of drained fluid and the formation of seroma were recorded and the results were compared between the two groups.

Results: In the adipodermal flap group, the drain was removed in significantly shorter time compared to the control group. Also, the total amount of drained fluid was significantly lower in the study group. The adipodermal flap group showed a significantly lower frequency of seroma formation compared to the control group. Also this technique enhanced breast shape, provided a special flap, and reduces subcutaneous tissue redundancy improving aesthetic outcome in obese patients.

Conclusions: This technique, of using the local adipodermal flap in obliterating the axillary space, seems to be a valuable procedure in decreasing the incidence of seroma formation, and remove the excess subaxillary skin and subcutaneous tissue redundancy in obese patients. A broader study with more cases and different surgeons is needed to confirm the value of this flap as an adjunct to reduce seroma formation after axillary lymph node dissection.

No conflict of interest.

Ipsilateral breast recurrence after breast-conserving surgery in young Japanese patients with breast cancer

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Background: The reported rate of recurrent ipsilateral breast tumor recurrence (IBTR) after breast-conserving surgery (BCS) is 5–20%. However, the rate may depend on age, ethnicity, and country, and be considerably influenced by the method of preoperative imaging such as enhanced breast MRI, postoperative pathological diagnosis, and adjuvant therapy. Some data from other countries have shown a tendency towards higher IBTR rates after BCS in young patients, but data derived from Japanese patients with breast cancer are scarce. We describe the incidence of IBTR and prognosis after BCS in young patients at our hospital.

Material and Methods: This retrospective review included patients with breast cancer who underwent BCS between January 2002 and December 2011 at Tokyo Metropolitan Cancer and Infectious Disease Komagome Hospital. Risk factors for IBTR and prognosis were evaluated using Kaplan–Meier and Cox regression analyses.

Results: Among 820 patients aged <60 years, 68 were excluded since they had undergone additional mastectomy to treat positive surgical margins. Fifty one (6.2%) and 769 (93.8%) patients were aged 35 (younger) and 36–60 years (older), respectively. During a median follow-up of 8.1 years, 19 (37%) younger and 247 (32%) older patients required additional partial resection and 6 (12%) younger and 62 (8%) older patients required mastectomy. Six (13.3%) younger and 16 (2.7%) older patients developed IBTR at a median follow-up of 7.95 (range 5.0–11.8) and 4.45 (range 1.2–10.2) years, respectively (p = 0.02). Univariate analysis selected younger age, node-positive (N1/2 vs. N0) tumors, the absence of radiation therapy after BCS, and a positive pathological margin as significant predictors of IBTR. Multivariate analysis selected only younger age as an independent significant negative predictor of IBTR (RR, 6.18; 95% CI, 1.88–17.63; n = 0.009).

Conclusion: Risk for IBTR after BCS was higher in younger, than in older Japanese patients. Young patients should be informed of the risk of IBTR before choosing to undergo mastectomy or BCS.

No conflict of interest.
231 Preferences of women in deciding on treatment for low-grade ductal carcinoma in situ (DCIS)

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Background: Ductal Carcinoma In Situ (DCIS) is a true precursor of invasive breast carcinoma. If untreated, it is estimated that 10–15% of low-grade DCIS will develop into invasive breast carcinoma. Because there is little data about the prognosis of DCIS, in most cases women detected with DCIS will be treated as if it is invasive breast carcinoma; mastectomy or lumpectomy and radiotherapy. Knowing that a substantial number of DCIS lesions will never form a health hazard, most women with low grade DCIS might be over treated. Currently, an European randomized inferiority trial (LORD) is set up to test if screen-detected low-grade DCIS can be safely managed by an active surveillance (AS) strategy only. Because future patients will be confronted with this decision option, we studied the preferences of women about low grade DCIS treatment using a Discrete Choice Experiment (DCE).

Methods: In a convenient sample of the general population, women between 45 and 75 were asked to fill in a questionnaire that consisted of background questions, the Dutch Cancer Worry Scale (CWS) and the DCE questions. Treatment attributes included interval follow-up; risk of nerve pain; 10 year iBC risk free rate; level of disfigurement due to choice of intervention. A conditional logistic regression analysis was performed to calculate the coefficients of each attribute level. Subsequently, the relative importance of attributes and predicted choice probabilities were calculated.

Results: From a total of 216 responders, the mean age was 52.6 (SD = 6.5) years. Ninety-two (43%) women scores high on the CWS (>13). The attribute "Level of disfigurement" had the largest impact (40%) on the predicted choice and stated preference. For women with a high CWS the impact of this attribute was higher than for women with a low CWS score (relative importance: 51% and 34%, respectively). Women with a high CWS score (>13) had a higher probability to opt for AS than for surgical treatment (47% vs. 53%, respectively), in contrast women with a low CWS score (≤13) they had a higher probability to opt for AS than for surgical treatment (61% and 39%, respectively). Furthermore, women with a history with cancer had a higher probability to opt for surgical treatment than for AS (55% vs 45%, respectively). In contrast women without a history of cancer had a higher probability to opt for AS than for surgical treatment (62% vs 38%, respectively).

Conclusions: Based on the results, the level of disfigurement due to choice of intervention was the most important attribute for choice of low-grade DCIS treatment. Understanding the preferences of women in the general population may help to enhance and informed decision-making process and based on the needs of the patients.

No conflict of interest.

232 Attitudes and beliefs of breast cancer patients toward their disease in urban South Africa: a cross-sectional descriptive study

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Background: Breast cancer is the most common cancer affecting women in South Africa. There is little knowledge of beliefs to help identify key areas to improve support and education in this demographically and culturally diverse population.

Material and Methods: Women with breast cancer accessing one government and one private breast clinic, with a variety of demographic and socioeconomic characteristics were asked to agree to statements of knowledge, attitudes and beliefs of breast cancer.

Results: Of the 259 participants, positive statements of medical cure (87.9%) and family support (90.5%) were most commonly believed. Beliefs in faith-based cure and alternative treatments were also present (79.5% and 24.9% respectively).

Negative beliefs were more likely in patients in the government hospital (RR: 3.73, 95% CI: 0.46–30.70) and in black patients (RR: 11.57, 95% CI: 1.37–97.89) as well as belief of cancer as a punishment (RR: 6.85, 95% CI: 1.41–33.21). However in multivariate analysis adjusting for age, education and access to information (by newspaper, internet, and confidence in reading and writing) there was no difference between racial groups or hospital used. Newspaper (aRR: 0.29, 95% CI: 0.05–1.54) and internet use (aRR: 0.00, 95% CI: 0.00–0.00) were the most protective against the negative beliefs of cancer, belief of cancer was a punishment or curse (Internet use: aRR: 0.12, 95% CI: 0.02–0.99) and belief in alternative methods of cure (Newspaper use: aRR: 0.91, 95% CI: 0.27–0.96). Positive expressions of cure and beating cancer were found equally in all women.

Conclusions: Attitudes and beliefs about cancer showed little independent demographic or socioeconomic variance. Negative beliefs were mitigated by access to information, and confidence in literacy. This study illustrates that information and education are important to promote positive attitudes in breast cancer treatment.

No conflict of interest.

233 Correlation of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) to lymph node (SLN) involvement in breast cancer

K.H. Tolani1, T. Canbak1, A. Acan1, S. Yuksekdağ2, M. Ozbagriacik1, M. Yucel1, E. Uinal1, F. Ezberco1. 1Health Sciences University Umraniye Training and Research Hospital, Department of General Surgery, Istanbul, Turkey

Background: There are a number of biochemical markers;包括 the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), which are insensitive markers of systemic inflammation. Since the presence of inflammatory cells, growth factors, activated stroma and DNA damage promoting agents in the inflammatory environment leads to sustain cell proliferation and causes an increase in the neoplastic risk, these peripheral blood elements were suggested to be independent prognostic factors associated with poor survival with various cancers, including breast carcinoma.

Material and Methods: 170 consecutive nonmetastatic patients with breast cancer operated between January 2012 and January 2016 in our clinic were included in the present study. Patients with active infection, any known other cancer history, hematologic disorders, chronic or current steroid treatment, and chronic inflammatory or autoimmune disorders were excluded. A venous blood sample was obtained from each patient one week prior to surgery and collected in the EDTA (anticoagulant) tube. All patients underwent breast conserving surgery with SLN biopsy. Statistical analysis was performed with IBM SPSS software version 23 (IBM SPSS, Armonk, NY, USA). The differences between clinico-pathological characteristics grouped by NLR or PLR were compared using the Pearson χ² test or Fisher's exact test for categorical variables and Student’s t test for continuous variables.

Results: All of the patients were women and mean age at diagnosis was 52.4±13.93. NLR positivity and NLR–PLR correlations are summarized in Table 1. PLR ratio was shown to be significantly increased in sentinel node positive patients.

Table 1. Serum NLR and PLR values correlated with SLN biopsy results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SLN involvement</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLR</td>
<td>1.91±0.89</td>
<td>2.15±0.95</td>
</tr>
<tr>
<td>PLR</td>
<td>132.40±56.36</td>
<td>153.44±59.73</td>
</tr>
</tbody>
</table>

*Statistically significant.

Conclusions: Our findings support the hypothesis that high level of PLR can influence the lymph node metastasis in breast cancer. However, further studies are required to better understand the role of PLR value in predicting lymph node metastasis, in particular, during sentinel lymph node biopsy before a precise conclusion can be drawn.

No conflict of interest.

234 Distress among women taking part in surgical continuity of care for breast cancer: a mixed methods study

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Background: Women often experience distress in relation to the diagnosis, treatment and care for breast cancer, which can give rise to reduced quality of life. The aim of this study was to evaluate the distress, resource use and coping strategies experienced by women with breast cancer during and after surgical continuity of care.

Method and Results: A mixed methods design was used. A semi-structured interview guide was developed and tested before data collection. Data were collected through interviews and questionnaires with 15 breast cancer patients in Aalborg, Denmark. The interviews were conducted by two trained interviewers and were audio-recorded and transcribed. The interviews focused on distress, resource use and coping strategies. The data were analyzed using qualitative content analysis.

Conclusions: The results showed that women experienced distress in various aspects of their lives, including physical, emotional and social aspects. The women also reported using a variety of coping strategies, including support from family and friends, as well as professional support from healthcare providers.

No conflict of interest.
of life and increased hospitalisation. Nevertheless, distress often remains unnoticed and untreated.

**Purpose:** To examine the prevalence and changes in distress among women taking part in surgical continuity of care for breast cancer and to identify indicators of distress, and furthermore to explore distress in more depth.

**Methods:** In this multistage mixed methods study three questionnaires were developed and content validated. Subsequently, a survey including 1079 women with newly diagnosed breast cancer was performed. The women were asked to score their distress level on a visual scale and complete a questionnaire to identify indicators of distress at three specific times in surgical continuity of care. Furthermore, 12 women were interviewed.

**Results:** At time of diagnosis 24.3% reported no or minor distress, 29.1% were moderately distressed and 39.8% severely. For most women the distress level remained unchanged, whereas it worsened for some women and decreased for others during surgical continuity of care. Indicators were time since diagnosis, age, children living at home, prior emotional status, and feelings regarding sexual attractiveness, and one hospital was associated with reduced distress. To feel supported it seemed important to be treated as a person in a caring human way, which involved the perspective of the life world.

**Conclusion:** Two thirds of women experience moderate to severe distress in surgical continuity of care for breast cancer. This study emphasise the importance of identifying women with distress to support them adequately.

No conflict of interest.

**234A**

**POSTER**


A. Bosieva1, C. Khutiev2, I. Khutiev2, U. Beslekoev2

1990

The state of cancer care in breast cancer in women and the ways to be treated as a person in a caring human way, which involved the perspective of the life world.

No conflict of interest.

**235**

**POSTER DISCUSSION**

Patient nutritional status: serum albumin levels a predictive indicator of survival in patients with metastatic breast cancer

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**Introduction:** As many as 20–30% (1) of breast cancer patients develop metastasis. Despite recent treatment advances and earlier detection, median survival approaches 2 years (2). Nutritional status and serum albumin levels in patients prior to cancer surgery has been investigated with higher levels of serum albumin associated with improved outcome (3). Serum albumin in patients with metastatic disease, however, has not been widely studied. We investigate serum albumin levels as a predictor of survival in patients with metastatic breast cancer.

**Methods:** Data was collected on all breast cancer patients who developed metastases while undergoing treatment or surveillance at tertiary referral breast centre between 2000–2016. Clinicopathological details including site of primary to score that tumour were recorded. The serum albumin on the date of diagnosis was recorded and the overall survival of each patient was calculated. A Kaplan–Meier and log rank test was performed to assess serum albumin levels on length of survival.

**Results:** The age [median (range)] was 55.2 (27.9–87.2). Of the cohort of 209, 168 were deceased (n=168). The median length of time until development of metastatic disease was 30 months (1–180). The sites of metastases included 131 who developed bone metastases, 144 who developed visceral metastases and 57 who developed brain metastases. The median length of survival post diagnosis of metastatic disease was 13.7 months (0.28–122). Low serum albumin (<35 mg/mmol) was shown to impact length of survival ([mean (SE)] 11.3 months (7.8) when compared to normal levels (28.8 months (3.3)). This was shown to be statistically significant (p < 0.01).

**Conclusion:** Serum albumin at time of diagnosis has shown to have an impact on the length of patient survival and may act a prognostic indicator. Further recording and interpretation of serum albumin and nutritional assessment at time of diagnosis in those patients who develop metastatic breast cancer may serve to optimise patient management and survival.

No conflict of interest.

**236**

**POSTER**

Prevalence of pain after six month of breast cancer surgery

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**Background:** This study was to evaluate the prevalence of pain after six month of surgery of breast cancer

**Methods:** This was a cross sectional study conducted on fifty breast cancer patients after 6 month of surgery.

**Results:** At 6 months 50% patients reported pain. Most patients (60%) have mild pain. Prevalence of pain was similar between those who underwent BCS and MRM. Most common site of pain was mastectomy scar followed by drain site. Upper arm dysesthesia was main problem in 20% patients

**Conclusion:** Pain is a major problem following breast cancer surgery. It can even persist after several months of treatment.

No conflict of interest.
236A  Poster

Patients’ perspectives on symmetrising breast reduction after oncoplastic surgery

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Background: Oncoplastic surgery aims at maintaining the shape of the breast when breast conserving surgery is performed. When larger volumes are excised it may also result in substantial asymmetry. Reduction mammoplasty for the contralateral breast is then offered. This study was performed to explore reasons why only 22% of our population proceeded with reduction mammoplasty.

Material and Methods: Semi-structured interviews were conducted with a purposive sample of 25 patients who had undergone oncoplastic surgery between 2010 and 2015 in a university hospital. The hospital policy was to perform symmetrising surgery after completion of breast cancer treatment. Nine of 25 patients had undergone symmetrising surgery, 16 did not. The interviews contained the following main themes: decision making, external influences (work / family), timing of the operation on the healthy breast, personal significance of symmetry.

Results: The interviews revealed that key factors determining the decision to have symmetrising surgery were: the extent of postoperative breast asymmetry, adaption to asymmetry in daily life, self-esteem in relation to asymmetry and postoperative outcome of oncoplastic surgery of the affected breast. Complications of previous breast surgery. Of the 16 patients who did not have symmetrising surgery, 7 stated that they did not experience significant breast asymmetry, of whom 4 had a LTD-flap as oncoplastic technique. Four patients wished to have symmetrising surgery but were not yet scheduled. The interviewees frequently denied that offering symmetrising surgery simultaneously with the oncological breast surgery would have favored them. 22 of 25 patients stated that they felt they had sufficiently been informed on the options for symmetrising surgery.

Conclusions: Patients who underwent oncoplastic surgery confirmed that asymmetry was the most important factor to decide to have symmetrising contralateral breast surgery. Complications of first surgery was a strong predictor of not proceeding with surgery on the contralateral breast. A broad range of motivations was encountered that contributed to their final decision. The extent to which patients turned out to be able to adapt to the asymmetry was influencing the perceived need for symmetrising surgery.

No conflict of interest.

237  Poster

Breast reconstruction using modified inferior dermal flap, implant, and nipple areola complex repositioning technique. Experience at MISR Cancer Center

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Background: Immediate breast reconstruction is routinely used for mastectomy candidate patients at MISR Cancer Center. Due to the patient preferences and advanced professional patient care. More and more cosmetic expectations are demanded every other day. Inferior dermal flap with implant is widely practiced. We added modification to this procedure using the autologous tissue as an inferolateral local sling, avoiding the costs in the low resource setting and reducing the morbidity of lengthy operating time. After using this modification many patients avoided a second procedure for subsequent nipple reconstruction and re-positioning that will decrease further appointments and costs.

Method: This study involved 24 patients (29 breasts) previously treated at our center from September 2014 to August 2016. Skin markings and a suitable nipple areola complex position is suggested. Reconstruction was performed following a periareolar skin deepithelialization to obtain the new nipple areola complex position. A Wise pattern skin incision and an inferior deepithelialized dermal sling was sutured to the pectoralis major to form a pocket for a silicone implant. And the nipple areola complex was sited at the time of reconstruction, with biopsies taken from retroareolar tissue before proceeding with the procedure.

Results: Patient average age was 51 years (range 38–64). 11 mastectomies were for invasive carcinoma, 8 for ductal carcinoma in situ, 5 for lobular carcinoma, and 5 of 19 mastectomies were prophylactically high risk and 2 Atypical lobular hyperplasia. Average operative time was 150 min. There were no immediate complications requiring reoperation. All retroareolar biopsies were benign and no locoregional recurrences have occurred. 4 nipples had partial superficial necrosis of the lower pole but healed with conservative treatment. No patients required any subsequent procedures to their reconstructed breast.

Conclusions: The modified inferior dermal flap with implant and nipple areola complex re-positioning is an excellent one stage breast reconstruction option. This method presents a potentially safe, trusted, and aesthetically accepted outcome for Egyptian women with large and ptotic breasts.

No conflict of interest.

238  Poster

Novel monastrol derivatives exert potent anti-breast cancer activity via inhibition of ubiquitin conjugating enzyme Rad6B

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Background: Rad6B is the first cloned ubiquitin-conjugating enzyme (E2) found to be essential for post-replication DNA repair. The over-expression of Rad6B is reported in breast cancer cell lines and tumours. Thus, interfering with Rad6B could serve as a novel target for anticancer drugs that contribute
Material and Method: All the compounds were evaluated for their anticancer activity against HeLa (cervical cancer), MCF-7 (breast cancer), HL-60 (Human promyelocytic leukemia) and HepG2 (Hepatocellular carcinoma). The compounds were also tested against Rad6B expressing human breast cancer cell lines MDA-MB-231. Molecular docking study was also carried out onto a human Rad6B protein crystal structure (PDB ID: 2Y6B) to define precise key interaction needed for inhibition. Results: Entire set of compounds showed considerable bioactivity against all the four cancerous cells in MTT assay with prominent inhibition against MCF-7 (IC50 = 41−97 μM) in comparison to cisplatin as standard. The compounds also showed considerable inhibition of MDA-MB-231 cells (IC50 = 2.31−45 μM). Docking study of ligands with Rad6B protein showed the formation of close H-bond and hydrophobic contact including pi-pi stacking interaction with Tyr82, Asp90, Tyr88 and Ser120 which makes it stable at the binding site with Kd of 102.45 μM.

Conclusion: A novel series of potent anti-breast cancer agent has been developed as potent anti-breast cancer agent via inhibition of Rad6B.

No conflict of interest.

239 POSTER
Assessment of EpCAM intensity of expression and outcome in breast carcinoma neoadjuvant chemotherapy treated patients
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Background: The wide use of Neoadjuvant chemotherapy nowadays became so wide to the degree that it is more or less established as a standard regimen in management of breast neoplasmia, in spite of different outcome results. Expression of epithelial cell adhesion molecule (EpCAM) is deregulated in epithelial malignancies. It is found that it acts as signaling molecule with tumor-promoting functions in addition to its role in cell adhesion.

Aim of work: It is aimed to assess the expression intensity of malignant mammary cells of EpCAM and its relation to the patient out come and their response to neoadjuvant chemotherapy.

Patients and Methods: 140 patients with breast carcinoma and undergone treatment with neoadjuvant chemotherapy were included in the study. Both Tru-cut tissue biopsy and radically-excised breast tissues; before and after neoadjuvant chemotherapy, were examined for intensity of staining by EpCAM.

Results: High intensity of EpCAM expression pattern is found correlated with lympho-vascular invasion status and higher nuclear grade (P = 0.01 and 0.008, respectively), and was associated with poor outcome (P < 0.001). We also found that patients with high EpCAM expression before and after neoadjuvant chemotherapy showed worse pathological and clinical outcome (P = 0.008 and <0.001, respectively) than the patients with high intensity before and low intensity after neoadjuvant chemotherapy. The overall survival rate of the first group is less than the second one (P = 0.049).

Conclusion: Strong EpCAM intensity in carcinoma of breast is correlated with bad response to neoadjuvant chemotherapy and subsequently with worse prognosis than in patients with negative or low staining intensity.

No conflict of interest.

240 POSTER
The role of topoisomerase IIα (TOPO IIA) as a predictive factor for response to neoadjuvant anthracyclines based chemotherapy in locally advanced breast cancer
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Background: Topoisomerase IIα (TOPO IIA) is a molecular target of anthracyclines; several studies have suggested that TOPO IIA expression is related to response to anthracycline treatment. The objective of this study was to evaluate if TOPO IIA overexpression predicts response to anthracycline treatment in locally advanced breast cancer patients.

Material and Methods: This prospective study included 50 patients with primary non metastatic locally advanced breast cancer according to American Joint Committee For Cancer Staging (T3-4,N0-3) who were treated between January 2012 and June 2012 at Clinical Oncology Department, Tanta University Hospital. TOPO IIA, HER2, estrogen receptor (ER), progesterone receptor (PR) expression and Ki-67 were evaluated by immunohistochemistry in formalin-fixed, paraffin-embedded breast tumors from 50 patients presenting with locally advanced breast cancer.

Results: Tumors from 50 patients, 45 (90%) showed TOPO IIA overexpression, 34 patients (68%) were ER positive, 32 (64%) PR positive, 10 (20%) had HER2 overexpression and 16 (32%) had high Ki-67.

Significant correlation between clinical and pathological response to TOPO IIA, HER2 and Ki-67 (p values < 0.001, 0.005 and 0.015, respectively).

1. Responders:
   • Clinical (CR): 3 patients had co-expression of TOPO IIA and HER2, hormonal receptor negative and high Ki-67.
   • Clinical (PR): 43 patients majority of them had TOPO IIA overexpression.

2. Non responders: 4 (8%) patients all had negative (TOPO IIA/HER2), low Ki-67 and 2 had hormonal receptor positive and another 2 had hormonal receptor negative.

No conflict of interest.

241 POSTER
Demonstration of pharmacokinetic and pharmacodynamic equivalence in healthy volunteers for B12019, a proposed pegfilgrastim biosimilar
K. Roth1, B. Gast1, D. Lehnick2, K. Jacob3, R. Jankowsky4.
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Background: B12019 is being developed as a biosimilar to Neulasta® (INN pegfilgrastim), a long-acting, pegylated form of recombinant human granulocyte-colony stimulating factor (r-metHuG-CSF, INN filgrastim) for the prevention of chemotherapy-induced neutropenia. A comprehensive analytical, functional and preclinical comparability program has already demonstrated a high degree of similarity of B12019 as compared to Neulasta®. In order to confirm the similarity on the clinical level, a pharmacokinetics/pharmacodynamics (PK/PD) study was conducted with B12019 in comparison to EU-authorised Neulasta® for treatment of chemotherapy-induced neutropenia.

Study design: The study was designed as a single-dose, randomized, double-blind, two-way crossover study. The study was based on a two-stage design according to Potvin et al, 2007 to address potential high variability for the PK endpoints. 172 healthy male volunteers were enrolled in stage 1 of the study, whereas stage 2 would allow the recruitment of additional 102 subjects. The subjects received B12019 as well as Neulasta®. The primary PK endpoints were the Area Under the Curve for concentration (AUC(0-∞)) and maximum concentration (Cmax). The primary PD endpoint was the Area Under the Effect Curve (AUEC) for Absolute Neutrophil Count (ANC). PK endpoints were assessed with a 94.32% confidence interval (CI) accounting for the two-stage study design, whereas the PD endpoint was assessed with a 95% CI. Furthermore, safety and immunogenicity were investigated.

Results: 161 subjects were eligible to contribute to the model-based PK and PD comparison based upon the first stage of the study. For the PK endpoints, the 94.32% CIs for the geometric mean ratios were 0.86–104.73% for AUC(0-∞) and 84.36–102.18% for Cmax. Both PK endpoints fulfilled the predefined acceptance criteria of being within the range of 80–125%. For the PD endpoint, the 95% CI for the geometric mean ratio of the ANC AUEC was 98.67–101.75 so falling within the predefined acceptance range of 80–125%. Since the primary PK endpoints were met in stage 1 of the study, stage 2 was not required. The safety profile of B12019 did not show any clinically meaningful difference as compared to Neulasta®. Neither anti-G-CSF nor neutralising antibodies were detected for both, B12019 and Neulasta®.

Conclusions: The study demonstrated PK and PD comparability as well as comparable safety and immunogenicity profiles of B12019 as compared to EU-authorised Neulasta®. No clinically meaningful differences were detected between B12019 and Neulasta®. The high analytical and functional similarity of B12019 was confirmed on clinical level.

No conflict of interest.

242 POSTER
Predictive factors for recurrence following neoadjuvant chemotherapy and definitive surgery for stage II and III breast cancer: A retrospective review
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Background: Neoadjuvant chemotherapy (NACT) for breast cancer is a therapeutic option for both locally advanced breast cancer and in large...
primary tumours. The aim is to downstage disease with the potential for offering more conservatory surgery. A proportion of patients will achieve a complete pathological response (pCR) conferring a significant survival advantage over patients who receive either partial or no response to NACT. Identifying patients that may contribute to a poor outcome in patients treated with NACT, and so hopefully better predict which tumours may benefit from alternative treatments such as targeted therapy or primary endocrine therapy, would be beneficial. The aim of this study was to analyse data from patients treated with NACT followed by definitive surgery for Stage II and III breast cancer, quantify survival and progression to potentially identify factors that may contribute to poor outcome.

Methods: A retrospective review of patients who had received NACT between 2009 to 2014. All patients had negative preoperative staging and received definitive surgery to the breast, with preoperative staging of the axilla. Patients who had recurred or died were compared to the group that were free of recurrence. Age, menopausal status, date of diagnosis, clinical findings, nodal stage at assessment, tumour type/grade, ER, PR and HER2 status, chemotherapy and cycles planned/given was recorded, along with final histology, surgery and post NACT receptor status, date of recurrence and death. cPR was defined as absence of invasive or in-situ tumour, in the breast and absence of any tumour in lymph nodes.

Results: 35 patients were identified between 2009–2014, 51.4% developed recurrence. Age distribution and menopausal status, and HER2 positivity was similar in both groups. In the group that recurred/died there was a higher percentage of triple negative tumours, progesterone receptor negativity, larger tumours on final pathology, greater lymph node positivity and lack of lymph node response, compared with the group that were recurrence-free. Lymphovascular invasion and extranodal spread on final histology was higher in the group that recurred reaching statistical significance. The percentage of patients not receiving the planned number of cycles of NACT was higher in the recurred/died group but this did not reach statistical significance.

Conclusion: The importance of a pCR following NACT continues to be demonstrated in large prospective trials. Identifying patients who will achieve the greatest benefit from primary chemotherapy or endocrine therapy is therefore important when managing patients with locally advanced or large primary breast cancer. This review demonstrated previously reported risk factors for recurrence, limited response in breast, and menopausal status. The presence and evidence of lymphovascular invasion/extranodal spread on final histology.

No conflict of interest.

243 POSTER SPOTLIGHT

Pembrolizumab for metastatic triple-negative breast cancer (mTNBC): long-lasting responses in the phase Ib KEYNOTE-012 study

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Background: In the multicenter, multicohort, nonrandomized phase Ib KEYNOTE-012 study (NCT01848834), the anti-PD-1 antibody pembrolizumab demonstrated promising antitumor activity (18.5% ORR in patients [pts] with measurable disease at baseline based on RECIST v1.1 as assessed by central radiology review; 6-mo PFS rate of 24%; 12-mo OS rate of 43.1%; data cutoff date, March 23, 2015) and a manageable toxicity profile as later-line therapy for previously treated pts with PD-L1+ mTNBC. Here we present updated follow-up data for KEYNOTE-012.

Materials and Methods: Patients ≥18 yr, with ER-negative, PR-negative, HER2-negative, recurrent or metastatic breast cancer, measurable disease per RECIST v1.1, ECOG PS 0–1, any number of prior systemic treatments in the metastatic setting, and PD-L1+ tumors (defined as expression in stroma or ≥1% of tumor cells by IHC using the 22C3 antibody) received pembrolizumab 10mg/kg Q2W for 2 yr or until disease progression or unacceptable toxicity. Response was assessed every 8 wk by central radiology review per RECIST v1.1. Survival was assessed every 3 mo. OS was estimated using the Kaplan–Meier method. Data cutoff date was April 26, 2016.

Results: Of the 32 female pts (median age, 50.5 yr [range, 29–72 yr]) enrolled, 46.9% had received ≥3 lines of therapy, and 25.0% had received ≥5 lines of therapy for metastatic disease. Duration of median follow-up was 10.7 mo (range, 0.4–32.7 mo). Median OS was 10.2 mo (95% CI, 5.3–17.5 mo); 12-mo OS rate was 78% (71.3%); 25 (78.1%) pts had died as of the data cutoff. Median PFS was 1.9 mo (95% CI, 1.3–4.3 mo); 12-mo PFS rate was 15.0%. Of the 5 responders (1 complete response [CR] and 4 partial responses [PRs]), 3 have had long-lasting benefit from pembrolizumab. The pt with CR discontinued pembrolizumab 11 mo after achieving CR and has remained in CR for approximately 15 mo without receiving additional anti-cancer treatment. Two pts with PR discontinued pembrolizumab after completing 2 yr of treatment. The first pt has maintained response for 22.7 mo; the second pt had disease progression after 7.7 mo. Median duration of response has not been reached (range, 15–58+ wk). Thirty (93.8%) pts discontinued pembrolizumab (27 [84.4%] for progressive disease and 3 [9.4%] for AEs) before reaching 2 yr of treatment. Six (18.8%) pts experienced grade 3–5 treatment-related AEs; 1 treatment-related death occurred (disseminated intravascular coagulation with decreased blood fibrinogen).

Conclusions: Pembrolizumab provides long-lasting responses in pts with mTNBC, with 22% of pts alive at 2 yr, thereby supporting its further development for heavily pretreated pts who have generally poor prognosis. The phase II KEYNOTE-086 study (NCT02447003), which is evaluating efficacy and safety of single-agent pembrolizumab as later-line treatment for mTNBC, is ongoing.

Conflict of interest: Advisory Board: R. Nanda has served on advisory boards for Genentech, Novartis, and Puma Biosciences; J. Specht has served on advisory boards for Advaxis and AbbVie, Inc.; L. Pusztai has received honoraria from Merck for consulting. Corporate-sponsored Research: R. Nanda has received research grants from Merck, Celgene, and Janssen. Clinical Trial: J. Specht has received research grants from Juno Therapeutics, Inc, Celldex Therapeutics, Pfizer, Genentech, Janssen LLC, Celgene, AbbVie, Nektar Therapeutics, and Seattle Genetics; E.C. Dees’ institution has received research grants from Novartis, Pfizer, Merck, Bayer, Roche-GNE, Cereulan, Lilly, and Medimmune; R. Berger has received research grants from Merck, Aveo, Bayer, Eli Lilly, New Link Genetics, Novartis, and Pfizer; L. Pusztai has received research grants from Merck, Other Substantive Relationships: E.C. Dees’ spouse has received consulting income from Novartis, unrelated to this work; K. Pathiraja, A. Ray, and V. Karantza are employees of, and V. Karantza owns stock in, Merck.

244 POSTER

Cardiovascular risk factors in breast cancer survivors: Analysis of NHANES 2010–2013

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Introduction: There are 1 million breast cancer survivors in Uganda. With improved survival from breast cancer, cardiovascular disease has emerged as one of the leading causes of morbidity and mortality. However, few studies have assessed CVD risk factors among breast cancer survivors.

Methods: We analyzed the National Health and Nutrition Examination Survey (NHANES) 2010–2013 to assess CVD risk factors, as defined by ASCVD, in adult women with and without a history of breast cancer.

Results: A total of 537 women, age 20 and older, with breast cancer history and 17,902 women without cancer history were included in the analysis. Among women with breast cancer, the mean (SE) age at diagnosis was 56.6 (0.81), 32.8% had the diagnosis <5 years; 39.9%, survived more than 10 years after diagnosis. Compared to women without cancer, the breast cancer survivors were older (mean age 65 (0.80) vs 46 (0.23)), and more likely to be white (84.2% vs. 67.6%) (both p < 0.0001), with similar education level. In stratified analyses, after adjustment for age, in older women with breast cancer compared to young women without cancer history had significantly higher SBP (128.9 vs 124.5, p = 0.003), and were more likely to be obese, have hypertension and diabetes (Table). In contrast, there were no significant differences in CVD risk factors in young women. There were no differences in lipids profiles between women with and without breast cancer.

Conclusion: CVD risk factors are very prevalent in breast cancer survivors. Improving cardiovascular health through lifestyle change and preventive strategies, particularly in older women with breast cancer, is a public health priority.

No conflict of interest.
245 POSTER 
Role of patient organizations in the fight against cancer

Mamma HELP, its projects, activities and experiences


Nowadays oncological patients form a large group, only in Europe there are 2½ million of them. The national health services of the states in Western and Central Europe provide the care for breast cancer patients at a high professional, technical and medication level. However, somewhere there is a lack of needful supportive care, especially psychological one, enough prevention and education. This is sometimes provided with patient organizations. These fields are a broad scope for patient organizations.

Mamma HELP is the largest female breast cancer patient organization in the Czech Republic included nowadays 8 centers in the regional and district towns. Since 1999 the association has been providing free consulting service and strong background for both female breast cancer patients and their families. The Mamma HELP professional guarantors are eminent experts. Our organization has been a member of the European Cancer Patient Coalition (ECPC) since 2015.

In the field of supportive care the organization provides individual consulting, after noon education and rehabilitation programs. One can use both our oncology consulting services on the website www. mammahelp.cz and free Breast Cancer Hotline sponsored by Avon Company. Our rehabilitative staff is trained to improve mental and physical health, to gain self-confidence. Mamma HELP organizes various motivational campaigns and events for a support and integration into everyday life of patients.

In the field of prevention and education Mamma HELP has offered the public lectures focused on the prevention of breast cancer since 2003. This year there are 60 lectures with the certificate trained by specialists from the Czech Association of Mammalogists. Mamma HELP has had a long-term cooperation with this Association. To increase awareness of breast cancer Mamma HELP uses international campaigns.

Our organization publishes a regular monthly journal as well as many other publications aimed at both prevention and support patients during and after treatment. Patients may receive from them quality needful information.

No conflict of interest.

246 POSTER 
Treatment with eribulin mesilate could suppress epithelial–mesenchymal transition (EMT) in tumors of patients with metastatic breast cancer – preliminary report of a prospective study

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Background: Recent evidence suggests that epithelial–mesenchymal transition (EMT) contributes to metastasis in patients with breast cancer, leading to their poor prognosis. Pivotal phase II trials have shown that eribulin improved overall survival in patients with triple negative metastatic breast cancer (MBC). Preclinical studies have demonstrated that eribulin suppressed EMT and this phenomenon could be one of reason for an improved prognosis of MBC patients treated with eribulin. However, there is no direct clinical data on the effect of eribulin treatment on EMT in tumors of MBC patients. We designed a prospective study to clarify if eribulin treatment suppresses EMT in tumors of MBC patients.

Patients and Methods: Patients with recurrent or MBC were treated with eribulin (1.4 mg/m² intravenously on days 1 and 8 of a 21-day cycle). Treatment continued until disease progress, unacceptable toxic effects, or discontinuation requests from patients or physicians. Breast cancer tissue samples were obtained from patients before and on day 15±4 of 1st cycle of eribulin treatment. EMT markers (E-cadherin, claudin, N-cadherin, vimentin) were analyzed by western blot. Primary outcome measure was to assess the change from baseline to day 15±4 in protein expression of EMT related markers in tumor tissue (UMIN Clinical Trials Registry number, UMIN000023300).

Results: Eleven patients were enrolled. Median age of the patients was 63 years old (44–72). Of the 11 tumors, 6 were luminal B and 5 were triple negative. Median number of prior chemotherapy regimen for recurrent or metastatic disease was 0 (0–3). After the treatment, E-cadherin protein levels were increased in 3 (75.0%), decreased in 1 (9.1%), and were decreased in 3 tumors (27.3%). Claudin protein levels were increased in 8 tumors (72.7%) and were decreased in 3 tumors (27.3%). Vimentin protein levels were increased in 2 tumors (18.2%), were not changed in 1 tumor (9.1%), and were decreased in 8 tumors (72.7%). N-cadherin protein levels were increased in 1 tumors (9.1%), were not changed in 4 tumor (36.4%) and were decreased in 6 tumors (54.5%).

Conclusions: This is the first prospective study to investigate the effect of eribulin treatment on expression of EMT marker in MBC patients. This study demonstrated that eribulin treatment suppressed EMT in tumors. These results suggested that eribulin showed antitumor effect by improving the tumor microenvironment. Our findings may provide a light to a scientific basis for solving underlying mechanisms for improvement of overall survival of patients with MBC treated with eribulin.

No conflict of interest.

248 POSTER
Interplay of MDM2 and PSMA modulates the secretion of the MMPs through AKT phosphorylation in breast cancer cells

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Background: In this study we investigated a possible interplay between two pro-oncogenes, Mouse Double Minute 2 homolog (MDM2) and Prostate-Specific Membrane Antigen (PSMA), in modulating the secretion of breast cancer cells through AKT phosphorylation in breast cancer cells.

Materials and Methods: Knockdown of MDM2 and PSMA in the breast cancer cell lines MDA-MB-231 and ZR-75-1 was performed using siRNA. Gene and protein expression was determined by qRT-PCR and western blot analysis, respectively. Following siRNA treatment, secreted protein levels of Matrix Metalloproteinases (MMPs) and Tissue Inhibitor of Matrix (TIMPs) were assessed using human MMP kits and flow cytometry. Western blots were also undertaken in order to determine the levels of phosphorylated AKT (ser473) and MMP2 (ser188).

Results: Treatment of MDA-MB-231 and ZR-75.1 cells with MDM2 siRNA results in a decrease in MMP2 expression (MDA-MB-231 p = 0.0051; ZR-75-1 p = 0.002) and treatment with PSMA siRNA results in a decrease in MMP2 expression in ZR-75.1 (MDA-MB-231 p = 0.001; ZR-75-1 p = 0.002; PSMA siRNA p = 0.0085); however, this trend is not replicated at protein level. Following treatment with both siRNAs, MDA-MB-231 showed a decrease in both MMP2 (MDM2 siRNA p = 0.0021; PSMA siRNA p = 0.0081) and MMP8 (MDM2 siRNA p = 0.0325; PSMA siRNA p < 0.0001), with ZR-75.1 cells showing significant decreases in the same MMPs (MMP2: MDM2 siRNA p = 0.0078; PSMA siRNA p = 0.0492; MMP8: p = 0.0491; PSMA p = 0.0278). Flow cytometric analysis showed a decrease in intracellular MMP2 levels following MDM2 or PSMA siRNA treatment, but no change in MMP8 levels. Since MDM2, PSMA and MMP8 all have previously been linked to AKT, protein levels were assessed, and it was shown that total levels increased upon treatment with PSMA siRNA; however, phosphorylation at AKT ser473 was decreased. AKT phosphorylation has been shown to be involved in the phosphorylation of MMP2 at ser187 and western blotting confirmed a decrease in phosphorylated MMP2 at ser187 following PSMA siRNA treatment of both cell lines.

Conclusion: Our data indicate that MDM2 and PSMA may interplay through their involvement in AKT phosphorylation at ser473, with PSMA knockdown resulting in a decrease in phosphorylation of AKT, and this leading to a decrease in MMP2 phosphorylation at ser187. This interplay may lead to a decrease in MPP2 and MMP8 secretion from breast cancer cells, when each of the molecules is knocked down.

No conflict of interest.

249 POSTER
Serial blood draws in metastatic breast cancer patients undergoing systemic treatment analysed by size based CTC detection and mFAST Seq cell free DNA analysis

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Background: Blood-based biomarkers such as circulating tumor cells (CTCs) and cell free circulating tumor DNA (ctDNA) provide dynamic real-time assessment of molecular tumor characteristics beyond the primary tumor. The aim of our study was to evaluate the performance of a size-based microfilter for CTC count analyses and of the mFAST-SeqS method in a prospective proof-of-principle study.

Materials and Methods: Patients with metastatic breast cancer diagnosed with progression in 7 tumors (63.6%) prior to the start of a new line of systemic treatment were eligible for inclusion in the study. 29 metastatic breast cancer patients were included and two tubes of peripheral blood were drawn. One CellSave tube for the size-based enrichment and detection
of CTC by immunofluorescence for PanCK and CD45 and one EDTA tube with paraformaldehyde for plasma DNA extraction and subsequent mFAST-SeqS analysis to estimate the percentage of ctDNA based on the amplification of the uniquely mappable LINE1-sequences across the genome.

Results: Using a size-based enrichment platform and immunofluorescence for CK and CD45 we were able to detect CTCs in 50% of patients at baseline with a median of 1 cell (0–58). Longitudinal blood draws during the treatment revealed a better correlation of the treatment response with mFAST-SeqS analysis than CTC counts. Genomewide mFAST-SeqS z-scores, which correspond to the amount of ctDNA in the circulation were clearly associated with response to treatment, whereas the CTC count was less predictive.

Conclusion: This proof-of-principle study demonstrates the feasibility of repeated blood draws for monitoring of treatment response, with mFAST-SeqS analysis indicating better prediction of response than CTC cell counts. These data should be validated in a larger cohort of patients with metastatic breast cancer.

No conflict of interest.

251 POSTER The efficacy and tolerability of eribulin for advanced or metastatic breast cancer: a case series from the Norfolk and Norwich University Hospital NHS Foundation Trust, United Kingdom

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Background: Eribulin (HALAVEN ®) is an antineoplastic agent which exerts its effects via a tubulin-based antimitotic mechanism leading to G2/M cell-cycle arrest and ultimately apoptotic cell death. It is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapy regimen. Prior therapy should have included an anthracycline and a taxane in either adjuvant or metastatic setting.

The use of eribulin at Norfolk and Norwich University Hospital was analyzed retrospectively in order to evaluate its effectiveness and side effect profile as per its current indication within our cohort population.

Material and Methods: We reviewed retrospectively 30 patients who had received eribulin between November 2012 and December 2015. All patients must have completed 2 or more previous lines of chemotherapy and at least 2 cycles of eribulin. The data was sourced from electronic patient records (MedOnc system version 10), patient hard notes, Somerset cancer registry, Web-ICE for Pathology, and PACS/Synapse for Radiology. The RECIST criteria v. 1.1 were used to assess treatment response.

Results: In our study 26 patients fulfilled inclusion criteria and were included in the analysis. The median age was 60.18 patients (70%) were ECOG performance status (PS) 0, 7 (27%) were PS 1 and 1 (4%) was PS 2. 25 (97%) had metastatic disease and only 1 (4%) had locally advanced disease. 21 (81%) patients were ER positive and 3 (12%) were HER2 positive. 7 (27%) patients were triple negative.

All 26 patients received at least 2 but no more than 3 lines of prior chemotherapy including an anthracycline and a taxane. On average, patients received 5 cycles of eribulin.

In the final analysis 63% had a clinical response and 40% had either a partial response or stable disease on CT as defined by RECIST criteria. No patient progressed after at least 3 cycles of eribulin.

Adverse effects were seen in 23 patients (88%). The majority were grade 1 or 2 however 5 patients (19%) experienced grade 3 neutropenia. Only 2 (8%) patients had to discontinue the treatment due to intolerability. There were no treatment related deaths.

Conclusion: In our population, eribulin (HALAVEN®) has exhibited good clinical and radiological response rates. The median PFS and median OS in patients with triple negative disease. The side effect profile is both acceptable and manageable with no deaths attributable to the treatment.

No conflict of interest.

252 POSTER Safety and effectiveness of anti-HER2 therapy in patients with advanced breast cancer: A case series from the Norfolk and Norwich University Hospital NHS Foundation Trust, United Kingdom

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Background: Patients (pts) with HER2-negative (HER2−) advanced breast cancer (MBC) may present with elevated serum levels of the HER2 extracellular domain (sHER2) or HER2 overexpressing circulating tumor cells (CTCs), potentially qualifying for anti-HER2 therapy. This retrospective study sought to clarify the value of HER2-directed Tx in these ‘occult’ HER2-positive (tissue-HER2 negative) patients with pathological or HER2+ CTCs in the clinical routine.

Methods: 32 pts with HER2− MBC (ER+, n = 28) exhibiting sHER2 values >15 ng/mL (n = 8), HER2+ CTCs (n = 8), or both (n = 16) were included. Pts had failed 2−16 prior systemic treatments (median: 7). Pts received trastuzumab (T: n = 20), lapatinib (L: n = 4), T+L (n = 2), or T+peruzumab (T: n = 6). Anti-HER2 Tx was given alone (n = 5), or in combination with endocrine agents (n = 7), cytotoxics (n = 17), or other targeted drugs (n = 3).

Responses were scored according to RECIST 1.1, OS was calculated from the start of Tx until death from any reason or loss to follow-up.

Results: Anti-HER2 Tx was well tolerated. Median treatment duration was 17.0 wks. In 2 pts with L and 1 pt with T+L, Tx was discontinued due to toxicity (diarrhea, fatigue), 13 PR, 13 SD, and 6 PD accounted for an objective response rate of 40.6% and a clinical benefit rate of 81.3%.

Median OS was 76.1 wks. In 25 pts, 9 with PR, 12 with SD, and 4 with PD, sHER2 measurements at baseline and after 3 wks were available. Most pts with PD showed increasing sHER2 levels. In the majority of pts with PR or SD, sHER2 dropped by more than 20% from baseline. Median OS was 76.1 wks. In 25 pts, 9 with PR, 7 with SD, and 5 with PD, serial CTC counts 6 wks from baseline were available. 4 pts with PD showed increasing CTCs. All pts with SD and PR presented with declining CTCs, mostly normalizing within 6 wks.

Conclusions: Anti-HER2 Tx was effective in pts with heavily pretreated HER2− MBC presenting with either elevated sHER2 or HER2+ CTCs or both. Thus, determination of both sHER2 and HER2 overexpressing CTCs is reasonable in tissue HER2-negative MBC pts in the clinical routine. Compared to sHER2, serial CTC measurements may be the more accurate predictor of response to anti-HER2 treatment in these ‘occult’ HER2+ MBC pts, particularly in those receiving L as part of their Tx.

No conflict of interest.

253 POSTER A pharmacokinetics (PK) bioequivalence trial of proposed trastuzumab biosimilar, Myl-1401O (A) vs EU-Herceptin (B) and US-Herceptin (C)

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Background: Myl-1401O is a proposed trastuzumab biosimilar. The biosimilarity of Myl-1401O to EU-Herceptin has been demonstrated in biochemical analyses, non-clinical studies, and one previous PK study. Methods: This single-center, randomized, double-blind, three-arm, parallel-group, phase I study was conducted in healthy adult male volunteers. The primary objective of this study was to establish PK similarity of A to B and C. The subjects were randomized to receive either A, B or C as 8 mg/kg over 90 minutes as an intravenous infusion. For the primary endpoint, the bioequivalence criterion was that the 90% confidence intervals (CI) of the mean ratios of AUC0–t, AUC0–∞ and Cmax were bounded within 80.00−125.00% calculated using natural log-transformed data. As secondary endpoints, t1/2, tmax and z, tmax and t1/2 along with assessment of safety (including immunogenicity) was performed.

Results: A total of 132 subjects (44/treatment) were enrolled and 120 [42 (A), 41 (B), 37 (C)] subjects were included in analysis. Statistical
analyses reveal that the 90% CI fall within 80–125% for all parameters. Eighty-three [31 (A), 28 (B), 24 (C)] subjects experienced a total of 227 [91 (A), 80 (B), 56 (C)] treatment emergent adverse events that were mild or moderate in severity. No serious adverse events were reported and there were no instances of treatment related anti-drug antibodies.

Table: PK results (dose-normalized)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AUC0-24h (mg h/mL)</th>
<th>AUC0-∞ (mg h/mL)</th>
<th>Cmax (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arithmetic mean (95% CI)</td>
<td>A (N=42) 48055 (15.92) 48241 (16.19) 200.4 (12.34)</td>
<td>B (N=41) 49623 (19.61) 50075 (19.81) 192.6 (14.13)</td>
<td>C (N=37) 49626 (13.86) 50181 (13.86) 197.9 (16.25)</td>
</tr>
<tr>
<td>LSMEAN Ratio (95% CI)</td>
<td>A/B 0.97 (91.17–102.97%)</td>
<td>A/C 0.96 (90.34–102.24%)</td>
<td>Cmax (mg/mL)</td>
</tr>
<tr>
<td>Ratio (A/B) = exp[LSMEANS of (LNA−LNB)]</td>
<td>Ratio (A/C) = exp[LSMEANS of (LNA−LNC)]</td>
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</table>

Conclusions: These results confirm pharmacokinetic bioequivalence for MYL-1401O vs. EU-Herceptin and US-Herceptin. All treatments were well tolerated and no significant safety issues emerged. Clinical trial information: NCT02594761.

No conflict of interest.

255 POSTER

HERITAGE: a phase III safety and efficacy trial of the proposed trastuzumab biosimilar MYL-1401O versus herceptin

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Background: Trastuzumab has revolutionized treatment of HER2+ breast cancer. Globally accessible alternatives are a critical need. We evaluated MYL-1401O, a proposed trastuzumab biosimilar, as treatment for HER2+ metastatic breast cancer (MBC), based on physicochemical analyses, nonclinical, pharmacokinetic and pharmacodynamic studies. Methods: Heritage is a double-blind, randomized clinical trial designed to evaluate comparative efficacy and safety of MYL-1401O vs Herceptin. Eligible patients (pts) had centrally confirmed HER2+ MBC without prior chemotherapy or trastuzumab for metastatic disease. Pts were randomized to receive either MYL-1401O or Herceptin with docetaxel or paclitaxel for a minimum of 8 cycles. Trastuzumab was continued until progression. The primary endpoint was overall response (ORR) at Week 24 by blinded central evaluation using RECIST 1.1. Secondary endpoints include progression free survival (PFS), overall survival, and safety. A sample size of 456 pts was calculated to demonstrate equivalence in ORR at Week 24 for MYL-1401O vs Herceptin, defined as a 90% confidence interval (CI) for the ratio of best ORR within the equivalence margin (0.81, 1.24).

Results: 500 pts were randomized, 458 were evaluable for efficacy. 44% of patients were hormone receptor positive MBC, 84% received docetaxel. Week 24 ORR was 69.6% for MYL-1401O compared to 64% for Herceptin. The ratio of ORR was 1.09; both 90% CI (0.974–1.211) and 95% CI (0.954–1.237) were within the pre-defined equivalence margin. Median PFS is not yet available. The ratio of median PFS was 1.24). The ratio of median PFS was 1.24. The ratio of median PFS was 1.24. Safety was comparable; serious adverse events (primarily neutropenia related) occurred in 38% (MYL-1401O) vs 36% (Herceptin), with 4 fatal events in each arm. There was no significant change in cardiac function from baseline to Week 24 in either arm.

Conclusions: MYL-1401O was equivalent to Herceptin, given in combination with a taxane as first line therapy for MBC, as measured by 24 week ORR. Safety was comparable. The proposed trastuzumab biosimilar MYL-1401O could be a new treatment option for HER2+ MBC.*

Phase 3 efficacy and safety trial of proposed pegfilgrastim biosimilar MYL-1401H vs EU-Neulasta® in the prophylactic treatment of chemotherapy-induced neutropenia


Background: MYL-1401H is a proposed pegfilgrastim biosimilar to the reference product EU-Neulasta®, based on physicochemical characterization, in vitro bioassays, toxicokinetics (TK), pharmacokinetics (PK), and pharmacodynamics (PD) studies.

Methods: This is a phase 3, multicenter, randomized, double-blind, parallel-group trial of MYL-1401H vs EU-Neulasta®. Chemotherapy and radiotherapy naive patients with newly diagnosed Stage II/III breast cancer were eligible to receive docetaxel, doxorubicin, and cyclophosphamide anti-cancer chemotherapy planned every 3 weeks for 6 chemotherapy cycles. A total of 194 patients were randomized in a 2:1 ratio to receive 6 mg/mL of either MYL-1401H or EU-Neulasta® on Day 2 of each cycle.

The primary efficacy endpoint was the duration of severe neutropenia (DSN) in Cycle 1, defined as days with absolute neutrophil count (ANC) <0.5 × 10^9/L in the per protocol population.

The sample size provides 90% power to declare that MYL-1401H is comparable to Neulasta® in the analysis of duration of severe neutropenia (DSN) in cycle 1. Equivalence is declared if the two-sided 95% confidence interval (CI) of the difference between these mean DSNs falls wholly within an equivalence region defined as [-1, +1] day. A sensitivity analysis in the intent-to-treat population was also carried out.

Results: The mean ± SD DSN in the MYL-1401H and EU-Neulasta® groups were 1.2±0.93 and 1.2±1.10, respectively. The 95% CI of LS means difference [-0.285 day, 0.298 day] was within [-1 day, +1 day] range, that was also corroborated by the sensitivity analysis. Other endpoints of the study including Grade 3–4 neutropenia, time to ANC nadir, and duration of post-nadir recovery were comparable too. The overall safety profile of MYL-1401H was similar to EU-Neulasta® with bone pain, an expected AE, as the most frequently reported treatment related AE.

Conclusions: MYL-1401H demonstrated equivalent efficacy to EU-Neulasta® in the prophylactic treatment of chemotherapy induced neutropenia in patients with breast cancer. MYL-1401H was generally well tolerated and there were no particular safety concerns identified with overall safety profile being similar to EU-Neulasta®.

No conflict of interest.
Clinical outcomes: Outcomes under consideration were as overall survival (OS), disease free survival (DFS), time to loco-regional recurrence (LRR) and time to distant recurrence (DR).

Bio-statistical methods: As all considered outcomes were time to event, hazard ratio was extracted. For the hazard ratio directly, it was extracted using Pemmar & colleagues method. The statistical heterogeneity was assessed by I² statistics. Risk of bias and quality of the included studies were assessed by the Cochrane bias assessment tool and Jadad score. None of the outcomes had publication bias as assessed by Egger's test and funnel plot. To synthesise the effect size, fixed effect and random effect methods were used in the case of low and high heterogeneity respectively. The protocol was registered in PROSPERO register (CRD4201523339).

Results: OS, LRR and DR were reported by 14, 13, 11 and 12 studies with 12 statistics 0%, 35.4%, 2.3% and 46.7% respectively. Toxicity and treatment compliance was similar in both of the groups. There was no significant difference between NACT and ACT for Distant recurrence (HR = 1.24 (1.05–1.45)). DFS (HR = 1.05 (0.95–1.15)) as well as OS (HR = 0.98 (0.89–1.08)) was similar in both of the groups.

Conclusions: The current systematic review and meta-analysis showed no statistically significant importance of neo-adjuvant chemotherapy in comparison to adjuvant chemotherapy for survival. No conflict of interest.

259 POSTER

Total preoperative NACT vs sandwich in breast cancer patients: systematic review and meta-analysis

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Introduction: Neo-adjuvant Chemotherapy (NACT) plays important role in the management of breast cancer patients. It is given in two types of setup, total preoperative or sandwich. There is lack of consensus, which is optimal. This Systematic review and meta-analysis was conducted to assess the impact of NACT administered either as total preoperative, or sandwich chemotherapy comparative to adjuvant chemotherapy (ACT) alone.

Material and Methods: Search Strategy: A comprehensive search of PubMed and Cochrane database with a predefined sensitive search strategy including the search terms as “Breast Neoplasms”, Breast Cancer; neoadjuvant, preoperative, upfront, primary; induction; and adjuvant and postoperative was performed on Jan 21, 2016.

Inclusion Criteria: All RCTs comparing NACT with ACT in the management of breast cancer measuring at least one of the considered outcomes were included.

Study material: Out of 1239 retrieved records, a total of 17 RCTs including 8 all preoperative NACT and 9 sandwich NACT trials were found eligible for inclusion. Data extraction form was prepared, to extract study level information of demographic, clinical and tumour factors along with outcomes, as per the Cochrane guideline.

Clinical outcomes: Outcomes under consideration were overall survival (OS), disease free survival (DFS), time to loco-regional recurrence (LRR) time to distant recurrence (DR), pathological complete response (pCR) and breast conserving surgery (BCS).

Bio-statistical methods: Hazard ratio (HR) was considered as all of the outcomes being time to event except BCS, for which relative risk was extracted. HR was extracted by method discussed by Pemmar & colleagues, if not reported directly. The statistical heterogeneity was assessed by I² statistics. Risk of bias and quality of the included studies were assessed by the Cochrane bias assessment tool and Jadad score. Egger’s test and funnel plot revealed no publication bias for any of the outcome.

Result: OS, DFS, LRR, DR and BCS were reported by 14, 13, 11, 12 and 9 studies respectively. Respective pCR rates in preoperative and sandwich groups were 14.6% (1.16–18.1) and 13.1% (11.4–15.0). LRR was higher in preoperative group (HR = 1.25 (1.05–1.50)) but not in the sandwich group (HR = 1.16 (0.81–1.66)). BCS rate was also higher in preoperative group (HR = 1.40 (1.08–1.81), n = 5), but not in sandwich group [HR = 1.06 (0.90–1.15), n = 4]. There was no significant difference between NACT and ACT for Distant recurrence [0.96 (0.80–1.15)], DFS [1.05 (0.95–1.15)] and OS [HR = 0.98 (0.89–1.08)], neither in preoperative nor in sandwich group.

Conclusion: No difference for DR, DFS and OS was found between preoperative and sandwich group. Preoperative chemotherapy indicated increase in the chance of BCS but at the cost of higher LRR. No conflict of interest.
Sub-group analysis was conducted on 69 cases who had full clinical data in order to identify the predictors of Miller pathological response after NAC (see table). Presence of peau d’orange (p = 0.016), >1 breast mass (p = 0.026), T4 stage (p = 0.013), TNM stage 3 (p = 0.052) showed better pathological response. Pre-menopausal females showed a trend towards better pathological response (48%, p = 0.108). Adjuvant tamoxifen and radiotherapy were more common in responder cohort (80.6%, p = 0.094 and 87.1%, p = 0.036 respectively).

### 263 Clinical factors associated with overall survival (OS) for patients with HER2-positive (HER2+) metastatic breast cancer (MBC) treated with HER2-targeting systemic therapy (HER2Tx)

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**Background:** The introduction of HER2Tx has significantly improved the objective response rate and overall survival (OS) of pts with HER2+ MBC. Although HER2+ MBC remains incurable, a meaningful minority of pts on first line HER2Tx can have a prolonged phase of disease control. Clinical factors at presentation of MBC can be associated with OS has not been fully elucidated and are not part of pts assessments at baseline.

**Material and Methods:** Data from a Departmental database of pts treated with HER2Tx for metastatic or inoperable locally advanced HER2+ BC were reviewed and retrospectively analysed. Oncomine and TCGA data on tumour pathology, first line HER2Tx administered, subsequent lines of therapy and long-term FU were included in the analysis. First and subsequent progression-free intervals and OS were calculated. This study focuses on OS data analysis.

**Results:** A total of 134 consecutive pts treated between January 2000 and June 2016 were eligible and analysed. Pts characteristics at the time of initiation of HER2Tx for MBC: median age 55yrs (range 25–83), ER/PR pos 76 (57%)/neg 47 (35%)/unknown 11 (8%), <2 metastatic sites 98 (73%)/>2 sites 36 (27%), visceral disease 85 (63%), HER2Tx+chemotherapy (CTX) 116 (86%). Median follow up is 23 months (range: 0.3–193). The proportion of pts treated for Relapsed (R) HER2+ MBC decreased significantly from the years 2000–2005 (R-MBC 83%) to 2011–2016 (R-MBC 42%), whereas DeNovo (DN) HER2+ MBC has increased significantly (DN-MBC 17% to 58%) in the same time interval. This is most likely an effect of the introduction of HER2Tx for early stage (ES) BC started routinely from 2005. Pts with DN-MBC had a longer median OS (44 months [95% CI: 29–94]) compared to R-MBC (38 months [95% CI: 23–47]). Longer OS was significantly associated with <2 sites of metastatic disease (p = 0.015), absence of visceral metastases (p = 0.048), treatment with HER2Tx+CTX (p = 0.022). On multivariate analysis, DN-MBC (p = 0.048) and <2 metastatic sites at diagnosis (p = 0.001) were associated with significantly longer OS and reduced risk of death. Within our pts cohort a disease complete response (CR) was obtained in 21 pts (16%), 16 of whom never relapsed. All of 16 durable CR received HER2Tx+CTX, <4 sites of metastatic disease and were not previously pre-treated with HER2Tx.

**Conclusions:** The introduction of HER2Tx for ESBC has significantly altered the presentation of HER2+ MBC in the last decade. Pts who present with DN-MBC, have a <2 sites of metastatic disease and no visceral involvement are more likely to achieve a prolonged OS when treated with HER2Tx in combination with CTX. These clinical factors may be used to prognosticate pts outcome and could be incorporated into clinical trials of HER2Tx.

**No conflict of interest.**

### 264 Roles of CD44 and CD24 in predicting response to neoadjuvant chemotherapy

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**Background:** Predicting the effect of the Neoadjuvant chemotherapy (NAC) in treating primary breast cancer is important in many aspects. In diagnosing with core needle biopsy, a previous study considered multiple factors using immunohistochemical staining and reported the effect of NAC on its possible prediction using a machine learning technique with an alternating decision tree (ADTree) in addition to statistical analyses (Horuguchi K et al. J Med Dent Sci 2010; 57; 165–175). In this study, we have further considered for new patients.
**Material and Methods:** Samples obtained from the core needle biopsy of patients who anticipated NAC were used. In addition to the regular examination, immunostaining with CD44 and CD 24 that are also known as breast cancer stem cell markers was conducted. During NAC, FEC (5-Fluorouracil, Epirubicin, Cyclophosphamide) followed by Docetaxel was done 4 cycles in each. In 11 human epidermal growth factor receptor 2 (HER2) positive cases, both Docetaxel and Trastuzumab were used. Based on the results from samples obtained after the surgery, the relationship between pathological therapeutic effect and the prognosis was investigated. We examined HER2 status, CD24, Stage, progesterone receptor (PgR) and CD44 as factors in applying ADTree to predict pathological response.

**Results:** 100 primary breast cancer cases that underwent NAC between August 2004 and January 2008 were investigated. The median of the patients’ ages was 54 (31−77) and the median of the follow-up period was 2.548 (411−3,396) days. During the follow-up period, 13 recurrences and 9 deaths were observed. Stages were I, II, and III with 3, 72, 25 cases respectively. There were 48 estrogen receptor (ER) positives, 27 PgR positives, and 27 HER2 positives. The effectiveness of NAC was determined by looking into the presence of pathological complete response (pCR). It was concluded that there were 26 pCR cases. There were significant correlations between pCR cases and HER2 positives (p = 0.0003); higher nuclear grade (p = 0.0105); and ER negatives (p = 0.0001). The sensitivity with the ADTree analysis in predicting pCR cases was 38.5% and the specificity was 83.8%. There was a positive relationship between CD44 and HER2 (p = 0.0474).

**Conclusions:** The study confirmed that in predicting the effectiveness of NAC, multiple factors including CD44 and CD24 were useful. The previous study did not use the Anti-HER2 treatment as part of NAC, therefore the effect has not been reflected to ADTree. In this study, out of 27 HER2 positive cases, 11 cases were treated with Trastuzumab, and of those, 7 cases were with pCR. It can be anticipated that HER2 positive cases would likely to find pCR, and a close correlation between HER2 and CD44 can be identified. Further data collection is essential to obtain more precise prediction of the treatment effects.

**No conflict of interest.**
Conclusion: The results indicate a role of Mena INV as a diagnostic marker to assess the migratory potential of transformed cells. The study identifies a novel signaling mechanism mediated by HIF-2 in regulating invasiveness and stemness characteristics suggesting that, under hypoxic conditions, some tumor cells acquire more migratory potential by increased Pan Mena and Mena INV expression along with increased stemness characteristics. This may increase the efficacy of successful local spread and metastasis, making tumor cells more aggressive. **No conflict of interest.**

318 POSTER
FAT1 knockdown led to reduce EMT and stemness genes expression in hypoxic glioma
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Introduction: Glioblastoma multiforme (GBM) is the most common and malignant of the glial tumors. Therapeutic targeting of pathways operative in GBM has had limited success and thus new targets are needed to be identified for therapeutic intervention. Our lab found oncogenic role of FAT1 gene in human gliomas. It is a transmembrane protein of 506 kDa, non-classical cadherin protein family. Our lab identified the role of FAT1 in migration/invasion as well as in regulating the expression of pro-inflamatory molecules in glioma. Since hypoxia is an integral part of GBM, Here, we analyzed the correlation of FAT1 gene expression with the expression of EMT and stemness markers in GBM under hypoxia.

Material and Methods: FAT1 and putative markers of hypoxia, EMT and stemness were analyzed at mRNA level in 31 GBM tissue samples. Correlation and cluster analysis were done using SPSS 11.5 and Cluster 3.0 softwares. U87MG and A172 glioma cell lines, increased FAT1 expression along with the expression of hypoxia, EMT and stemness markers was observed 72 hrs post-siRNA transfection.

Results: In GBM, a positive correlation of FAT1 expression with hypoxia (HIF1α, VEGF, PGK1 and CA9), EMT marker (LOX) and the stemness marker (SOX2) was observed. SPSS correlation showed an inverse relationship of GBM patient’s (N=21) survival with FAT1 expression. In U87MG and A172 cell lines, increased FAT1 expression along with the expression of hypoxia, EMT and stemness markers was observed on treatment with severe hypoxia. Upon transfection with FAT1 siRNA, we observed decreased mRNA expression of hypoxia (HIF1α, VEGF, PGK1 and CA9), EMT (Vim and LOX) and stemness markers (SOX2 and OCT4) in cells maintained under severe hypoxia.

Conclusions: Our results suggest FAT1 to be a novel molecule regulating the expression of hypoxia, EMT and stemness markers in GBM and FAT1 may emerge as a target for therapeutic intervention. **No conflict of interest.**

320 POSTER
Role of glossopharyngeal nerve block in palliation of pain from head and neck cancer
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Background: Pain is most troublesome feature in advanced or recurrent Head and Neck cancer. Carcinoma of Tongue, Buccal Mucosa, Central arch region, Alveolobucal region often present in advanced stage where cure is not possible even with multidisciplinary management. In these scenarios palliation of symptoms remains one of the goals of treatment. As these patients had difficulty in deglutition and compliance of oral analgesics is poor therefore an alternate mode of analgesia is required. Glossopharyngeal nerve block produces effective palliation of pain and adds to the quality of life to the patients.

Material and Methods: During past two year 46 patients were managed by Glossopharyngeal nerve block for the management of pain in head and neck region for carcinoma of head and neck. 30(63.62%) Patients were having carcinoma buccal mucosa, 15 (32.60%) patients were having carcinoma Tongue and 1(2.17%) patient had carcinoma central arch region. 2.5 ml of 0.5% Bupivacaine was injected to confirm the position of the nerve with respect to needle and 4ml of 50% lignocaine was used to block Glossopharyngeal nerve near tip of styloid process.

Results: 26 (56.52%) patients were blocked in single attempt 19 (41.30%) patients’ required two attempts and one patient required three attempts to block the nerve. Patients felt pain relief after nerve block and were able to swallow without pain and were able to eat. Pain relief was adequate till 4 weeks in 10 (21.73%) patients 3 to 4 weeks in 26 (56.52%) patients, 2–3 weeks in 9 (19.56%) patients and less than 1 week in 1 (2.17%) patient.

Conclusion: Glossopharyngeal nerve block is an effective method to treat pain in advanced head and neck carcinoma **No conflict of interest.**
Management of symptomatic paediatric vertebral haemangiomas by an innovative technique

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Background: Paediatric vertebral haemangiomas (VH) are exceedingly rare benign and highly vascular tumours of spine. Purpose of study was to evaluate the outcome of patients with single level vertebral haemangioma presenting with myelopathy treated by laminectomy + alcohol embolization + instrumentation.

Materials and Method: Twelve patients (mean age 14.85 years, range: 10–17 years; 8 females and 4 males) were treated using laminectomy + alcohol embolization + instrumentation from December 2004 to June 2016. Demographical, clinical, radiological, operative details and postoperative events were retrieved from hospital records. Outcome was assessed using modified ASIA score and U118MG, were used for in vitro analysis of NSC-745887 effects on tumor metabolism and size by using animal positron emission tomography (animal-PET). Cell viability was measured by MTT assay.

Result: Myelopathy was present in all patients. The pre-operative ASIA score was A in 7, B in 2, C in 2 and D in 1 patient. All had pain vertebral body VH with severe cord compression in thoracic region on imaging study. Immediate embolization was achieved in all patients, which made laminectomy and soft tissue haemangioma removal relatively easy. Post-surgery, at mean follow up of 38.82 months all patients showed improvement in power. ASIA score was E in 8, D in 1, C in 2 and B in 1 at last follow up.

Conclusion: Present study is largest series of paediatric symptomatic VH. This procedure of laminectomy + alcohol embolization + instrumentation is safe, efficient method to treat symptomatic VH with severe cord compression with good results. No conflict of interest.

Surgical outcome of microsurgical excision of brain and spinal cord cavernomas: Our 13 year single center experience

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Background: These are rare lesions of brain and spinal cord. Cavernoma causes morbidity and mortality due its mass effect on surrounding structure or due to effect of hemosiderin and other blood components on it. Various treatment options like conservative management, radiosurgery and microsurgical excision are available for treating these lesions but there are no clear guidelines available. Objective of this study was to analyze the outcome of microsurgical excision of central nervous system cavernomas.

Material and Method: All patients with brain and spinal cord cavernoma, who were treated with microsurgical excision at AIIMS hospital between 2001 and 2013 period, were included in the study and their case records, imaging details and follow up data retrieved retrospectively from the hospital database.

Results: Total 135 patients were enrolled in the study that underwent surgical excision. Patients were ranged between 3 to 66 years. Around 75% of patients were male. 120 patients had cavernoma in brain with involvement of supratentorial compartment in 63.3% patients and 15 patients had spinal cavernoma. 44 patients had cavernomas in infratentorial location. Frontal lobe was most commonly involved in supratentorial cavernomas while most of infratentorial cavernomas were present in Pons. Seizure (68%) was most common presentation in supratentorial cavernomas followed by neurodeficit while most of brainstem cavernomas had motor and cranial nerve deficit on admission. 43.7% of brain stem cavernomas patients had history of clinically significant hemorrhage compared to 18.4% of supratentorial cavernomas. Various common surgical approaches were used according to the location of cavernoma and intraoperative adjuncts like neuronavigation, ultrasound, eccocitography etc. were used for better lesion localization. Outcome was assessed using Engel score for supratentorial cavernoma with Seizures, glasgow outcome scale for brain cavernoma and McCormick outcome scale for spinal cord cavernoma. All the patients presenting with seizure had relief in the seizure including 96.1% patient achieving Engel score I. Overall neurodeficit improved in 88.3% patients. However 5.1% patient developed new onset neurodeficit including 3 patients who died in post operative period due to poor preoperative neurological condition.

Conclusion: We conclude that aggressive approach with microsurgical excision of cavernoma is associated with excellent outcome with acceptable morbidity and mortality with the use of routine common surgical approaches. No conflict of interest.

Poster Session, Sunday 29 January 2017 Abstracts S47

Objective arguments for discussions between care teams on the quality of neurosurgical care for patients with a glioblastoma.

No conflict of interest.

NSC-745887, a novel small molecule, modulates Dcr3 and ATM signalings in brain cancer

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Background: NSC-745887 is a novel small compound derived from the antheraquinone, which have been reported to have anticancer effects. However, the anticancer effects of NSC-745887 and antheraquinoine have never been investigated in brain cancer. The aims of this study was to investigate whether NSC-745887 has specific cytotoxic activity in cultured human glioblastoma cells and in growing glioblastoma in mice, and to analyze whether some biomolecules are the involved in the underlying mechanism. Furthermore, we examined the effects on glioblastoma growth in vivo.

Material and Methods: Human glioblastoma cell lines, including U87MG and U118MG, were used for in vitro. analysis of NSC-745887 effects on cell viability, cell-cycle arrest and apoptosis, while nude mice bearing xenograft of the tumor cells were used for in-vivo analysis of NSC-745887 effects on tumor metabolism and size by using animal positron emission tomography (animal-PET). Cell viability was measured by MTT assay, DNA fragmentation, cell cycle arrest, mitochondrial membrane potential change and apoptosis were labelled with fluorescent tracers or antibodies, and followed by measured with flow cytometry. Un-phosphorylated and
phosphorylated proteins were quantified by immunoblot analysis. Tumors in animals were labelled with $^{18}$F-fluorodeoxyglucose (FDG), and imaged by animal-PET.

**Results:** We found that NSC-745887 exerted antitumor activities on cell cycle through DNA damage by activating pH2AX, ATM/ATR and CHK1/CHK2 phosphorylation. The cell cycle-related proteins including cyclin A, cyclin D, CDK2, CDK4 and CDK6 were regulated to promote G1 and S phase arrest. The apoptotic-protein such as p53 and caspase-3, were activated after NSC-745887 treatment for 24 hours. However, NSC-745887 also repressed DCR3 expression and encouraged Fas/FasL signaling. In our animal model, administration of NSC-745887 reduced the standard uptake value (SUV) of $^{18}$F-FDG and tumor volume in nude mice bearing with U118MG cells.

**Conclusions:** NSC7–45887 can repress glioblastoma growth and may provide the potential of NSC-745887 to target therapies for human malignant gliomas.

**No conflict of interest.**
Gastrointestinal Malignancies – Colorectal Cancer

Two countries – two treatment strategies for rectal cancer

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Background: Trials have shown that radiotherapy (RT) or chemoradiotherapy (CRT) decreases local recurrence rates, whereas the effects on survival are uncertain except in the most locally advanced cases. Sweden and Norway had different treatment recommendations. The two countries have population-based rectal cancer registries. The purpose was to compare local recurrence rates and survival in the two countries.

Material and Methods: Between 1995 and 2012 all rectal cancer patients registered in the national quality registries in Sweden and Norway were included. Patient characteristics, stage, radiotherapy and surgery, recurrence, metastases, and survival were analyzed.

Results: In total, 29029 Swedish and 15456 Norwegian patients were analyzed. RT was given to 49% of patients in Sweden and 26% in Norway. In Sweden, no major changes in the proportion irradiated were observed, most patients received short-course RT, long-course (CRT) was given to 10-15%. In Norway, an increase in radiotherapy from about 10% in 1996 to 40% in 2012 was observed, most patients were given long-course (CRT). Survival improved in both countries during the time period, and there was no difference in survival between countries. Patients with stage I-II disease who underwent major radical surgery (18541 in Sweden and 10421 in Norway) were further analyzed. Local recurrence rates were initially lower in Sweden (about 8%) than in Norway (about 12%) whereas they were equally low (4%) in both countries during the latter time period. About 20% of patients in both countries developed distant metastases within 5 years. The 5-year relative survival after curative resection increased in both countries from about 77% in 1996 to about 81% in 2009.

Conclusions: Two entirely different approaches to preoperative radiotherapy in rectal cancer, mostly preoperative short-course RT to every other patient in Sweden and selective preoperative CRT to initially very few followed by an increase towards 40% in Norway, resulted in similar survival. Local recurrence rates were initially lower in Sweden, but were in later years similar at a very low level of 4%. This opens for discussions regarding the optimal RT rate and technique. The quality of rectal cancer care is at a very high international level in both countries.

No conflict of interest.
Conclusions: Significant correlation between the numbers and type of intratumoral T-cells to those in pre-surgical blood was found. Whether T-cell count could be a useful tool to stratify immunestatus in patients with CRC using “liquid biopsies” rather than tissue analyzes warrants further investigation.

References

No conflict of interest.

382 Nationwide survey on patients' and professionals' expectations on prognosis of metastatic colorectal cancer (mCRC)

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Background: Accurate understanding of illness, prognosis and treatment effect enables discussions of benefits and harms of treatments with patients, and them to make informed decisions. The use of new biological agents (BAs), may have changed the perception of mCRC and its prognosis.

Methods: As part of a nationwide study the survey included all University and Central Hospitals with cancer centers in Finland. The questionnaire was delivered during a two-week period to all patients visiting these centers, and their personnel. Background information included sex, age and education for all, and in addition, marital and working status, and type and stage of cancer for patients. Patients were asked if they had received accurate information on their cancer and treatment objectives. There were 4 given potential options for mCRC: curative, survival gain (sg) years, sg months, or no sg but relief of symptoms. Estimates for the benefits and harms of biological agents were asked.

Results: 291 professionals (31% doctors and 69% nurses) and 1879 patients (19% CRC, 78% other cancers, 3% unknown) responded. Of patients 86% felt they had received accurate information, 5% did not, and 8% did not know. 90% answered they understood the objective of their treatment, 8% did not, and 2% did not answer. 82% of professionals, 75% of all patients, 92% of CRC patients and 93% of mCRC patients responded that treatment of mCRC is either curative or sg is years (P<0.0005), whereas 17%, 2%, 1% and 1%, respectively, estimated sg to be months.

The gain using biological agents were estimated to be great or moderate by 94%, 68%, 77% and 82%, respectively. 27% of all patients, 15% of CRC, and 11% of mCRC patients did not answer the question. 13% of professionals considered the harm of treatment to be potentially serious, whereas <1% of all and 0% and 3% of CRC and mCRC patients did.

Conclusion: Both professionals and patients overestimate the treatment effect and underestimate the potential harms. Patients who have been informed on mCRC treatment (mCRC patients) overestimate the most. Perception of mCRC and its prognosis does not reflect reality and patients treated for it do not get accurate information or do not understand it. No conflict of interest.

Poster Session (Saturday 28 January 2017)

Gastrointestinal Malignancies – Colorectal Cancer

433 POSTER

The results of neoadjuvant chemoradiation therapy in combined treatment of rectal cancer

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Background: Improve long-term results of treatment of resectable rectal cancer stage I-III through the optimization scheme of neoadjuvant chemoradiation therapy.

Materials and Methods: The study of the efficacy of the developed neoadjuvant chemoradiation protocol for preparation of treatment of the ileocaecal area and with the use of frequent large-fraction radiotherapy SD 5gr, Cumulative dose 25gr conducted in patients receiving capcitabine at a dose of 1700mg/2 during the entire course of radiation therapy, local intracavitary microwave hyperthermia 3, 4 and 5 days, and a course of metronidazole intracavitary administration radiosensitizing mixture consisting of 3 or 5 days of the course. The treatment included Study group: 53 patients with resectable rectal cancer (LFTR + CT + microwave hyperthermia + metronidazole). The Control group included 54 patients with resectable rectal cancer who receive the standard neoadjuvant large-fraction radiotherapy (LFTR). After a neoadjuvant treatment, all patients were operated in a radical amount within 5–7 days.

Results: Evaluation of the composition of the study and control groups of patients showed their complete identity for the main prognostic features. In the study group, postoperative complications were seen in 5 (9.4%) cases in the control group, which held LFRT postoperative complications were seen in 6 (11.1%) cases, respectively. The use of preoperative large-fraction radiotherapy in patients receiving capcitabine, microwave hyperthermia and metronidazole has increased the 5-year survival rate of up to 69.8% compared with the control group, received LFTR, where 5-year survival rate was 61.5%, respectively. The incidence of local recurrence was 2.2%, and the frequency of distant metastases of 5.6% in the study group and the control group of local recurrence rate of 2.6%, and distant metastasis rate of 11.6%.

Conclusions: The preoperative treatment method using (LFTR + CT + microwave hyperthermia + metronidazole) in the combination therapy of resectable rectal cancer does not affect the incidence of postoperative complications and increases the performance of 5-year survival compared with those receiving standard neoadjuvant large-fraction radiotherapy.

No conflict of interest.

434 POSTER

Colorectal cancer and its awareness

A. Fatima1, S.S.A. Zaidi1. 1Fatima Jinnah Medical University; MBBS, Lahore, Pakistan

Objective: To promote awareness regarding increased occurrence of colorectal cancer in younger population and its clinical and pathological features compared to older patients.

Methods: The cross-sectional study was conducted from February 2014 to January 2016 on patients with diagnosis of colorectal carcinoma admitted through emergency or outpatients in Sir Ganga Ram Hospital Lahore. Data regarding age, gender, presentation, site of tumor, surgery performed and Dukes staging was collected and analyzed.

Results: A total of 23 patients were operated during the study period: 13 (56.52%) males and 10 (43.47%) females. Of them 12 (52.17%) were below the age of 40 years, while 3 (13.04%) patients were in the 11-20 age group. In 7 (30.43%) patients, tumor was unrespectable at the time of presentation so a palliative procedure (diversion colostomy or ileostomy) was performed. There was a higher proportion of younger patients with metastatic disease at the time of presentation (n=9; 75%) while 10 out of 12 patients in the younger age group (83.3%) had a tumour of left colon, particularly rectum.

Conclusion: Although colorectal cancer is usually a disease of older patients, it is increasingly becoming more common in younger population. Data suggests a leftward distribution for colorectal carcinoma and that younger patients present with more advanced disease and poorer prognosis. No conflict of interest.
Comparison of expectations between medical oncologists (MO) and hepatobiliary surgeons (HS) regarding the indications for liver metastasectomy

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1Cross Cancer Institute – University of Alberta, Medical Oncology, Edmonton- Alberta, Canada; 2Princess Margaret Cancer Centre, Surgical Oncology, Toronto, Canada; 3University of Alberta, Medicine, Edmonton, Canada; 4Cross Cancer Institute – University of Alberta, Experimental Oncology, Edmonton- Alberta, Canada; 5 BC Cancer Agency Vancouver, Medical Oncology, Vancouver, Canada

Background: Resection of liver metastases is curative for specific patients with advanced cancers. There is increasing aggressiveness in the use of metastatic resections, but guidelines describing appropriate indications for metastasectomy are lacking or obsolete in the era of novel systemic therapies and advanced surgical techniques. We compared expectations of MO vs HS in the management of liver metastases from colorectal cancer (CRC).

Methods: MO and HS across Canada were surveyed to evaluate their criteria to determine resectability of liver metastases, their current access to and availability of multidisciplinary care, and their views regarding imaging in guiding management of these complex patients.

Results: Of 220 experts surveyed, 145 (66%) responded of whom 137 (95%) had received specialized training in oncology. Among them, 109 (75%) reported the lack of institutional criteria to determine resectability of liver metastases while only 37 (26%) indicated that they had access to multidisciplinary tumor boards and clinics. MO and HS disagreed in terms of absolute contraindications (CI) for liver metastasectomy. For example, MO were more likely to consider significant liver parenchymal involvement, proximity to major vessels, and poor performance status as absolute CI compared to HS. MO also more often considered liver parenchymal involvement in a bilobar pattern and as a single lesion. Likewise, there were notable discrepancies between physicians with respect to the types of clinical or radiographic findings that would modify their perspectives on resectability.

Conclusion: The proposed preoperative HART with co-administration of two cycles of 5FU had acceptable toxicity profile and provided satisfactory rate of ypCR. This created rationale to initiate a phase III randomized study that was registered under ClinicalTrials.gov Identifier: NCT01814969.

No conflict of interest.

Poster Session, Saturday 28 January 2017

Abstracts

S51

Poster Spotlight

Comparison of expectations between medical oncologists (MO) and hepatobiliary surgeons (HS) regarding the indications for liver metastasectomy

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1Cross Cancer Institute – University of Alberta, Medical Oncology, Edmonton- Alberta, Canada; 2Princess Margaret Cancer Centre, Surgical Oncology, Toronto, Canada; 3University of Alberta, Medicine, Edmonton, Canada; 4Cross Cancer Institute – University of Alberta, Experimental Oncology, Edmonton- Alberta, Canada; 5 BC Cancer Agency Vancouver, Medical Oncology, Vancouver, Canada

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No conflict of interest.
context, the likelihood of the evaluation of a patient in a MDT meeting is clearly related to the prognosis and surgical complexity. MDT assessment is not established because of limited number of reported cases. We reviewed the treatment results of preoperative chemoradiotherapy (CRT) and combination 5-fluorouracil (5FU) + Oxaliplatin for locally advanced rectal cancer with LPLNM.

Material and Methods: Between 2006 and 2013, eighteen patients with LPLNM from low rectal adenocarcinoma underwent preoperative CRT. All patients have clinical stage T3–4 tumor with LPLNM (short diameter 10mm or more with a high resolution MRI) were treated with oxaliplatin (50 mg/m², weekly for 5 weeks) and continuous infusion 5FU (225 mg/m²/day, 5-week infusion) and radiotherapy (RT). The preoperative pelvic RT schedules total 50.4 Gy/28 fractions. Radical resection was performed four to eight weeks after the end of CRT.

Results: There were 9 men and 9 women with a median age of 48 (14–67) years. A median distance between the anal edge of tumor and the anal verge was 3 (0–5) cm. Stages of primary tumor were cStageIIb or more. One patient experienced grade 3 neutropenia. Response rate after CRT were 83% (CR 3, PR 12, PD 3). Fifteen patients were performed surgery, fourteen patients were complete resection (APR 8, LAR 3, TPE 2, ISR 1), one patient experienced exploratory laparotomy. All complete resection patients underwent radical lateral pelvic lymph node dissection. Histologic diagnosis included adenocarcinoma in 14 cases, T-stages of tumor were ypT0 in 3 patients, ypT2 in 3, ypT3 in 7 and ypT4 in 1. N-stages of tumor were ypN0 in 4 patients, ypN1 in 3, ypN3 in 7. Six patients had negative pathological lateral pelvic lymph node metastasis. All patients had negative surgical resection margin. Median follow-up of the all patients was 44 months, eight patients developed recurrence. The initial site of recurrence included the lung in 4 patients, the liver in 2, the para-aortic lymph node in 1.

Conclusion: Radical resection after CRT for advanced rectal cancer with LPLNM, may be effective for local excellent control and prolonging survival. Contrameasures for lung metastasis are necessary. Intensive preoperative CRT may suggest the possibility of prolongation of overall survival.

No conflict of interest.

440

OUTCOMES OF PREOPERATIVE CHEMORADIOThERAPY FOR RECTAL CANCER WITH LATERAL PELVIC LYMPH NODE METAStASIS

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Background: Clinical picture of lateral pelvic lymph node metastasis (LPLNM) from rectal adenocarcinoma is unclear and treatment strategy is not established because of limited number of reported cases. We reviewed the treatment results of preoperative chemoradiotherapy (CRT) and combination 5-fluorouracil (5FU) + Oxaliplatin for locally advanced rectal cancer with LPLNM.

Material and Methods: Between 2006 and 2013, eighteen patients with LPLNM from low rectal adenocarcinoma underwent preoperative CRT. All patients have clinical stage T3–4 tumor with LPLNM (short diameter 10mm or more with a high resolution MRI) were treated with oxaliplatin (50 mg/m², weekly for 5 weeks) and continuous infusion 5FU (225 mg/m²/day, 5-week infusion) and radiotherapy (RT). The preoperative pelvic RT schedules total 50.4 Gy/28 fractions. Radical resection was performed four to eight weeks after the end of CRT.

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Conclusion: Radical resection after CRT for advanced rectal cancer with LPLNM, may be effective for local excellent control and prolonging survival. Contrameasures for lung metastasis are necessary. Intensive preoperative CRT may suggest the possibility of prolongation of overall survival.

No conflict of interest.
Institut J. Bordet, Surgery, Brussels, Belgium; 2Institut J. Bordet, Statistics

G.Liberale1, S. Vankerckhove2, M. Gomez Galdon3, B. Ahmed2,

Materials and Methods: Retrospective analysis of our homogeneous series of PSS from 2003 to 2015. PSS used all type of resectionsRefeeding low HL and intraoperative ablation (IOA), favoring one-stage.

Results: 387 patients underwent a PSS. 328 patients received a median of 12 cycles of oxaliplatin or irinotecan with targeted therapies for half of them. Resection was major in 128 patients, combined with IOA in 137 patients and IOA was alone in 50 cases. 38 patients had a portal vein obliteration by strict necessity. The 5-years overall survival was 50.3%. 78 of 9 pre-operative cycles of oxaliplatin or irinotecan with targeted therapies.

G.Liberale1, S. Vankerckhove2, M. Gomez Galdon3, B. Ahmed2,

Conclusion: At the opposite of non-parenchymal sparing surgeries, preoperative chemotherapy does not impair PSS and must be considered to be part of the concept, a multidisciplinary, soft and iterative procedure.

No conflict of interest.

442 POSTER DISCUSSION

Near infrared fluorescence imaging after intraoperative injection of indocyanine green to improve the staging during cytoreductive surgery for peritoneal carcinomatosis of colorectal origin: results of a pilot prospective study (NCT02032485)

G. Liberale1, S. Vankerckhove2, M. Gomez Galdon3, B. Ahmed2,

Patients and Methods: Patients with CRC from PSS admitted for study and the decision taken after the multidisciplinary discussion. Proposals were recorded as similar, different but acceptable and inappropriate. The proportion of decision modifications related to the MDM approach was recorded. Implementation of different decisions was registered.

Results: One hundred seventy-four patients were presented to the MDM. All patients with GI cancer, leading to a modification of the therapeutic management plan in 39% of the cases and avoiding inappropriate decisions in 18% of patients. MDMs clearly increase the proportion of guidelines directed decisions. MDM decisions were followed by therapeutic implementation in 93% of patients.

No conflict of interest.

443 POSTER DISCUSSION

Evaluating the scientific basis of quality indicators in colorectal cancer care: results of a systematic review

L. Keikes1, C. Punt1, P. Tanis1, M. Koopman2, V. Lemmens3,

Material and Methods: All patients with GI cancer presented at the GI-MDM were included in this study for a period of 6 months. The MDM included at least 4 physician specialists (medical-, radiation-, and surgical oncologist, a radiologist and a pathologist). Before discussion, the doctor responsible for the patient suggests what he thought to be the most appropriate treatment. Those propositions were collected before and/or during the meeting and compared to the decision taken after the multidisciplinary discussion. Proposals were recorded as similar, different but reasonable, or considered as inappropriate. The proportion of decision modifications related to the MDM approach was recorded. Implementation of different decisions was registered.

Results: One hundred seventy-four patients were presented to the MDM. All patients with GI cancer, leading to a modification of the therapeutic management plan in 39% of the cases and avoiding inappropriate decisions in 18% of patients. MDMs clearly increase the proportion of guidelines directed decisions. MDM decisions were followed by therapeutic implementation in 93% of patients.

No conflict of interest.
Clinical impact of MRI vs computed tomography in the diagnostic work-up of colon cancer patients

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Background: Traditionally, colon cancer patients are mainly staged with CT. However, MRI is superior to CT for detecting hepatic disease. Preliminary reports indicate that MRI is able to stage colon tumors and as such may replace CT for integrated local and liver staging. Aim of this study was to evaluate the clinical impact of replacing CT for MRI in abdominal staging of colon cancer patients.

Materials and Methods: Thirty colon cancer patients were included: 10 underwent abdominal CT (including 4-phase liver scan) and 30 patients underwent abdominal MRI (including 4-phase liver sequences and DWI). Both groups were retrospectively assessed regarding primary tumor stage, presence of liver metastases and whether additional imaging was needed in case of inconclusive results. Histology and clinical/imaging follow-up was the reference standard.

Results: All colon tumors(100%) were detected and could be staged in both groups. 43/30 patients in the CT-group and 3/30 in the MRI-group presented with liver metastases at primary staging; 2 additional patients from the CT-group developed metastases within 1 year (versus none in the MRI-group). In the CT-group 8/30(27%) had inconclusive results concerning hepatic disease; in 5/8 patients additional imaging was performed in the MRI group no inconclusive results occurred and no additional imaging was needed.

Conclusion: Simultaneous staging of hepatic disease and the colon tumor with MRI is feasible and has a clear clinical impact. As such MRI could become a valuable integrated staging tool for colon cancer.

No conflict of interest.

445 POSTER DISCUSSION

Long-term follow-up features on rectal MRI during a 'watch-and-wait' approach in clinical complete responders after chemoradiotherapy: an update of 140 patients

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Background: Non-operative treatment with stringent follow-up (watch-and-wait) is emerging as an alternative to surgical resection in rectal cancer patients that show a clinical complete response after chemoradiotherapy. An important question is how (frequently and with what modalities) to monitor patients once surgery is omitted. In addition to clinical examination and endoscopy, imaging – mainly MRI – plays an important role. Given the novelty of the watch-and-wait approach, limited data exists yet on what we can expect to see on MRI during long-term follow-up after chemoradiotherapy. A small pilot study described various patterns of a complete response during watch-and-wait in a group of 19 patients (Lambregts et al. Diseases of the Colon and Rectum 2011).

Aim of this study was to follow-up on this previous study in a larger patient cohort and describe the morphology of the rectal wall in patients with a complete response after chemoradiotherapy and study the evolution in rectal wall morphology during long-term clinical follow-up in these patients.

Materials and Methods: A total of 140 patients with a sustained complete response (i.e. no evidence of recurrence on sequential imaging and endoscopy +/- biopsy examinations) were analysed during long term follow-up within the scope of a ‘watch-and-wait’ protocol. Patients underwent MRI (as well as corresponding clinical examination and endoscopy) 3-monthly in the first year, 6-monthly during the second year to fifth year. Two readers in consensus analysed the rectal wall morphology on the initial post-chemoradiotherapy scan and studied the evolution in morphology on the various sequential follow-up MRIs.

Results: Median follow-up time was 18 months (range 6-82). A total of 801 MRIs was analysed (median 5, range 2-13/patient). In 9% of patients the rectal wall completely normalised post-CRT. The other 91% showed a fibrotic remnant (64% minimal fibrosis limited to the bowel wall; 21% thickened fibrotic wall and 6% irregular fibrosis). Histology and clinical/imaging follow-up showed that residual fibrosis remained unchanged during long-term follow-up, in 4% initial fibrosis later developed into a normalised wall, in 4% the fibrosis slightly thickened (without evidence of recurrence).

Conclusions: In the vast majority of patients with a complete response residual fibrosis is present post-CRT, which remains unchanged during long-term follow-up in almost all patients. A completely normalised wall is observed in approximately 1 out of 10 complete responders. These findings may serve as a reference and provide teaching for radiologists involved in the clinical follow-up of patients selected to undergo a watch-and-wait policy.

No conflict of interest.

447 POSTER

Safety of bevacizumab versus no-bevacizumab treatment used on metastatic colorectal cancer: a systematic review and metaanalysis

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Background: Biologic agents are widely used in the treatment of metastatic colorectal cancer (mCRC) and has achieved variable results.

Aim: Evaluate safety of bevacizumab (a monoclonal antibody that binds to vascular endothelial growth factor - VEGF) versus no-bevacizumab therapies (include Chemotherapy alone and/or other monoclonal antibodies, in patients with advanced colorectal cancer).

Methods: We performed a systematic review and metaanalysis of observational cohort studies based on PRISMA recommendations. The research was made on MEDLINE/Pubmed, LILACS, COCHRANE Library and EMBASE, including search on literature by hand searching (until march 2016). The Newcastle-Ottawa scale was used to evaluate the observational studies methodological quality. The outcome measures were safety/severe adverse events.

Results: Sixteen OCS (Observational Cohort Study) were selected. The quality of the evidence on the question was considered moderate and data from seven studies were included in this meta-analysis. The treatment with bevacizumab was, in general, more toxic. Severe adverse events related to comparative group included hypertension, gastrointestinal perforation, bleeding, diarrhea, neutropenia and thromboembolic events (Table 1). Metaanalysis results showed that: Bevacizumab was associated with an increased risk of gastrointestinal perforation and hypertension, was not statistically significant, compared to no-Bevacizumab group.

Table 1: Comparison: Bevacizumab vs no-Bevacizumab – Outcomes: severe adverse events

<table>
<thead>
<tr>
<th>Outcome/Adverse Event</th>
<th>Comparison Group</th>
<th>Participants</th>
<th>Effect size estimate</th>
<th>I2 (%); [95% CI]; p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Bevacizumab</td>
<td>2436</td>
<td>1.36</td>
<td>2% [0.90, 1.58]; 0.36</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>183</td>
<td>1.09</td>
<td>1.00 [0.63, 1.58]; 0.81</td>
</tr>
<tr>
<td>Arterial thrombembolism</td>
<td>Bevacizumab</td>
<td>2948</td>
<td>0.89</td>
<td>0% [0.17, 2.31]; 0.40</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>302</td>
<td>0.85</td>
<td>0% [0.49, 1.73]; 0.15</td>
</tr>
<tr>
<td>Venous thrombembolism</td>
<td>Bevacizumab</td>
<td>4009</td>
<td>0.97</td>
<td>0% [0.17, 2.31]; 0.40</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>391</td>
<td>0.91</td>
<td>0% [0.49, 1.73]; 0.15</td>
</tr>
<tr>
<td>Gastric intestinal perforation</td>
<td>Bevacizumab</td>
<td>5182</td>
<td>1.89</td>
<td>17% [0.90, 3.59]; 0.01</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>408</td>
<td>1.51</td>
<td>17% [0.90, 3.59]; 0.15</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Bevacizumab</td>
<td>2436</td>
<td>1.62</td>
<td>43% [0.68, 3.87]; 0.17</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>371</td>
<td>1.07</td>
<td>31% [0.17, 3.13]; 0.17</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Bevacizumab</td>
<td>371</td>
<td>0.63</td>
<td>0% [0.17, 3.13]; 0.17</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>371</td>
<td>0.56</td>
<td>0% [0.17, 3.13]; 0.17</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Bevacizumab</td>
<td>371</td>
<td>1.19</td>
<td>0% [0.17, 3.13]; 0.17</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>371</td>
<td>1.08</td>
<td>0% [0.17, 3.13]; 0.17</td>
</tr>
<tr>
<td>Other events</td>
<td>Bevacizumab</td>
<td>4176</td>
<td>1.46</td>
<td>29% [0.64, 3.32]; 0.24</td>
</tr>
<tr>
<td></td>
<td>No-Bevacizumab</td>
<td>4176</td>
<td>1.56</td>
<td>29% [0.64, 3.32]; 0.24</td>
</tr>
</tbody>
</table>

Net. Heterogeneity: Source: RCM/illan 5.3 modifications

Conclusion: Bevacizumab group was associated with more adverse events than without Bevacizumab, demonstrated in this studies.

No conflict of interest.
Poster Session, Saturday 28 January 2017

Abstracts S55

Supported by FAPEMIG – Fundação de Amparo à Pesquisa de Minas Gerais, Brazil.

No conflict of interest.

448

POSTER

The Prospective Dutch ColoRectal Cancer cohort (PLCRC) – a prospective nationwide observational cohort study

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Background: While diseases like colorectal cancer were once seen as a single disease, there now exist multiple molecular subclasses. This has implications for treatment and hampers feasibility of prospective clinical trials, which require large sample sizes. With currently less than 10% of all cancer patients being enrolled in clinical trials, innovative alternatives are urgently required. Prospective observational cohort studies can provide standardized and validated collection of clinical data, tissue and blood samples and patient-reported outcome measures, and can serve as an infrastructure for registry based trials with improved recruitment.

Methods: All patients >18 years with histologically proven colorectal cancer are asked to participate. The informed consent includes consent for systematic collection of long-term clinical follow-up data. Optional consent is given for: 1) filling out patient-reported outcome questionnaires; 2) standardized collection of tissue and blood samples; 3) being informed when clinically relevant DNA mutations are detected and 4) invitation for future interventional studies according to (amongst others) the cohort multiple randomized controlled trial design. This design allows patients to participate in multiple non-conflicting interventional clinical trials. PLCRC is set up in close collaboration with other national data collection initiatives, including the Netherlands cancer registry (hosted by IKNLS), the national pathology registry PALGA, the national biobanking infrastructure BBMRI-NL, and the Dutch Surgical Colorectal Audit (DSCA).

Results: Currently 11 centers are open for inclusion, more than 850 patients have been included in PLCRC, and a total of 10 studies are using the PLCRC infrastructure. In the second half of 2016, at least 10 more centers will open. Of the included patients, 85–90% have consented to receive questionnaires, to be approached for future trials and to be informed about DNA mutations. More than 95% of patients have given consent for the collection of tissue and extra blood samples.

Conclusions: PLCRC is expected to provide long-term clinical data, tissue and blood samples, and patient-reported outcome measures of a large cohort of patients with colorectal cancer. PLCRC is well received by patients with the great majority giving consent for all options in the consent form. The available data and material will facilitate basic, translational and clinical research.

Conflict of interest: Corporate-sponsored Research: PLCRC is supported by Bayer, Lilly, Merck, Roche, Servier, Sirtex.

449

POSTER

Ways to improve long-term results of combined treatment of patients with colorectal cancer liver metastases

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Background: Choice of treatment tactics in patients with metastatic colorectal cancer (CRC) is ambiguous and depends on clinic’s capabilities and standards that determine the need of optimal model of treatment for such patients. Study evaluated possibility of complete (R0) resection in patients with CRC liver metastases after preoperative chemotherapy.

Material and Methods: Study enrolled 139 patients with CRC liver metastases treated in surgical department of abdominal oncology from January 2013 to September 2015: 100 patients had synchronous metastases and 39 patients had metachronous metastases. 37 patients (26.6%) underwent preoperative 3–12 cycles of FOLFIRI/FOLFOX. 102 patients due to complicated primary tumor or contraindications to chemotherapy underwent surgical treatment as first step.

Results: Multiple lesions (more than three) occurred significantly more frequently in patients with synchronous liver mets than in metachronous: 52.9% and 26.1%, respectively, p<0.005. Preoperative chemotherapy performed in 12 patients with metachronous lesions, objective response was observed in five patients (41.7%); 27 patients with metachronous lesions (69.2%) underwent R0 surgical treatment. 25 patients with synchronous metastases underwent preoperative chemotherapy with 14 patients (56.0%) achieved an objective response. R0 resection after neoadjuvant chemotherapy was performed in 10 of 22 operated patients received preoperative chemotherapy (45.5%). 80 patients with synchronous disease (57.6%) due to complicated primary tumor underwent surgery as first step; RO managed only in 21 patients (26.3%). Resectability in patients with metachronous metastases was 69.2%, in patients with synchronous metastases it was only 26.3%. 3-year survival was 15% in group with metachronous metastases and nobody of patients with synchronous survived the 3-year mark (p<0.06). Survival of patients with 3 or more lesions was significantly less than in patients with 1–2 lesions: 1-year survival was 67% and 92% and 2-year survival 54% and 82%, respectively, (p<0.004).

Conclusions: R0 resection is possible in 45.5% of CRC patients with synchronous liver disease after neoadjuvant chemotherapy and only in a quarter of patients (26.3%) if surgery is first step of treatment. Time of occurrence and number of liver metastases are independent prognostic factors.

No conflict of interest.

450

POSTER SPOTLIGHT

The International Watch and Wait Database (IWWD) for rectal cancer, an update

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Background: In 2014 the International Watch-and-Wait Database (IWWD) for rectal cancer was established under the umbrella of EURECCA and the Champalimaud Foundation. The main goal of this database is to collect all available data to expand knowledge on the benefits, risks and oncological safety of organ preserving strategies in rectal cancer [Beets, ESJO 2015 41(12): 1562–4]. In April 2015 the database was opened for retrospective and prospective data registration.

Methods: An international multicentre observational study. Data was collected by participating centres and stored in a highly secured NEN7510 certified and encrypted research data server. Each centre always retains full ownership of their data.

Table 1. Data for 679 patients with clinical complete response

| Gender | Male | 449 (66%) |
| Age | Mean | 63.8 years |
| BMI | Mean | 26.7 kg/m² |
| Imaging | Endo/rectoscopy | 598 (87%) |
| MRI | 434 (64%) |
| ERUS | 42 (6%) |
| CT-pelvis | 172 (25%) |
| Stage baseline | cT1 | 13 (2%) |
| cT2 | 146 (28%) |
| cT3 | 335 (64%) |
| cT4 | 27 (5%) |
| N stage baseline | cN0 | 208 (40%) |
| cN1 | 185 (35%) |
| cN2 | 132 (25%) |
| M stage baseline | M0 | 635 (99%) |
| M+ | 8 (1%) |

Results: In August 2016 the database included 775 patients from 11 countries and 35 participating institutes. 90% of all patients were included because of a clinical complete response (n = 679). All other reasons for a watch-and-wait regimen, such as a near-complete response, were excluded for the present analyses. The year of decision for a watch-and-wait regimen ranged between 1991 and 2016. As shown in Table 1, imaging modalities used to assess response after induction therapy were variable, most frequently used modalities were endoscopy and MRI. Induction treatment consisted of chemo-radiotherapy in 90% of all cases. Median follow-up time is 2.6 years (range 0–24 years). Local regrowth occurred in 25% (n = 167)
of all patients, of which 64% within the first year of follow up and 84% in the first 2 years. A local regrowth was located endoluminal in 96% (n = 161) and of which 65% in the first two years of follow-up. The overall 3 year survival of all patients was 91% and for patients with a local regrowth this was 87%.

Conclusions: This is the largest retrospective series of patients with rectal cancer in which surgery was omitted after induction therapy. These data illustrate differences in induction therapy as well as baseline or follow-up imaging strategies and provide some crude outcome data. Further prospective data collection on the Watch-and-Wait strategy for rectal cancer is needed to increase our knowledge on oncological safety of omitting surgery. This may contribute to international consensus on staging, treatment and surveillance guidelines in rectal cancer care.

No conflict of interest.

451

POSTER

Vitamin D receptor and calcium sensing receptor polymorphisms and colorectal cancer survival in Newfoundland population

Y. Zhu1, P. Wang1, G. Zhai2, B. Bapat3, S. Sevtap2.

Vitamin D receptor (VDR) and calcium sensing receptor (CASR) polymorphisms have previously been implicated in colorectal cancer (CRC) survival. We evaluated genetic variation in VDR and CASR in a large cohort of colorectal cancer patients from Newfoundland, Canada. Methods: A total of 608 colorectal cancer patients were prospectively recruited from Memorial University of Newfoundland Cancer Centre and Cancer Clinic. A 9028 SNP genotyping panel was used to evaluate VDR and CASR single nucleotide polymorphisms (SNP). The primary outcome was overall survival (OS). Results: rs1801725, rs1042636, and rs1802757), with decreased OS associated to the most common haplotype (HR, 0.29; 95% confidence interval (CI), 0.13–0.68). Additionally, a significant interaction was observed for these genetic variants in VDR and CASR with colorectal cancer survival and whether the associations vary by dietary vitamin D and calcium intake. Material and Methods: A cohort of 532 colorectal cancer patients diagnosed from 1999 to 2003 in Newfoundland and Labrador, Canada, was followed for mortality and recurrence until April 2010. Germline DNA samples were obtained with the Illumina Omni-Quad 1 Million chip. Using a single nucleotide polymorphism (SNP) tagging approach, we selected a total of 24 tag SNPs in VDR and 17 SNPs in CASR for this analysis. Principal component analysis was utilized to examine the overall association of the genes with colorectal cancer. Kaplan–Meier curves and multivariate Cox models assessed single SNPs and relative haplotypes on VDR and CASR and their relation to overall OS and disease-free survival (DFS). Results: We observed a gene-level association for CASR and colon cancer overall survival (P = 0.014). CASR SNP rs1354162 had a borderline significant association with colon cancer OS (unadjusted P = 0.0052; adjusted P = 0.077). Haplotype analysis within linkage blocks of CASR showed a global association between haplotypes based on four SNPs (rs1814740, rs35274320, rs1354162, and rs18367874) and the OS of colon cancer patients (P = 0.047). In particular, the AGAC haplotype was correlated with a marked reduced OS of colon cancer in comparison to the most common haplotype (HR, 0.29; 95% confidence interval (CI), 0.13–0.68). Although no gene-level associations were noted for VDR, the association between VDR SNP rs1544410 and colorectal cancer OS was of borderline significance after the adjustment of multiple comparison (hazard ratio (HR), 1.50; 95 CI, 1.17–1.94; unadjusted P = 0.060). Additionally, a significant interaction was seen between prediagnostic dietary calcium intake and a CASR GTGGGG haplotype (rs10222635, rs10934578, rs3804592, rs17250717, rs1801725, rs1042636, and rs1802757), with decreased OS associated with this haplotype limited to only patients consuming dietary calcium below the median (HR, 1.87; 95% CI, 1.17–2.97; Pinteraction = 0.026).

Conclusion: Our results suggest that polymorphic variations of CASR are associated with OS of colon cancer patients. The associations on survival among colorectal cancer patients may differ according to dietary calcium intake.

No conflict of interest.

452

POSTER

Tumor hypoxia in colorectal cancer evaluated by 18F-fluoromisonidazole PET/CT

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Background: Tumoral lesions invariably receive less oxygen than the normal tissues from which they grow. This phenomenon is called tumor hypoxia (THPX). THPX has a negative impact on patients with cancer due to mechanisms of chemoradio resistance. The study of molecular imaging 18F-fluoromisonidazole (18F-FMISO) PET/CT has been validated as a diagnostic test for THPX. Which is a non-invasive alternative to electrode Eppendorf. However, there is no evidence of the behavior of the hypoxia in colorectal cancer (CRC).

Objective: To determine tumor hypoxia in primary and metastatic lesions of colorectal cancer with a 18F-FMISO PET/CT study.

Method: A positive patients diagnosed with CRC in 18F-FDG PET/CT scan was performed with 18F-FMISO to assess the presence of THPX. Without receive cancer treatment between both scans. With acquisition 60 and 120 min and provide scans of 18F-FDG and 18F-FMISO respectively. The maximum standardized uptake value (SUV) or (SUVmax) of each tumor drawing regions of interest was obtained. SUVmax >1.2 was the cutting range to define THPX. SPSS statistical software was used; with central tendency and dispersion measures for the descriptive component and hypothesis testing according to data distribution for the analytical component. P value (p < 0.05) were considered significant differences. With the intention of clearing the effect of the obtained sample size, the test was pondered with an expansion factor of 4 (minimum necessary to observe differences).

Results: 28 patients were studied (16 F, 12 M, 38–77 years, mean 60.89). The most frequent location for the primary colorectal cancer tumor was descending colon (28.6%), sigmoid colon (25%), rectum (25%), and finally ascending colon (21.4%). 60 lesions were examined in total: 14 lymph nodes, 12 hepatic metastases, 12 lung metastases, 10 peritoneal lesions, 5 gastrointestinal tract lesions, 4 mesenteric lesions, 3 bone lesions, 3 in soft tissues, and 3 in other regions (retroperitoneal and adrenal lesions). When the objective of finding the correlation between the tumor hypoxia and the metastasis locations, these were grouped into: bone and soft tissue, abdomen, and thorax. In this correlation test, no significant statistical differences were found. After pondering the sample with an expansion factor of 4, difference between THPX soft tissue and bone were found. The relation between hypoxia and the examined lesions' location did not show statistical significant values. After the sample was expanded by the same factor (4), statistical significant values were observed for the gastrointestinal tract, mesenteric and peritoneum groups.

Conclusion: The CRC metastases located in GIT, mesentery and peritoneum are more likely to manifest THPX, compared with those located in the liver, lung, soft tissue and bone.

No conflict of interest.
**Poster Session, Saturday 28 January 2017**

**Abstracts**

**454**

**POSTER**

Intra operative sentinel lymph node positivity by methylene blue dye and its association with other dissected lymph node by histopathological examination in colorectal cancer

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**Background:** In colorectal cancer presence of lymph node involvement signifies stage III disease and a marked decrease in the survival rate compared to stage I and II disease. Thus, the ability to identify nodal involvement more accurately is an important challenge in colorectal cancer.

The sentinel lymph node (SLN) concept is based on the premise that lymphatic drainage of tumors initially occurs through a small number of lymph nodes prior to draining into the lymphatic basin. The SLN is therefore the one most likely to harbour metastatic cells.

**Aims:** To find out the effectiveness of methylene blue dye in diagnosis of sentinel lymph node in colorectal cancer. To determine association between proportion of sentinel lymph node positivity and other dissected lymph nodes histopathological examination node in colorectal cancer.

**Materials and Methods:** The study was conducted in the Department of General Surgery, SMS Hospital, Jaipur. A total of 50 patients were studied and the results compared to other similar studies and differences analysed.

**Results:** There were 42 (84%) tumours in the colon and 8(16%) rectal tumours. Out of the total colon tumour, the sigmoid colon was the commonest site for colonic tumours (18 (36%)). There were 5 (10%) tumours in the rectum, 1 (2%) hepatic flexure tumour, 1 (2%) transverse colon tumours, 1 (2%) splenic flexure tumour and 7 (14%) descending colon tumours. The tumor was moderately differentiated in 44% of case, poorly differentiated in 10% of case, well differentiated in 44% and rest 2% is extent of malignancy. The stage was found to be stage III with 21 (42%) patients, followed by stage II with 17 (34%) patients, stage I with 12 (24%) patients. The total number of lymph nodes examined by the routine pathological method was 298, with a mean of 5.96 nodes retrieved per patient (298/50). Successful Sentinel lymph node mapping is done 45 patients out of 50 (90%). 5 out of 50 did not shown sentinel lymph node mapping. 5 out of 5 patients also negative for lymph node metastasis in histopathological examination.

**Conclusion:** In this study we observed satisfactory result of SLN biopsy in CRC even with methylene blue. Only in patients who received neoadjuvant CT/RT SLN detection was difficult and we could not detect SLN in 5 patients out of 12 who received neoadjuvant CT/RT and this difference was significant. We noted that SLN mapping do not have any significant correlation with age, sex, stage and grade of the tumor. In Patient where SLN was negative on HPE we didn’t find any other positive node which predicts 0.0% false positive result. So we can conclude SLN biopsy in CRC reliable tool to predict lymph node metastasis.

**No conflict of interest.**

**455**

**POSTER**

Unique gene expression signature of cancer initiating cells in colorectal cancer

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**Background:** Colorectal cancer (CRC) is one of the most common gastrointestinal malignancies in the world. The absolute burden of CRC has increased recently with high proportion of relatively younger patients. In India, CRC is characterised by delay in diagnosis with a ratio of deaths to incidence of 70:3, which is amongst the highest in the world. New data suggest that CRC in younger patients exhibited novel and unique mutations, with a higher percentage of advanced-stage, aggressive tumors and poor survival outcomes. The high death rate in CRC is due to its metastatic spread. Recent research has revealed the role of Cancer initiating cells (CIC) in metastasis of CRC. CIC possess self-renewal, differentiation and drug resistance potential and are present in all tumors but only some metastasize. We aim to study the differences between CIC of different grades of CRC to understand their role in metastasis. This would help to identify critical targets for clinical intervention to halt the progression and metastasis of CRC.

**Materials and Methods:** Fresh colorectal tissue was obtained from primary untreated CRC tumors, after taking permission from the Institute Ethics Committee and informed written consent from the patients. The study was conducted in the Department of General Surgery, SMS Hospital, Jaipur. A total of 50 patients were studied and the results compared to other similar studies and differences analysed.

**Results:** There were 42 (84%) tumours in the colon and 8(16%) rectal tumours. Out of the total colon tumour, the sigmoid colon was the commonest site for colonic tumours (18 (36%)). There were 5 (10%) tumours in the rectum, 1 (2%) hepatic flexure tumour, 1 (2%) transverse colon tumours, 1 (2%) splenic flexure tumour and 7 (14%) descending colon tumours. The tumor was moderately differentiated in 44% of case, poorly differentiated in 10% of case, well differentiated in 44% and rest 2% is extent of malignancy. The stage was found to be stage III with 21 (42%) patients, followed by stage II with 17 (34%) patients, stage I with 12 (24%) patients. The total number of lymph nodes examined by the routine pathological method was 298, with a mean of 5.96 nodes retrieved per patient (298/50). Successful Sentinel lymph node mapping is done 45 patients out of 50 (90%). 5 out of 50 did not shown sentinel lymph node mapping. 5 out of 5 patients also negative for lymph node metastasis in histopathological examination.

**Conclusion:** In this study we observed satisfactory result of SLN biopsy in CRC even with methylene blue. Only in patients who received neoadjuvant CT/RT SLN detection was difficult and we could not detect SLN in 5 patients out of 12 who received neoadjuvant CT/RT and this difference was significant. We noted that SLN mapping do not have any significant correlation with age, sex, stage and grade of the tumor. In Patient where SLN was negative on HPE we didn’t find any other positive node which predicts 0.0% false positive result. So we can conclude SLN biopsy in CRC reliable tool to predict lymph node metastasis.

**No conflict of interest.**

**455A**

**POSTER**

Translation initiation separates low and high grade colon and rectum carcinoma


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**Background:** Colorectal cancer (CRC) is the third most common cause of cancer related death worldwide. Protein deregulation has received considerable attention as a major step in cancer development and progression. The step of initiation, regulated by eukaryotic initiation factors (eIFs), is assigned as rate limiting step in protein synthesis. eIFs become major targets for cancer therapy and are functionally linked to the PI3K/Akt/mTOR signaling. However, little is known about their contribution in CRC. Therefore, we aimed to investigate the role of eIFs and mTOR members in CRC.

**Material and Methods:** eIF and mTOR expression was analysed in primary low and high grade CC and RC samples in comparison to controls without any disease-related pathology on protein and mRNA expression. To assess the therapeutic potential of targeting eIFs, siRNA knockdown experiments in HCT116 cells were performed. We evaluated the eIF knockdown on protein and mRNA level and investigated proliferation, apoptosis, invasion, colony forming and polysome associated fractions.

**Results:** Protein and mRNA levels of low grade and high grade CC and RC patients revealed a significant up-regulation of mTOR members and most eIF subunits. Reducing eIF1, eIF5 and eIF6 expression by inducible knockdown in the HCT116 cell line led to increased levels of free ribosomal subunits, suggesting reduced mRNA translation. As consequence, CRC cell proliferation, viability, invasion, clonogenicity and apoptosis were found to be decreased.

**Conclusion:** Various eIFs are altered; particularly eIF1, eIF5 and eIF6, in low and high grade CC and RC thus aberrant translation initiation might represent a novel mechanism in CRC carcinogenesis.

This research received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no. 115234, Oncotrack.

**No conflict of interest.**
Radiomics signature of primary diffusion MR for treatment response prediction in rectal carcinoma

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Background: The standard procedure for Locally Advanced Rectal Carcinoma (LARC) is neoadjuvant chemoradiotherapy (CRT) followed by total mesorectal excision (TME). Proposed alternatives aim to avoid TME for patients showing good response, offering a better functional outcome. Poor responders still need TME with a higher risk of morbidity and worse functional outcome. The challenge is to predict response before treatment and to intensify CRT in responders, and avoid futile CRT in non-responders. In this pilot study, we aim to assess Radiomics signature [1] of LARC for prediction of response to CRT.

Material and Methods: We retrospectively assessed the primary staging diffusion-weighted MRI scans (b-values: 0–1000/1000) of 124 patients with locally advanced rectal carcinoma, treated with CRT. Tumours were semi-automatically segmented on DWI1000. Radiomics signatures [1] were extracted from the DWI1000 for each of the five segmentations (1129 features). Features showing sufficient stability (ICC ≥ 0.75 and reproducibility performance [Wilcoxon test, False Detection Rate (FDR) 10%]) across different readers were selected to test their performance in predicting response to CRT (complete tumour regression versus residual tumour) by means of ROC curve analysis.

Results: Out of 1129 initial features, 1010 were stable across different readers. For the manual delineations, 1200/1129 features per reader remained significantly performed after FDR correction, however, none of these survived FDR correction for the fully automated segmentation. A final subset of 60 features remained stable and performed across all readers. These 64 features resulted in mean AUC of 0.67 (range 0.65–0.69) to predict a complete response and a mean ICC of 0.83 (range 0.73–0.88). Best results were obtained for textural features and volume confounding features, and volume confounding features like total energy, showed the highest performance and stability.

Conclusions:
1. Various features extracted from pre-treatment diffusion-weighted MRI correlate to neoadjuvant treatment response and may be used to predict a complete response after CRT of rectal cancer.
2. Best results are obtained for textural features and volume confounding features.
3. Features extracted from automated segmentation showed inferior performance compared to the features extracted from the manually adjusted segmentations, emphasizing the need for adequate tumour segmentation. Interestingly, delineations by both experienced and inexperienced readers were able to generate stable and high performing features, suggesting that the selected features are robust and do not necessarily require highly expert input.

References

No conflict of interest.

456A POSTER IMRT and simultaneous hypofractionated boost combined with chemotherapy for squamous cell cancer anal cancer: All in 25 fractions

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Background: Squamous cell anal canal carcinoma is a rather rare malignancy, no more than 4% of all gastrointestinal tumors although is incident is increasing. Definitive chemoradiation is the standard management for anal squamous cell carcinoma. The aim of this study is to evaluate the outcome and toxicity of our institutional new schedule with intensity modulated radiation therapy and simultaneous boost plus concurrent chemotherapy for these patients.

Material and Methods: A consecutive series of 14 patients was enrolled between August 2013 and June 2016. Treatment schedule consisted of 8 GY embarked in 25 fractions (1.8 Gy daily) (DBE result support 93 from 1.8 Gy daily) to the gross tumor volume (boost), while the elective nodal volumes were prescribed 45 Gy/25 fractions (1.8 Gy daily) for patients having a N0 disease. Non affected inguinal nodes were prescribed 39.6 GY/22 fractions (1.8 Gy daily) and gross nodal volumes were prescribed 57.5 GY/28 fractions (2.5 Gy daily). Chemotherapy was administered concurrently according to the Nigo’s regimen (mitomycin and 5-FU), Xelox (oxaliplatin plus capecitabine) or capecitabine alone.

Results: We got 8 male and 5 female patients all of them with biopsy of squamous cell anal carcinoma. The stage distribution was: T3N0 (3 pts: 21.4%), T2N3 (3 pts: 21.4%), T2N2 (2pts:14.2%), T3N3 and T4N2 (21.4% and 28.5% for each one) Mean follow up was 16.14 months (range 9–30). Until November 2016, we got 7 patients in complete response confirmed by radiology and biopsy guide by endoscopy; 5 patients in partial response and 2 who progressed 9 and 13 months after treatment respectively. In one of this case, there were 14 days of interruption of concomitance due to hematological toxicity. Maximum detected acute toxicities were as follows: Skin G3 only in 2 patients, G2 in the rest, gastrointestinal G3 in one patient, G2 in five and G1 in the rest. No urinary toxicity was observed.

Conclusion: Our study shows comparable results to the literature with respect to toxicity and local control with a decrease of treatment time although we need a greater number of patients and longer follow up for better comparative.

No conflict of interest.
**457A**

**POSTER**

Tumour infiltrating (TINK) and Tumour associated (TANK) natural killer cells: novel inflammatory orchestrators in colorectal cancer (CRC) progression and angiogenesis

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**Background**: Tumour infiltrating immune cells often show a skewed phenotype that reflects attenuation of anti-tumour activity and enhancement of pro-tumour and pro-angiogenic activities. Natural Killer (NK) cells are effector lymphocytes of innate immunity, primarily involved in immunosurveillance against tumours through their cytotoxic activity. We reported that NKs from Non Small Cell Lung Cancer patients are able to acquire the decidual-like CD56dimCD16+VEGFR2+IL-8+IFNγ− phenotype and promote angiogenesis in vitro, similar to NK cells found in the decidua.

**Material and Methods**: Here we extend our findings to colorectal carcinoma (CRC) using multicolour flow cytometry on NK cells derived from peripheral blood and tissue samples of CRC patients. Functional assays were conducted on conditioned media (CM) from FACS-sorted NK cells for secretomic profiling and in vitro angiogenesis correlates using human umbilical endothelial vein cells (HUVECs).

**Results**: We found that CD56+CD16− NK cells predominate in CRC adjacent and tumour tissues, show decreased NKGD2 surface expression and impaired tumour cell lytic abilities. Further, peripheral blood (TANKs) and tumour infiltrating (TINKs) NK cells from CRC patients express the decidual NK A.D. CD56dimCD16+VEGFR2+IL-8+IFNγ− phenotype and promote angiogenesis in vitro, similar to NK cells found in the decidua.

**Conclusion**: The coefficients of significant predictive variables (p < 0.001) for each outcome and specific FUP time, with the correspondent training and validation performance and brier score, are shown in the table.

<table>
<thead>
<tr>
<th>FUP</th>
<th>Outcome</th>
<th>Covariates</th>
<th>Coefficients</th>
<th>Area under curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>DM</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.42; -0.49</td>
<td>0.74 0.78 0.08</td>
</tr>
<tr>
<td>3</td>
<td>OS</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.16; -0.15; 0.74</td>
<td>0.73 0.76 0.12</td>
</tr>
<tr>
<td>5</td>
<td>LR</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.74; -0.81; 0.74</td>
<td>0.74 0.76 0.08</td>
</tr>
<tr>
<td>10</td>
<td>DM</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.17; -0.13; 0.73</td>
<td>0.74 0.76 0.19</td>
</tr>
<tr>
<td></td>
<td>OS</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.09; -0.01; 0.72</td>
<td>0.76 0.76 0.19</td>
</tr>
</tbody>
</table>

**Conflict of interest**: No conflict of interest.

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**458A**

**POSTER DISCUSSION**

Updated prognostic models for local recurrence, distant metastases and overall survival in a pooled dataset of 3770 rectal cancer patients

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**Background**: Several prognostic and predictive models (PMs) for locally advanced rectal cancer (LARC) patients (pts) have been developed in the last years. Aim of this study was to update the previous PMs [1] developed for local recurrence (LR), distant metastases (DM) and overall survival (OS) at 2, 3, 5 and 10 years; based on a pooled set of LARC pts.

**Material and Methods**: The PMs were developed using the data of the following LARC trials: Accord 12/0405, EORTC 22921, FFCD 9203, CAGI/AIRO/AIO-94, CAGI-AIO-94, INTERACT, I-CNR-RT and TROG 01.1. This dataset contained 7670 pts were selected after applying the following exclusion criteria: neoadjuvant (NAD) and adjuvant (ADJ) oxaliplatin based chemotherapy (CT), no surgery procedure (SP), short-course radiotherapy (RT) and no NAD RT. As the current pooled dataset contains different trials, we used 20% of the data (stratified per trial) as a validation dataset. Due to variable influence over time, a logistic regression model was used. Follow-up times (2, 3, 5 and 10 years) for the respective outcomes (LR, DM and OS) were used as the model outcomes. Variable selection was performed using a stepwise Akaike’s information criterion (AIC) feature selection to determine the optimal subset of covariates. According to the TRIPOD [2], all PMs were validated using external validation of type 2b.

**Results**: The coefficients of significant predictive variables (p < 0.001) for each outcome and specific FUP time, with the correspondent training and validation performance and brier score, are shown in the table.

<table>
<thead>
<tr>
<th>FUP</th>
<th>Outcome</th>
<th>Covariates</th>
<th>Coefficients</th>
<th>Area under curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>LR</td>
<td>pT3; pT4; pN1</td>
<td>-0.56; 1.42; 2.15; 0.69</td>
<td>0.73 0.77 0.06</td>
</tr>
<tr>
<td>3</td>
<td>DM</td>
<td>pT3; pT4; pN1</td>
<td>-1.49; 2.15; 1.02; -0.45</td>
<td>0.73 0.74 0.14</td>
</tr>
<tr>
<td>5</td>
<td>OS</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.81; 1.24; 2.11; 0.74; 0.74 0.75 0.08</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>DM</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.42; -0.49; -0.34; -0.34</td>
<td>0.71 0.75 0.07</td>
</tr>
<tr>
<td></td>
<td>OS</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>0.74; 0.73 0.74 0.73 0.73 0.16</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>LR</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.48; 1.01</td>
<td>0.75 0.77 0.13</td>
</tr>
<tr>
<td>10</td>
<td>DM</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>-0.17; -0.13; -0.30; 0.73</td>
<td>0.74 0.75 0.19</td>
</tr>
<tr>
<td></td>
<td>OS</td>
<td>pT3; pT4; pN1; ADJCT; AR SP</td>
<td>0.02; 0.02; 0.73; 0.40; 0.95; 0.70</td>
<td>0.76 0.76 0.19</td>
</tr>
</tbody>
</table>

**Conclusion**: The logistic regression model performed well with high AUC and low brier score. The AUC higher in validation than in training would need further investigation. Nomograms will be showed at the meeting.

**References**

No conflict of interest.

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**459A**

**POSTER**

Addressing intraoperative adhesions, heat dissipation and uneven distribution of the perfusion fluid during HIPEC: The laparoscopy-enhanced HIPEC technique

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**Background**: Hyperthermic intraperitoneal chemotherapy (HIPEC) is delivered after cytoreductive surgery (CRS) in selected patients with peritoneal carcinomatosis. The closed-abdomen technique, preferred by many centers, prevents heat loss and drug spillage, but does not warrant homogeneous distribution of the perfusion fluid. The hypothesized formation of intra-abdominal adhesions that could hamper the distribution of the perfusion fluid during the closed-abdomen perfusion has never been described.

**Material and Methods**: From March 2014 to May 2016, 11 consecutive patients with peritoneal carcinomatosis, selected for CRS, underwent the Laparoscopy-Enhanced HIPEC technique to explore the abdominal cavity during the perfusion. The aim of the study was to investigate the incidence and the extent of intra-abdominal adhesions (IA) that are formed after CRS during the perfusion period of closed-abdomen HIPEC.

**Results**: During the perfusion, IA developed in 8 patients (73%). IA were formed among the loops of the small bowel in 3 patients, between the small bowel and the colon in 3 patients and between the bowel and the anterior abdominal wall in 6 patients. IA between the bowel and the anterior abdominal wall involved one abdominal region in 1 patient, two abdominal regions in 1 patient, three abdominal regions in 3 patients and seven abdominal regions in 1 patient. Adhesions developed mainly in the period before the closure of the abdomen and the subsequent filling of the abdomen with the PF. After their first division, during the following perfusion period, adhesions between the bowel and the abdominal wall reformed in 3 patients (27%).

**Conclusions**: Intra-abdominal adhesions are frequently formed during closed-abdomen HIPEC and can hamper the adequate circulation of the PF. The Laparoscopy-Enhanced technique enables the early detection and the division of any intra-abdominal adhesions.

No conflict of interest.
459A Elevated levels of peripheral blood T lymphocytes are predictors of complete response to chemoradiotherapy in patients with locally advanced rectal cancer

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Background: Neoadjuvant chemoradiotherapy (nCRT) has become a standard treatment for locally advanced rectal cancer, however great differences in treatment response still exist among treated patients. Some studies have been made to identify possible factors that can lead to a CPR, but predictive factors of CPR have not been totally identified. These are preliminary results of a prospective study than we’ll finish in the next two years. We aimed to identify if host immune response, analysed with peripheral blood leukocyte subsets, can be a predictive factors of response to CRT.

Material and Methods: Demographic and clinical data about 22 patients who had a locally advanced rectal cancer between July 2015 and November 2016, were prospectively collected. All patients received a nCRT followed by curative surgical resection. Pre-treatment numbers of blood lymphocytes subset were identified on each patients using cytometry. Patients were divided in those who achieved a CPR and those who did not achieve a CPR (nCPR) group. Patients were divided into two groups according to the nRCT response.

Results: Among 22 patients, we have able to have a pathologiscal stage only for 19 patients and among these, 3 (15.8%) patients had a pathological complete response (CPR). Patients with CPR had a significantly higher number of pre-nCRT T lymphocytes compared with patients without response to nCRT (1501.33 vs 684.18; p = 0.0476). Also patients with CPR had a significantly higher number of Helper T lymphocytes (Th lymphocytes) than patients without response to nCRT (964.33 vs 522.56; p = 0.0211). No difference was found between others blood leukocyte subsets (all lymphocytes, cytotoxic T lymphocytes, B lymphocytes and natural killer) and CPR.

Conclusion: Our study suggest that pre-nCRT high numbers of T lymphocytes and Th lymphocytes should predict the response to nCRT in patients with locally advanced rectal cancer. No conflict of interest.

460 A method for identification of tumor cells in the caval bloodstream in colorectal cancer with immunohistochemistry

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An intraoperative analysis of caval blood was made in 2014–2015 on 22 patients with metastatic colorectal cancer in liver by clinic procedure. 24 of these were suffering from a cancer of the sigmoid, 12 patients from a rectal cancer and 16 were suffering from a cancer of different colon parts. The local dissemination of process corresponded to T3–4. The analysis was performed in patients undergoing simultaneous operative treatment such as resection of affected colon part and anatomical liver resection. Caval blood samples were taken from a pool hepatic veins up to dissection of parenchyma only after abdomen cavity revision. In the beginning of experiment on the phase of developing the technique in patients not included in the trial, the microscopy of caval blood without destruction of erythrocytes was conducted. Despite on identification of tumor cells in 2 patients this technique has significant drawbacks: difficulties in preparation of a smear (usually a smear is thick, accumulate fat droplets and thread of fibrin); difficulties in identification of single tumor cells; duration and laboriousness of microscopy.

Taking into account the above disadvantages it was designed the method of caval tumour cells with destruction of erythrocytes identification: (the modification of the technique of tumor cells identification in blood by Grekh J.F. and Yakovleva M.P.). In this method of blood processing a complete destruction and stroma removing of erythrocytes occurs while saves morphological structures of leucocytes and tumor cells. During this trial tumor cells were verified in 37 patients: in 14 with a sigmoid cancer, in 7 patients with a rectal cancer and in 16 patients with a cancer of different colon parts. Thus, on the grounds of the obtained data it could be made a conclusion that in more than a half of patients with presence of metastases in liver there are circulating tumor cells in caval bloodstream, which identification determines a necessity of adjuvant chemotherapy correction taking into account the specific immunohistochemical tumor markers in these patients.

No conflict of interest.
postoperative fever and one patient in group A (2.3%) required readmission and re-surgery to manage anastomotic leakage and peritonitis.

**Conclusions:** Enhanced recovery program for elective colorectal cancer surgery has a very good impact on post-operative recovery as it shortens the patient’s hospital stay with high safety and good patient compliance, so we strongly recommend the application of such protocols provided that the availability of the well trained and adequately experienced personnel in equipped centers.

**No conflict of interest.**

**462**

**POSTER**

Curative partial pelvic exenterations for locally advanced rectal and sigmoid cancer with recto-vaginal and recto-vesical fistulas

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**Background:** Partial pelvic exenterations remains a gold standard for urgent abdominal surgery, Kharkiv, Ukraine; 2Institute of general and urgent surgery, Academy of sciences of Ukraine, Department of urgent abdominal surgery, Kharkiv, Ukraine; 3Institute of general and urgent surgery, Academy of sciences of Ukraine, Director, Kharkiv, Ukraine; 4Kharkiv medical postgraduate academy, Psychotherapy, Kharkiv, Ukraine

**Material and Methods:** Between 2003 and 2015, 72 partial pelvic exenterations was performed for the primary (47) and recurrent (25) rectal cancer complicated by the recto-vaginal (43) and recto-vesical (29) fistulas. An evaluation of prognostic factors for anastomotic leakage, mortality rate and overall survival was made.

**Results:** Combined operations were performed at 72 patients accounting for 8.3% of the total number (873) operations for rectal cancer. A total of 42 patients were treated by posterior exenteration (abdominal rectal resection and hysterectiony and vaginectomy en bloc), 30 patients were treated by anterior exenteration (rectal resection and resection of bladder/lef ureter). Primary colo-anal anastomoses were performed in 35 from 46 sphincter spared patients (76%). Urinary diversion was achieved by construction of a Boary-flap (10), ileal conduit (6), ileal bladder augmentation (6), transverse colon conduit (3) and double-barreled wet colostomy (2). Microscopically complete resections (R0) were achieved in 94%. The histological study identified the presence of the direct tumor invasion in the adjacent organs in the 63 patients (87.5%), inflammatory penetration was identified in 9 patients (12.5%).

Total of 84 anastomoses in 72 patients were performed (44 ureteral and 40 intestinal). Signs of leakage were found in 9 patients (leakage rate made up 10.7%). In the group of anastomotic leakage in comparison to non leaked anastomoses (9/39) were found an oppression of a cellular link of immunity, augmentation of cytotoxicity of blood serum, 10-fold increase urinary excre- tion of aminoacid oxypoline as a markers of the disintegration of collagen type 1 and early predictor of anastomotic leakage. Also risk factors for anastomotic failure were hypoproteinemia, incomplete resection (R1), male gender and 3 or more anastomoses. The average follow up from surgery was 42 months (range 8-96). The 5-year overall survival rate made up 48%.

**Conclusions:** Patients with rectal cancer complicated with recto-vaginal or recto-vesical fistulas without distant metastases can safely be treated by means of combined operations which lead to a satisfactory overall survival and local control. New methods of combined operations compared with total pelvic exenterations allowed to improve early and late outcomes with satisfactory medical and social adaptation of patients after resections of the adjacent organs.

**No conflict of interest.**

**463**

**POSTER**

5-Aminolevulinic acid-mediated fluorescence in colon cancer surgery: a histopathological analysis of fluorescent and non-fluorescent tumours

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**Background:** 5-aminolevulinic acid (5-ALA) is a prodrug that is metabolised in mitochondria to the fluorophore protoporphyrin IX. This se-lectively accumulates in cancer cells, enabling tumour-specific fluorescence to be observed upon exposure to excitation light. This principle has been used for fluorescence diagnosis in a number of cancer types, although the GLStest trial was the first time 5-ALA had been applied to the intraoperative detection of colon cancer and lymph node metastases. In this trial, 39 patients received oral 5-ALA preoperatively, however only 13 had visibly fluorescent primary tumours at laparoscopy, suggesting a fundamental difference between fluorescent and non-fluorescent cases. The aim of this study was to investigate whether differences in fluorescence were due to tumour composition – specifically tumour cell density, vascularity and T cell infiltration – which may be of prognostic significance.

**Material and Methods:** Primary tumour tissue was available from 30 trial participants. Tumour cellularity was quantified using digitally scanned tissue sections stained with haematoxylin and eosin. A grid of 300 points was randomly superimposed onto each tumour image and the structure indicated by each point categorised as ‘tumour’, ‘vessel’ or ‘other’. The proportion of points classified as ‘tumour’ gave the tumour cell density and the proportion of points classified as ‘vessel’ gave the vessel density. A tissue section was also stained for the T cell marker CD3 by immunohistochemistry. Microscopic spectral imaging was used to quantify staining in three high-density fields at the tumour’s invasive margin and in a further three fields in the tumour centre. The independent effect of the measured variables on tumour fluorescence status was assessed by binary logistic regression analysis.

**Results:** We were unable to detect any association between fluorescence status and tumour composition, with tumour cell density, vessel density and T cell infiltration not emerging as significant predictors of tumour fluorescence (P > 0.05) (see table). Furthermore, comparisons of the distributions of each variable demonstrated substantial overlap between the fluorescent and non-fluorescent cohorts.

<table>
<thead>
<tr>
<th>Fluorescent (n=21)</th>
<th>Non-fluorescent (n=21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour cell density 36.42% (12.72)</td>
<td>36.15% (12.86)</td>
<td>0.440</td>
</tr>
<tr>
<td>Vessel density 1.67% (0.82)</td>
<td>1.64% (1.20)</td>
<td>0.673</td>
</tr>
<tr>
<td>T cell infiltration (invasive margin) 2.13% (4.64)</td>
<td>2.45% (3.61)</td>
<td>0.509</td>
</tr>
<tr>
<td>T cell infiltration (tumour centre) 2.48% (6.45)</td>
<td>2.50% (4.92)</td>
<td>0.355</td>
</tr>
</tbody>
</table>

**Conclusion:** The results suggest that tumour composition is not an important discriminating factor between cancers that fluoresce with 5-ALA and those that do not. We therefore propose that cellular uptake and metabolism of 5-ALA is a more likely explanation for differential fluorescence in colon cancer.

**No conflict of interest.**

**464**

**POSTER**

Reversal of Hartmann’s procedure, experience in an Asian population

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**Introduction:** Hartmann’s procedure is normally performed for left sided colonic pathologies in emergency situations. It is now less frequently performed due to improvement in radiological modalities, endoscopic interventions and surgical techniques. Restoration of intestinal continuity after Hartmann’s procedure has traditionally been viewed to be technically demanding and associated with significant morbidity and mortality. This study has been done to show reversal rate after Hartmann’s procedure in an Asian population.

**Methods:** Data collected from database showed that 102 patients had undergone Hartmann’s procedure from Jan, 2006 to Dec, 2015 due to colorectal carcinoma. Patients who subsequently underwent Hartmann’s reversal were identified and their records reviewed retrospectively.

**Results:** Hartmann’s procedure was done under emergency situation in 74 patients due obstruction (62.7%), perforation (8.8%) and anastomotic leak (1%) and electively in 28 patients mostly due to poor bowel preparation (20.1%), and early predictor of anastomotic leakage. Also risk factors for anastomotic failure were hypoproteinemia, incomplete resection (R1), male gender and 3 or more anastomoses. The average follow up from surgery was 42 months (range 8-96). The 5-year overall survival made up 48%.

**Conclusion:** In our population, Hartmann’s procedure is more commonly performed for colorectal cancer under emergency situations. Reversal rate is more than 90% if there no locoregional recurrence and patient continue further ups.

**No conflict of interest.**
Next-generation sequencing for miRNA profiling of stool and plasma samples of patients with colorectal cancer or precancerous lesions

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Background: MicroRNAs (miRNAs) are key gene regulators in most biological and pathological processes, including colorectal cancer (CRC). The possibility of using circulating or fecal miRNA expression as non-invasive biomarkers open interesting possibilities for their potential clinical utility. In this respect, diet and other lifestyle factors may also modulate miRNA expression and need to be explored in the context of search of biomarkers for disease stratification. Next-generation sequencing (NGS) technologies have changed the approach to complex genomic studies, including those on RNA, providing a reliable and accurate method for grouping individuals on the basis of their molecular profiles. NGS allows the exploration of all potential miRNAs expressed giving the possibility to comprehensively define signatures at the basis of regulatory circuits that govern many pathways involved in carcinogenesis. We report our study on the search of CRC biomarkers in surrogate specimens by a concomitant evaluation of miRNA expression profiles in plasma and stools samples from healthy subjects and patients with CRC or precancerous lesions.

Materials and Methods: miRNA expression profiles is characterized by NGS (small RNA sequencing) in exosome isolated from plasma and in stool samples of a discovery set of CRC adenoma/inflammatory disease patients and healthy subjects recruited at colonoscopy. Samples from more than 100 subjects have already been collected. An optimized workflow for quantification of miRNAs obtained from NGS and an analysis pipeline has been developed for pre-processing the raw sequences, aligning the data to a known reference sequence and finally, analyzing the compiled sequence. The identified deregulated miRNAs will be validated by qPCR in an additional group with similar distribution of cases/controls. Information on lifestyle and dietary habits are collected at the time of enrolment, logobase.

Results: Stool miRNAs analyzed by NGS for the first time in the present study seem to provide reliable and comparable results to other specimens (number of mapped sequences/identified miRNAs). Preliminary results of a set of 96 plasma/stool samples shows that several miRNAs are dysregulated in patients with precancerous lesions and inflammatory diseases in comparison with healthy subjects.

Conclusions: The present study shows the importance to use high-throughput techniques and complex computational analyses to globally define miRNA signatures involved in colorectal carcinogenesis in surrogate specimens. Their future use in clinical practice may help to avoid unnecessary and expensive colonoscopies in low-risk patients.

No conflict of interest.

Analysis of factors affecting survival in patients with lung metastases from colorectal cancer who underwent VATS-assisted surgical excision

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Background: Colorectal cancer (CRC) is one of the most common malignancies, and the onset of liver or lung metastases (LMs) significantly affects overall survival. The main reported prognostic factors related to survival are the age of the patients, preoperative carcinoembryonic antigen (CEA) serum levels, lymph node involvement, neoadjuvant chemotherapy, disease-free survival, and number and size of LMs. We have previously reported that the primary tumor site should not be considered a major criterion in selecting patients for pulmonary metastasectomy. The aim of this retrospective study was analyze whether the age of the patients and the number and size of LMs could affect survival of patients who underwent curative surgery for CRC and developed LMs during follow-up.

Patients and Methods: We reviewed the medical reports of 36 patients who underwent VATS-assisted lung metastasectomy for LMs. There were 21 (58.3%) men (57.9±14.9 years of age) and 15 (41.7%) women (63.3±11.1). Because the data were not normally distributed, the Mann–Whitney U-test was used to evaluate difference between groups. The Pearson correlation coefficient (r) and the linear regression equation calculation was obtained to evaluate survival and the main risk factors, such as age of the patients, and size and number of the LMs. A p-value <0.05 was considered statistically significant.

Results: The age between men and women did not differ significantly (Z = 0.35, p = 0.71). The overall survival was 30.6±25.1 months (median 24.5, range 1–92 months). The mean number of the excised LMs was 2.1±1.8 (median 1.5, range 1–9) and the mean size of the greatest LM was 17.6±8 mm (median 15 mm, range 5–32 mm). No correlation was found between survival and age (r = 0.069, p = 0.56), mean size of LM (r = 0.209, p = 0.22) and No. of LMs (r = 0.196, p = 0.25). The Table reports each regression line equation and the relative intercept (α) and slope (β) value.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Regression line equation</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of the patients</td>
<td>survival = 18.34462437527571 + 0.1968832394193 age</td>
<td>-0.099</td>
<td>0.56</td>
</tr>
<tr>
<td>Size of largest LM</td>
<td>survival = 1.4946628510453 + 0.00615722356345 size</td>
<td>-0.209</td>
<td>0.22</td>
</tr>
<tr>
<td>No. of LMs excised</td>
<td>survival = 2.46796691013347 − 0.012554396779736 number</td>
<td>-0.196</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Conclusion: Overall survival of patients with LMs from CRC is independent of the number and size of LM and the age of the patients. Further studies will eventually confirm our results.

No conflict of interest.

Oncological outcomes of colon carcinoma: 10 year experience from a low income country

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Background: Colorectal cancer is ranked second in cancer related deaths in United States and Europe, and is the third most common epithelial malignant tumor of human body. Total mesorectal excision (TME) has been institutionalized worldwide and was first applied by Heald. We conducted this study to see the oncological outcomes of carcinoma colon managed at our hospital.

Material and Methods: Medical records of all the patients who presented to Shaukat Khanum Hospital from Jan 2006 to Dec 2015 with colon tumor and who underwent surgery were analysed of any age, either gender were included in this study. Their demographic, clinicopathological features, operative information and outcomes were recorded on a pre-designed proforma and were analysed. Primary end point was 5 year overall survival (OS).

Results: In total of 244 patients, male to female ratio was 2:25:1, most of the patients were above the age of 45 years (66.4%). The most common presenting symptom was per rectal bleeding (23.5%) followed by altered bowel habits (23.9%) and pain (22.5%). Right (43.8%) and left side (44.3%) of the colon were equally involved. Almost half of them were performed laparoscopically (44.2%) and half open (48%) and conversion rate to open surgery was only 7.8%. Right hemi and extended right hemi was the most commonly performed procedure (54.5%) followed by sigmoid colectomy (21.3%) and left hemicolectomy (9%). Adjuvant therapy was offered to 128 patients (52.5%), as majority of the patients were T3 (63.1%) followed by T4 (18.9%) and near to half were node positive (41%) with an overall 5 year survival rate of more than 60%.

Conclusion: Advance disease and late presentation is very common in this part of the world with lack of any screening programme, the overall survival can be improved by implementing a proper screening programme on national level.

No conflict of interest.

Evaluation of weight status during the time between ileostomy formation and closure in individuals who were operated due to rectal cancer

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Background: Approximately 50 percent of the patients who had undergone colorectal surgery may experience weight loss due to several reasons. Stoma is one of those reasons. The aim of this study is to evaluate weight changes during the time between ileostomy formation and closure in individuals who were operated due to rectal cancer.

Material and Methods: A total of 23 people (13 males and 10 females), who had undergone laparoscopy assisted low anterior resection with ileostomy formation and whose mean ages were 55.52 ± 12.40 (between
POSTER

469
Contributions of patient-, tumor-, and treatment-related factors to the patients' outcome after curative liver resection among Egyptian patients with metastatic colorectal tumor

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Background: This study was conducted to identify the influencing factors on the outcome of Egyptian patients of colorectal cancer with liver metastasis.

Materials and Methods: From June 2011 to June 2015, medical records of 44 patients who had undergone a first curative hepatectomy for colorectal cancer with liver metastasis were analyzed. Relationships between survival and patient demographics, selected biological tumor markers, degree of tumor differentiation, need for ≥3 resection(s), margin and lymph nodes (LNs) status were evaluated using Chi-square test.

Results: Median age was 50.73 years (SD=11.99). 61% of the patients were males. The baseline CEA was 98.67±166.71. LNs in the primary tumor was positive in 43.2%. About 65.9% and 34.1% underwent unilobar and bilobar resection respectively. Median tumor burden and size of largest tumor in cm was 8.39 ±3.64 and 5.59±2.41 respectively. Portal vein thrombosis was seen in 13.6% of the patients. Grade I, II and III was presented in 2.27%, 90.9% and 6.82% respectively. Positive resection margin was observed in 45.5%. Disease free survival in relation to primary colon cancer was 11.05±15.57 months. About 81.82% received induction chemotherapy while only 63.64% responded. In a median follow-up time of 36.0 months, recurrence was observed in 43.2%. Recurrence was hepatic, extrahepatic and both hepatic and extrahepatic in 20.5%, 6.8% and 15.9% respectively. The median survival after recurrence was 12.0±7.77 months. Of all variables tested, LN status of the primary colon tumor, overall tumor burden and size of largest tumor in cm was statistically significantly with the recurrence with p value of 0.01, 0.049 and 0.008 respectively. Only the LNs status of the primary colon tumor (p = 0.022) was statistically significantly with the mortality.

Conclusion: LN status of the primary colon tumor was affecting both the recurrence and mortality after curative hepatectomy liver resection in Egyptian patients with metastatic colorectal tumor.

No conflict of interest.

470
Impact of prolonged postoperative ileus on surgical outcome in elective colorectal cancer resections

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Background: Decrease of bowel motility is expected in postoperative period as part of complex response to surgery. The aim of this prospective study was to analyze development of prolonged postoperative ileus (PPOI) after elective colorectal surgery for cancer and its impact on early postoperative outcome.

Material and Methods: All eligible patients eighteen years or older scheduled for open colorectal resection for cancer during eight months period were included. Patients with metastatic disease, prior neoadjuvant chemo/theraphy, or any resection other than curative were excluded from the study. All patients were operated by the same group of surgeons using the same protocol of preoperative and postoperative care. All had mechanical bowel preparation. In cases of placement of nasogastric catheter for decompression, same was removed at the conclusion of the operation. Liquid diet was prescribed to all patients on postoperative day one, followed by solid food as tolerated. None of the patients received opiate based analgesia postoperatively, nor were epidurals used. The study duration was up to 30 days after the surgery. Primary outcome measure was development of PPOI according to strict definition. Prospectively we analyzed the impact of PPOI on early postoperative morbidity and mortality and hospital stay.

Results: Prospective analysis included 103 patients, 64 (37.9%) men and 39(62.1%) women, mean age 66.00±10.06 years, without statistically significant difference in age between men and women (p = 0.542). PPOI developed in 12 (11.3%) patients. Almost half of the patients (47.6%) had some grade of compicication, while one third had some type of surgical site infection (SSI). The rate of anastomotic leakage was 5.4%. Ten patients (9.7%) required reoperation. Total length of hospital stay was mean 12.60±0.65 days (range 7-49). Comparing the group of patients with prolonged postoperative ileus with those without, there were no statistically significant differences in rates of SSI and anastomotic leakage. There was statistically significant difference in terms of complications (χ² = 34.966; p < 0.0001), complications grade III (χ² = 23.43; p < 0.0001) and reoperations (χ² = 15.724; p < 0.0001). Patients who developed PPOI had statistically significant longer postoperative hospital stay (Z = 2.291; p = 0.022) and longer total length of hospital stay (Z = 2.377; p = 0.015). According to regression analyzes PPOI is a risk factor for reoperations (OR = 12.286; p = 0.001). PPOI is not risk factor for development of other complications (OR = 1.197; p = 0.773). Our results show that patient who develops PPOI has 12 times more chance to undergo reoperation (OR = 12.286; p = 0.001), while PPOI poses no risk for mortality (OR = 0.291; p = 0.170).

Conclusions: PPOI although not life-threatening complication effects surgery, increases length of hospital stay and contributes to poor surgical outcome.

No conflict of interest.
472

Results of total mesorectal excision with water-jet dissection in patients with rectal cancer

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Background: The total mesorectal excision (TME) technique includes mobilization of the rectum under visual control within the mesorectal fascia, along with preservation of the pelvic veins and the presacral vessels. Various versions across the world traditionally use scissors, coagulators, and, later, harmonic scalpels for this kind of mobilization. The aim of our study was to retrospectively evaluate local results of nerv-sparing total mesorectal excision in patients with rectal cancer using different dissection techniques.

Materials and Methods: We used the water-jet dissection technique to obtain tissue specimens in 20 patients with rectal cancer. The mean age of these patients was 56.1 ± 11.2 years (range, 44–78). The group consisted of 8 men and 12 women. The T2/T3a tumors were either in the middle part (14 patients) or in the lower portion (6 patients) of the rectum. We also used two reference groups consisting of 20 controls each; the rectum was mobilized in them using a monopolar coagulator and a harmonic scalpel. The study groups were comparable with regard to gender, age, tumor sites, and staging. All surgical interventions were performed by the same team of surgeons. Low anterior resections were performed in all 60 patients. Additionally to the routine morphological examination, we performed microscopy of the circumferential resection margin to assess the intensity and depth of damage to the mesorectal tissue.

Results: The mean duration of the surgical operation was 138 ± 36.1 minutes (range, from 100 to 190). There was no postoperative morbidity and mortality. Morphological examination showed the good quality of mesorectal plane (mesorectal plane) in majority of patients in all groups. The following data were obtained with regard to depth of tissue damage along the lateral margin of the excised tissue. There was virtually no tissue damage (in the fascia and cellular tissue) in patients in whom the rectum was mobilized by means of water-jet dissection. The worst lateral resection margin damage (as a result of the thermal impact, sometimes including foci of coagulative necrosis) was observed following the use of a monopolar coagulator – 1.7 to 3.0 mm deep. Lateral tissue damage was less pronounced when the rectum was mobilized with the harmonic scalpel, as compared with the monopolar coagulator. The maximal depth of tissue damage along the lateral resection margin was between 1.0 and 1.5 mm in this group.

Conclusion: Our initial experience in the use of the water-jet dissector in the process of total mesorectal excision indicates that this technique is safe and effective. The absence of lateral thermal tissue damage (primarily the pelvic vegetative nervous system elements) permits use of this type of dissection in the critical points of mesorectal excision without any risk of damage to the specified structures.

No conflict of interest.

473

Portal vein ligation vs ALPPS for colorectal metastatic liver cancer

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Background: Related data suggests that associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) effectively increases the volume of the FLR allowing for resection than conventional two-stage hepatectomy with portal vein ligation (PVL). The aim of this study is to compare the hypertrophic stimulus on the FLR and the clinical changes associated with both ALPPS and PVL.

Material and Methods: Thirty patients underwent two-stage hepatectomy at the abdominal oncology department PHERZEN MROI from January 2012 to January 2016. 25 patients with CLRM operated with two-stage hepatectomy technique were retrospectively analyzed.

Results: Twelve patients (5 male, 7 female), age 57 ± 11.6 years (39–75) were operated by portal vein ligation (PVL) techniques for 52 ± 4 months (2–10). Metastases of which the largest was 58 ± 27 mm (30–122). Nine (75%) patients received neo-adjuvant chemotherapy. The median volume of the FLR before PVL was 278.3 ± 73.6 mL (28 ± 8.3%) and 333.5 ± 69.7 mL (34.7 ± 4.9%) before the second step. After the first stage of hepatic resection FLR increased by 59.5 ± 65.9% (5–166%), p < 0.005. The second stage of hepatic resection was performed in 8 (66.7%) patients. The time between two steps of the procedure was 72.3 ± 32.8 days. There were no cases of liver failure. For stage 2, operation time was 291 ± 74.3 min and estimated blood loss 1428.5 mL (400–3000).

ALPPS was initiated in 13 patients whose mean age was 59.6 ± 6.3 (49–72) years. One patient had salvage ALPPS after failed PVL. Patients were operated for 2.8 ± 1.6 metastases of which the largest was 64.6 ± 18.8 mm (40–104). The calculated FLR volume was 313 ± 120 mL (28 ± 7%) before ALPPS-1 and 503 ± 128 mL (43 ± 7%) before ALPPS-2 (p < 0.001). The increase in FLR between the two procedures was 95.3 ± 53.6% (range: 1.4–164%, p < 0.001). The average time between the first and second stages of the procedure was 9.4 ± 1.4 days. The second surgery had a surgical time of 105.5 ± 35.5 min, an average volume of blood loss 281.2 mL (100–1000).

Twenty-three patients in both groups underwent the second stage of hepatectomy. The predominant cause for mortality of one patient in PVL group and two patients in ALPPS group between stages was postoperative liver failure. Unsuccessful left liver growth was observed in 2 (13.3%) patients after PVL-1. Two patients (13.3%) of PVL group were excluded due to the tumor progression between the stages.

Conclusion: Portal vein ligation effectively increased the future liver remnant in 6–8 weeks. However, it’s not possible to perform the second step in every third patient. The ALPPS technique can be associated with a hypertrophic stimulus on the future liver remnant (FLR) stronger than other techniques – such as portal vein ligation at early terms. Meanwhile, the ALPPS technique in patients with hepatocellular carcinoma associated with a high risk of fatal complications.

No conflict of interest.

474

Prediction and prevention of liver failure after major liver resections for liver metastases of colorectal cancer: the role of functional tests

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Background: Hepatic resection is the most important component of treatment of CRLM. The concept of remnant liver volume (RLV) has been introduced and can be assessed with CT. However, lack of correlation between morphologic hypertrophy and functional recovery fuelled the enthusiasm for functional imaging. The aim of the study is to improve the treatment results of patients with colorectal metastatic cancer of liver (CRLM) by reducing the risk of post-resection liver failure based on the assessment of liver functional reserve.

Materials and Methods: The study enrolled 2 independent branches of patients underwent surgery for CRLM in the department of abdominal oncology at the PA. Herzen Moscow Oncological Research Institute. Group I included 47 patients: in addition to the standard treatment algorithm they underwent 13C-methacetin breath test and dynamic scintigraphy of liver in the preoperative stage. Patients from the group II (n = 30) underwent standard clinical and laboratory examination, without preoperative evaluation of liver functional reserve. The level of total bilirubin, albumin and prothrombin time showed no decrease in liver function. Post-resection liver failure was established based on the 50/50 criterion when evaluated on the 5th postoperative day. According to results of preoperative liver function tests decision of changing surgical technique were made.

Results: A strong positive correlation (r = 0.75) was found between preoperative liver function reserve (LFR) determined with HBS and 13C-methacetin breath test results in patients with metastatic liver tumors. Receiver operating characteristic (ROC) curve analysis demonstrated high and good quality 13C-methacetin breath test and HBS for liver functional reserve in predicting postoperative liver failure (AUC = 0.89 and 0.78 respectively). The analysis of operational characteristics of functional tests showed absolute sensitivity of 13C-methacetin breath test (SE > 100%) and negative predictive value (NPV > 100%) in case of integrated application of diagnostic methods.

An incidence of post-resection acute liver failure by 50–50 criteria in the study group was significantly 2.2-fold lower than in the control group – 16.0% and 23.3%, respectively (p < 0.001). In conformity with functional tests results SVI–SVII bisegmentectomy was performed instead of right hepatic resection in 15 cases (31.2%). In 6 patients (12.7%) surgical approach was revised for two-stage liver resection.

Conclusion: Unique combination of preoperative 13C-methacetin breath test and dynamic scintigraphy with 13C-methacetin breath test used to perform comprehensive assessment of liver functional reserves and to estimate remnant liver function. That enables to improve postoperative results of anatomic resections in patients with liver metastases due to decreasing of incidence of postoperative liver failure.

No conflict of interest.
Individual diagnosis of chemotherapy-associated liver function impairment before surgery of hepatic colorectal metastases

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Background: Chemotherapy prior liver resection of colorectal liver metastases implies the risk of chemotherapy-associated liver injury leading to increased postoperative morbidity and mortality. The aim of this study was to evaluate the LiMAx test for diagnosis of chemotherapy-associated liver injury.

Material and Methods: Retrospective analysis of patients with colorectal liver metastases scheduled for liver resection. Preoperative assessment of liver function by biochemical parameters as well as LiMAx (Liver Maximum capacity) test. Analysis of history of chemotherapy during 12 months prior assessment including the regime, the number of cycles and the therapy-free interval.

Results: A total of 204 patients were analyzed. The majority (n=127; 62%) had received previous chemotherapy. Impaired LiMAx results were determined in 49% of patients after chemotherapy. No effect of chemotherapy on biochemical parameters was observed. The extent of LiMAx impairment was dependent on number of oxaliplatin cycles, therapy-free interval and obesity in multivariate analysis. Patients with impaired LiMAx showed regeneration during chemotherapy cessation. The history of chemotherapy did not influence the rate of resected patients, the type of resection, the incidence of postoperative complications or the survival.

Conclusions: The LiMAx test enables the non-invasive preoperative diagnosis of chemotherapy-associated liver injury. The preoperative performance of the test in patients after chemotherapy can augment the surgical strategy and timing, thus avoiding an increased postoperative morbidity.

Conflict of interest: Ownership: Martin Stockmann is the inventor of the LiMAx test and has capital interest in Humedics, the company marketing the LiMAx test. Advisory Board: Johan Lock receives revenues as medical consultant of Humedics.

Preoperated IntraPeritoneal Aerosole Chemotherapy (PIPAC) for unresectable peritoneal carcinomatosis: The French experience

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Background: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a novel technique designed for patients with peritoneal metastases of various origins that cannot benefit from surgery mainly due to the extension of the disease. Those patients, often resistant to systemic chemotherapy, have an ominous prognosis in the absence of innovative treatments. The PIPAC had promising results in the group of origin but there are few data elsewhere. The aim of the present study is to evaluate the postoperative outcome of PIPAC in the French centers that integrated this program to their peritoneal carcinomatosis management experience.

Material and Methods: All patients operated between December 2015 to June 2016 were included in this study. Different variables concerning personal, clinical, pharmaceutical and surgical factors were prospectively collected and then analyzed

Results: 45 patients underwent at least one PIPAC procedure in the mentioned period in all three French centers currently performing this operation. A total of 89 PIPAC cycles were performed for patients with a median PCI of 20. Colorectal, gastric, and ovarian cancers, as well as malignant mesothelioma, pseudomyxoma peritonei and others were encountered. The most common regimens included a combination of cisplatinum-doxorubicin, oxaliplatin and mitomycin C, respectively. The median hospital stay was 3 days. Major complications occurred in 18 patients (40.0%) and most frequent grade 3 toxicity was nausea-vomiting. Among the 31 patients presenting preoperative symptoms, at least a half presented with complete disappearance or significant improvement of the symptomatology.

Conclusions: Present results of PIPAC in the French centers are optimistic but more data is needed on specific subsets of peritoneal disease to conclude on the benefits of this procedure. A risk of postoperative morbidity even in experienced carcinomatosis centers is inherent but toxicities are acceptable. International consensus for PIPAC protocols is mandatory before more phase II and III trials should be performed.

No conflict of interest.

Role of lateral lymph node dissection in improving survival in low rectal cancer. A single institute, prospective study

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Background: The en bloc excision of primary tumor along with locoregional lymphadenectomy is the standard curative surgical treatment for rectal cancer. The development of local or locoregional recurrence is primarily due to sub-optimal surgical resection. The current standard technique of TME does not have satisfactory results in low rectal cancers. It has been stated that with the introduction of lateral pelvic lymph node dissection, local control has improved and survival is better in comparison to survival reports of surgery alone. We hypothesized that the rate of local recurrence in lower rectal cancers with LLND would be less if groups are balanced by minimization methods.

Material and Methods: This was a prospective randomized study of 240 consecutive patients who underwent curative surgery as TME + LLND or TME alone for lower rectal cancer stage II and III, located at or below the peritoneal reflection. After assessment of disease resectability and operability, the patients were randomized pre-operatively by third party with a ratio of 2:1. The groups were balanced by minimization methods for sex, tumor characteristics, age, clinical stage and pre-operative short course radiotherapy. The primary end point was disease free survival. The intra-operative and post-operative parameters as well as local control of disease were compared at the end of two years. The relation of lateral lymph node metastasis with clinic-pathologic characteristics was also analyzed.

Results: One hundred and sixty three patients were randomly allocated to TME with LLND (Group 1) and 77 patients to TME alone (Group 2), for a period of four years. Twenty patients with T1N0 tumor and 17 patients who were lost to follow up in both the groups were excluded from the study. Operation time was significantly longer in the Group 1 (median 294 min, IQR 239–357) than in Group 2 (214 min, 184–247, p <0.001). Blood loss was more in Group 1 (375 mL, IQR 305–700) than in Group 2 (305 mL, 180–500, p < 0.21) but the difference was statistically insignificant. Twenty-three (16.7%) patients had lateral pelvic lymph node metastasis in Group 1. Grade 3-4 postoperative complications were higher in Group 1 but the difference was statistically insignificant. The 2-year disease free survival in Group 1 was 94.9% and 86.2% in Group 2 (p = 0.942, d.f = 1, p = 0.002). Patients with metastatic lateral pelvic lymph nodes had a lower DFS in comparison with non-metastatic PLN in Group 1 (p = 4.113, d.f = 1, p = 0.042).

Conclusion: Tumor location, transmural extension, presence of mesorectal lymph nodes in lower rectum and differentiation are significant risk factors for lateral lymph node metastasis. Lateral pelvic lymphadenectomy with TME in lower rectal cancer improves DFS. Lateral lymph node metastasis is an important predictor of local recurrence and DFS in patients with low rectal cancer.

No conflict of interest.

A new effective enhanced recovery pathway after liver surgery using the LiMAx test – results from a multicenter prospective randomized controlled trial

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Background: Enhanced recovery after surgery (ERAS) protocols have been reported as an effective strategy to improve postoperative outcome after liver surgery, but liver function has not been incorporated into ERAS so far. This study presents a new approach implementing liver function as selection criteria for ERAS.
Methods: The LiMax test can validly determine liver capacity and has been successfully integrated in clinical management in liver surgery. A prospective randomized controlled trial (RCT) was conducted in six centers between 2013 to 2015 including patients with major open liver resection. Patients were randomized into LiMax group (with pre- and post-operative LiMax test) or control group. Stable patients with sufficient residual liver function (LiMax >150 μg/kg/h) were directly transferred to general ward to enable LiMax-ERAS.

Results: 148 patients were randomized. 80% of patients had malignant tumours and the majority of these (61%) had hepatocellular carcinoma (HCC). The rate of complications (in both groups) at 30 days was 8% with no statistical difference. In the LiMax group, the total length of stay (10 vs. 13 days, p=0.01). No readmissions were noted in the LiMax group (13.6% vs. 31.7%; p <0.007).

Conclusion: LiMax test controlled ERAS is safe and effective and could significantly improve the postoperative management after liver resection.

Conflict of interest: Ownership: Martin Stockmann is the inventor of the LiMax test and has capital interest in Hemedics, the company marketing the LiMax test. Other Substantive Relationships: Johan Lock receives revenues as medical consultant of Hemedics.

Abstracts

478A

POSTER

Is hepatic volumetry sufficient for avoiding postoperative liver failure? A correlative study between future liver remnant volume and mebrofenin scintigraphy function after major hepatic resections

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Introduction: Future liver remnant (FLR) volumetry after hepatectomy is the most frequent method of prevention of postoperative liver failure (LP) in the current practice. S-1-methylbenzene-2,3-dicarboxylic acid (Mebrofenin) scintigraphy (ScMeb) is a novel technique that estimates functional liver remnant after major hepatectomy. In the future the latter may become more useful than volumetry particularly in patients that received several lines of chemotherapy. The aim of this study is to evaluate possible correlations between the hepatic volume and function as measured by ScMeb as well as their clinical implications.

Method and Material: All patients that underwent a ScMeb before major hepatectomy between February 2014 and June 2016 were included in the present study. For the total number of 51 patients the liver volume-function correlation was calculated. For the patients that had a low ScMeb extraction rate (VS <2.69%/min/ml), portal embolization (PVE) was performed and the planned major hepatectomy was not performed in the absence of a sufficient vs after PVE. For dissected patients, morbidity and mortality were recorded according to Clavien-Dindo classification.

Results: 69% patients had liver metastases and 44% had been treated with triple chemotherapy +/- targeted therapy. For preoperative ScMeb, the CVP was satisfactory (r=0.8401). Globally, 29% of all patients presented with discordant volume-function measurements: 26% presented with superior liver function when compared with volumetry while the FLR volume was inferior in 30%. 3% had an insufficient function despite a good volume. In the resected patients subgroup (n=33), 14 were discordant with a volume <30%. Nevertheless, no significant difference was noted in terms of liver failure rates and morbidity between the discordant and non-discordant patients. Liver failure was only noted in 2 patients.

Conclusion: ScMeb seems to be a more reliable examination than volumetry before hepatic major resection. It allowed us to perform major hepatic resections in patients where the FLR volumetry would have been a counter indication. Larger studies are needed in order to confirm these results.

No conflict of interest.

479

POSTER DISCUSSION

Prognostic value of pre-operative neutrophil–lymphocyte ratio in predicting survival in lower gastrointestinal malignancy

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Background: Numerous pre-operative screening tools have been reported to aid in determining prognosis of colorectal cancer, but have poor severity prediction and lack accurate estimation of postoperative complications. Assessment of the hosts inflammatory response to the tumour may be easier in clinical practice. The ability of tumours to invade and metastasise is dependent both on the intrinsic characteristics of tumour cells and on the tumour microenvironment. The systemic inflammatory response also comprises changes in the relative levels of circulating white blood cells. It is widely accepted that neutrophilia is accompanied by a relative lymphocytopenia. The neutrophil–lymphocyte ratio (NLR) has been suggested as a simple index of systemic inflammatory response in critically ill patients. We hypothesised that NLR could be used as a prognostic indicator in colorectal cancer patients.

Materials and Methods: Five hundred and seven patients who underwent a colorectal resection for malignancy over a 5-year period (January 2009-December 2013) were evaluated. Demographics, types of surgical intervention, biochemistry, tumour grading and staging and five-year survival were noted.

Results: A total of five hundred and seven patients were included in the study of which (n =296) were male. Median (range) age was 70 (27–95) years. There was no statistical difference in NLR across tumour stage and lymph node positivity. Median NLR was statistically different regarding elective vs. emergency resection (3.5 vs. 6.4, p <0.0001, Mann–Whitney). A receiver operating characteristic (ROC) cutoff value of >3.61 was associated with higher 5-year mortality rate (sensitivity 65%, specificity 58%, p <0.0001).

Conclusion: We advocate that NLR is a useful adjunct in predicting survival in colorectal cancer.

No conflict of interest.
significantly worse OS, when compared to patients with desmoplastic type HGP. The obtained results can be used to improve prediction of survival outcome after resection of CRLM. **No conflict of interest.**

**POSTER**

**480**

Reassessing, revisiting and redoing incomplete lymph nodal clearance in colon cancer: our experience

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Background: Colon cancer accounts for almost 70 percent of all GI malignancies. Traditionally the surgeries of colon cancer (Colectomies) are considered to be a resident's operation in most of the places. The oncologic outcome of colon cancer depends on the complete clearance of tumor as well as removal of the lymph node bearing vascular pedicles. The colonic mesentery or mesocolon contains the vascular and lymphatic drainage systems of the colon and therefore adequate clearance with central vascular ligations is a mandatory part of surgical oncology surgery in rectum. We aimed to emphasize on the importance of proper lymphatic clearance in colon cancer.

Materials and Methods: We have done revision surgeries on few patients of colon cancer who were initially operated outside with subtotal lymph node clearance.

Results: Case 1: 65 years male underwent emergency right hemicolecotomy for hepatic flexure growth at a rural hospital. Biopsy showed adenocarcinoma of colon, 4 LN was isolated (pT3N0M0). He received 6 cycles of adjuvant chemotherapy(CapeOx). Pre-Chemo CEA was 2.18 but CEA started rising by 5th Cycle of chemo and reached 18.92 after sixth cycle. PET scan showed enlarged LN at ileo-colic pedicle with uptake. He underwent revision Colectomy with central vascular ligation (ileocolic and middle colic). Final Biopsy: 5/18 LN showed metastatic adenocarcinoma, ileo-colic pedicle.

Case 2: 42 years male underwent elective right hemicolecotomy at a rural hospital. Biopsy: Adenocarcinoma pT3N0M0. He was referred to surgical oncology department for completion surgery. CECT showed intact ileo-colic pedicle. He underwent revision colectomy with central vascular ligation (ileocolic vessel). Final Biopsy: 1 out of 7 nodes showed metastatic deposits.

Case 3: 69 years old female underwent sigmoid colectomy with primary anastomosis in Bangladesh. Biopsy: Adenocarcinoma T2N0(U4)/M0. She was referred to surgical oncology department. CECT showed enlarged LN at the IMA pedicle. She underwent revision surgery (Anterior Resection) with ileo-colic ligation at the root. Final biopsy showed all LN reactive (0/11).

Patient escaped from adjuvant chemotherapy.

Conclusion: Colonic lymph nodes tend to follow the arterial supply; hence complete mesocolic excision (CME) with central ligation would remove the highest draining nodes that may harbor occult metastases. The revision surgery to remove residual lymph node and lymph node bearing tissue helps to detect the actual stage of the disease and simultaneously increase chance of cure by removing the affected LN. Adjuvant chemotherapy can also be avoided in some patients if the final staging is completed and showed no LN metastasis. Thus revision surgery for suboptimally operated colon cancer has oncological benefits.

**No conflict of interest.**

**POSTER**

**480A**

Identifying best performing hospitals in colorectal cancer care; is it possible?

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Background: Comparing outcomes of hospitals and learning from best practice can be useful for improving quality of care. However, reliably identifying best performing hospitals based on outcomes is challenging. This study aims to assess whether high performing hospitals can be identified for individual outcomes and whether good performance on several outcomes is clustered in specific hospitals in colorectal cancer care.

Methods: Data were derived from the Dutch Surgical Colorectal Audit. Outcomes considered were complications (complication and in-hospital stay of >14 days, re-intervention, or death), mortality, irradical resections (colon), Circumferential Resection Margin (CRM) involvement (rectum) and failure to rescue (FTR, death after a serious complication). To include uncertainty in rankings we used random effect logistic regression models to calculate the expected rank of each hospital for each outcome. We calculated rankability, which can be interpreted as the percentage of between-hospital variation in outcome that might be due to quality of care instead of chance, as a measure of the reliability of ranking on that outcome. We considered rankability of <50% as poor, 50–70% as moderate and >70% as high. In addition we assessed whether high performance across outcomes was correlated in specific hospitals. We considered correlation below 0.40 as weak, 0.40–0.59 as moderate and above 0.60 as strong.

Results: We included 11,376 patients treated in 84 hospitals that received surgical treatment for colorectal carcinoma in 2015. Rankability of complications was highest after both colon (57%) and rectal (41%) surgery. Rankability of mortality was 17% after colon and 0% after rectal surgery. Rankability of FTR was lowest both groups. The tables show that overall correlation of outcomes is low to moderate.

<table>
<thead>
<tr>
<th>Colon</th>
<th>Complications</th>
<th>Serious complications</th>
<th>Mortality</th>
<th>Irradical resection</th>
<th>FTR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Serious complications</td>
<td>0.59</td>
<td>0.59</td>
<td>0.35</td>
<td>1.00</td>
<td></td>
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<tr>
<td>Mortality</td>
<td>0.04</td>
<td>0.04</td>
<td>0.35</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Irradical resection</td>
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<td>-0.11</td>
<td>-0.02</td>
<td>-0.03</td>
<td>1.00</td>
</tr>
<tr>
<td>FTR</td>
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<td>-0.24</td>
<td>-0.07</td>
<td>0.85</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rectum</th>
<th>Complications</th>
<th>Serious complications</th>
<th>Mortality</th>
<th>CRM</th>
<th>FTR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious complications</td>
<td>0.62</td>
<td>0.62</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>0.12</td>
<td>0.12</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRM</td>
<td>-0.17</td>
<td>-0.17</td>
<td>-0.19</td>
<td>0.06</td>
<td>1.00</td>
</tr>
<tr>
<td>FTR</td>
<td>0.00</td>
<td>0.00</td>
<td>0.11</td>
<td>0.94</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**Discussion:** Poor to moderate rankability of outcomes indicates that best performing hospitals cannot be reliably identified for most outcomes. A weak to moderate correlation across different outcomes indicates that high performance on several outcomes does not cluster in specific hospitals. Rankings were most reliable on the outcome complications and least reliable on mortality and FTR, but FTR may be a more clinically relevant outcome than complications for specific feedback. The balance between reliability and relevance is vulnerable when measuring quality of colorectal cancer care based on outcomes.

**No conflict of interest.**

**POSTER**

**481**

ONCOPRE: a new chemotherapy benefit prediction algorithm to assist with treatment decision making

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Background: Electronic support tools can facilitate treatment decisions and inform care. Existing web-based tools such as Adjuvant! Online and Numeracy are frequently used by clinicians to estimate the relative benefits of adjuvant therapy to guide conversations with patients. However, existing applications neither consider more contemporary disease characteristics (e.g. microsatellite instability) nor operate on modern handheld devices.

Methods: A novel adjuvant chemotherapy benefit calculator for early stage colon cancer was designed to address the limitations of existing platforms. It is based on historical outcomes, epidemiological data, and results of landmark trials that originally demonstrated the benefits of various adjuvant chemotherapy regimens on outcomes. We compared estimates generated by our calculator with those derived by existing tools and validated the findings with real world population-based data from 7 centers in Canada.

Results: An algorithm based on various patient factors, tumor characteristics, and prognostic biomarkers such as MSI, was developed that predicted 5-year disease-free and overall survival (OS) in colon cancer.
It provides unique predictions dependent on the selected disease stage and adjuvant treatment regimen. Results demonstrate that our outcome estimates compare favorably with survival findings from landmark clinical trials and those from population-based settings. Further, our estimates are more optimistic and precise when compared to historical data and estimates generated by existing calculators (see table).

Conclusions: ONCOPRE (www.oncopre.com/beta) represents a new decision support tool that can assist in adjuvant therapy decision-making in colon cancer. Calculators must consider biomarkers as they improve capacity for prediction. Our platform serves as a potential model on which to develop prediction tools for other cancers.

No conflict of interest.

482 POSTER Simultaneous, but not consecutive combination with folinate salts potentiates 5-fluorouracil antimutator activity in vitro

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Background: The combination of 5-fluorouracil (5-FU) and folinate salts has shown better clinical responses compared to the fluoropyrimidine alone. However, the simultaneous 5-FU and calcium levofolinate (CaLV) mix and infusion is impossible due to drug precipitation. Therefore, a sequential administration of CaLV followed by 5-FU was adopted in the clinical routine. At the beginning of the 2000s, disodium levofolinate (NaLV) was available which can be easily administered simultaneously with 5-FU instead. The aim of this study was to investigate if there were pharmacological differences between the simultaneous administration of folinate salts (1 h before) followed by 5-FU and the simultaneous administration of both drugs in vitro settings.

Materials and Methods: Proliferation and apoptotic assays were performed on human colon cancer (HT-29, Caco-2) cell lines exposed to 5-FU, CaLV or NaLV, or their simultaneous and sequential combination for 24 h, respectively. The synergistic, additive or antagonistic effects of the combinations were evaluated by the methods of Chou based on the combination index. Apoptosis was analyzed using the Cell Death Detection ELISA Plus Kit. Thymidylate synthase (TYMS) and reduced folate carrier (SLC19A1) gene expression was performed with realtime polymerase chain reaction and the quantification was obtained using the ΔΔCT calculation.

Results: As expected, the simultaneous combination of folinate salts and 5-FU was synergistic or additive in a 24 h treatment in both cell lines. In contrast, the sequential combination of both folinate salts (1 h before) and then 5-FU was surprisingly antagonistic in a 24 h treatment. Simultaneous NaLV+5-FU maintained its advantage, differently from CaLV+5-FU, even after 72 h of treatment. The sequential combination of NaLV or CaLV followed by 5-FU confirmed to be antagonistic also at 72 h. Moreover, the simultaneous combination (but not the sequential one) of 5-FU and NaLV or CaLV significantly increased the percentages of apoptotic cells and the inhibition of TYMS gene expression following 24 h exposure. On the other side, the sequential combination (but not the simultaneous one) of 5-FU and CaLV or NaLV significantly inhibited the SLC19A1 gene expression after 24 h treatment.

Conclusions: The simultaneous in vitro 24 h-treatment of 5-FU and both folinate salts formulations potentiated the antiproliferative effects of the drugs. This synergism was completely lost in the sequential combination at 24 h and 72 h of treatment. These preliminary in vitro findings seem to suggest that folinate salts are better given simultaneously in a single i.v. infusion (i.e. NaLV) or with the aid of CaLV rather than to anticipate their administration of 1 or 2 h for practical reasons.

Conflict of interest: Corporate-sponsored Research: Unconditioned grant from Medac Pharma Italia to G.B.

483 POSTER CXCR4 promotes adhesion capacity and activates the AKT signalling pathway in colorectal cancer cells

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Background: Colorectal cancer (CRC) is one of the most common cancers over the world. The major cause of CRC death is tumour metastasis to the liver and other organs. CXCR4 expression is positively associated with recurrence and poor survival of CRC patients. The axis of CXCR4/SDF-1 has been reported to show an important role in some cancer metastasis. The aim of this study was to explore the role of CXCR4 in the adhesive capacity of CRC cells, which is essential for CRC metastasis.

Materials and Methods: The technique of CRISPR/Cas9 genomic editing was used to knockdown CXCR4 on Colorectal cancer cell lines. Following electroporation of the sequence-verified CRISPR plasmids, the knockdown of CXCR4 was validated using T7EN1, FACS and Western Blotting, respectively. Cell proliferation was analysed using Alamar Blue assay following treatment. CRC cell adhesion to HUVEC cells was accessed by using DIO cell-labelling solution. CRC cell adhesion to Matrigel was determined using the Crystal violet assay. Cell migration and invasion were evaluated using transwell insert assays with or without Matrigel coating. The Electric Cell-Substrate Impedance Sensing (ECIS) system was also used to monitor cell behaviours.

Results: Knockdown CXCR4 slightly increased proliferation of HT115 CRC cells with time dependence until cells reached confluency. This knockdown however decreased the adhesion of cancer cells to HUVEC endothelial cells and Matrigel, respectively. The decrease of adhesion capacity was also confirmed by using the ECIS (Electric Cell-Substrate Impedance Sensing) system. The CRISPR-mediated CXCR4 knockdown reduced the level of total and phosphorylated AKT (ser473) proteins. The upregulation of ERK, MEK and IGF1R genes by CXCR4 knockdown was eliminated in the presence of stromal development factor 1 (SDF1), the CXCR4 ligand.

Conclusions: CXCR4 plays a role in promoting adhesion capacity of CRC cells, probably via activation of the inactivation of AKT signalling pathway. SDF-1 is able to eliminate the upregulation of ERK, MEK and IGF1R genes by CXCR4 knockdown, suggesting that the level of SDF-1 in tumour microenvironment is very crucial for the function of CXCR4.

No conflict of interest.

484 POSTER DISCUSSION Evaluation of guideline adherence in colorectal cancer treatment in The Netherlands: a survey among medical oncologists by the Dutch Colorectal Cancer Group (DCCG)

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1 Academic Medical Center, Medical oncology, Amsterdam, Netherlands; 2 Comprehensive Cancer Organisation INKL, Research, Eindhoven, Netherlands; 3 University Medical Center Utrecht, Medical oncology, Utrecht, Netherlands

Background: Clinical guidelines are generated to preserve high quality evidence-based care. In 2014, several adjustments for the systemic treatment in the adjuvant and metastatic setting were introduced in the Dutch colorectal cancer guidelines. Data on the implementation of guidelines into clinical practice are scarce, despite the fact that guideline adherence is known to prevent over- and undertreatment and is related to survival. Therefore, the aim of this survey is to investigate adherence to the Dutch guidelines for the systemic treatment in high risk stage II and stage III colon cancer and metastatic colorectal cancer.
**Material and Methods:** In all Dutch hospitals (n=88) one medical oncologist involved in colorectal cancer care was approached to participate. An online survey was conducted regarding the local standard of care for adjuvant chemotherapy in high-risk stage II and III colon cancer and for treatment of metastatic colorectal cancer. Frequency tables were provided for categorical variables and Fischer’s exact tests were performed to compare differences in guideline adherence according to hospital type (academic versus teaching versus regional hospital).

**Results:** The overall response rate was 70% (62/88). Adherence to guidelines was at least 60% in all settings that were presented. In high-risk stage II and stage III colon cancer, reported treatment strategies agreed with the national guidelines in 66% and 82% of hospitals, respectively. Disparities mainly concerned the implementation of mismatch repair status in treatment selection which resulted in overtreatment of 28% of hospitals in high risk stage II and 13% in stage III colon cancer. The main disparity in the treatment of metastatic disease concerned the use of targeted drugs as part of first-line treatment according to the guidelines. Bevacizumab was not administered in two thirds of hospitals. Adjuvant treatment in high-risk stage II and III colon cancer as observed in the implementation of mismatch repair status in the selection of patients with initially unresectable but potentially resectable metastases. Bevacizumab was not administered in two thirds of hospitals. Adjuvant treatment in high-risk stage II and III colon cancer as observed in the implementation of mismatch repair status in the selection of patients with initially unresectable but potentially resectable metastases. There was no difference in guideline adherence was observed between the different types of hospital.

**Conclusions:** Guideline adherence as reported by medical oncologists in The Netherlands leaves room for improvement. Suboptimal adherence was observed in the implementation of mismatch repair status in the selection of patients with initially unresectable but potentially resectable metastases in high-risk stage II and stage III colon cancer as well as the use of targeted drugs as part of first-line treatment regimens in metastatic patients. Reasons for nonadherence have not been enough revealed, but unawareness or disagreement with the guidelines with or without financial restrictions are speculative explanations. Our results demonstrate that more attention should be paid to guideline adherence in clinical practice, and in case of nonadherence to underlying causes.

**Conflict of interest:** Corporate-sponsored Research: This work was funded by an unrestricted grant from Amgen, Merck and Roche.

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**Poster Session, Saturday 28 January 2017 Abstracts**

**485 POSTER**

Tolerability of the oral fluoropyrimidine S-1 after hand-foot syndrome-related discontinuation of capecitabine in Western cancer patients

R.J. Kwakman 1, A. Baars 2, H. Boot 3, W. Smitt 4, S. WINther 5, P. Pfeiffer 5, C. Punt 7, A.M.C. Medical Oncology, Amsterdam, Netherlands; 2Hospital Gelderse Vallei, Department of Medical Oncology, Ede, Netherlands; 3The Netherlands Cancer Institute, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands; 4Jeroen Bosch Hospital, Department of Medical Oncology, Den Bosch, Netherlands; 5Odense University Hospital, Department of Medical Oncology, Odense, Denmark

**Background:** The oral fluoropyrimidine S-1 has comparable efficacy to capecitabine, but is associated with a lower incidence of hand-foot syndrome (HFS). Data on the tolerability of S-1 in patients experiencing severe capecitabine-induced HFS are not available. We retrospectively assessed the tolerability of S-1 after HFS-related discontinuation of capecitabine.

**Patients and Methods:** Medical records of patients treated with S-1 were reviewed to confirm previous HFS-related intolerance of capecitabine. The primary outcome was the incidence of any grade HFS in patients receiving S-1 after prior intolerance to capecitabine. Secondary outcomes were grade 3 HFS, other S-1-related adverse events, and S-1 dose reductions.

**Results:** A total of 52 patients with a diagnosis of metastatic colorectal cancer (n=29,56%), advanced pancreatic cancer (n=13,25%), metastatic breast cancer (n=7,13%), and stage III colon cancer (n=3,6%) were identified. Capecitabine had been administered as monotherapy (n=18,35%) or in combination schedules (n=34,65%), and dose reductions and delays had been applied in 26 (50%) and 21 (40%) patients, respectively. Reasons for capecitabine discontinuation were grade 2 HFS in 15 (29%) and grade 3 HFS in 37 patients (71%). S-1 was administered at full recommended dose in 49 patients (94%). Forty-nine patients (94%) experienced a lower grade of HFS after switching to S-1, with complete resolution of HFS-related symptoms in 29 patients (56%), despite the fact that S-1 was started without waiting for capecitabine-induced symptoms to resolve in 33 (67%) patients. Other S-1-related toxicities included diarrhea (n=15,29%) and fatigue (n=20,38%), but were generally limited to grade 1–2.

**Conclusion:** S-1 is a feasible and useful alternative for patients experiencing capecitabine-induced grade 2–3 HFS.

**Conflict of interest:** Advisory Board: Prof. dr. C.J.A. Punt (Servier, Nordic Pharma); Prof. dr. P. Pfeiffer (Lilly, Roche, Merck-Serono, Amgen, Celgene, Taiho, Servier, Nordic Pharma). Corporate-sponsored Research: Prof. dr. P. Pfeiffer (Lilly, Roche, Merck-Serono, Amgen, Celgene, Taiho, Servier, Nordic Pharma). Other Substantive Relationships: Drs. J.J.M. Kwakman (honorarium, Nordic Pharma).

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**Poster Session, Saturday 28 January 2017 Abstracts**

**486 POSTER**

Systemic therapy as adjunct to cytoreductive surgery with HIPEC for peritoneal metastases of colorectal cancer: a systematic review

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**Background:** Both systemic therapy and cytoreductive surgery with HIPEC are increasingly used for colorectal peritoneal carcinomatosis. However, there is no consensus on the value and risks of perioperative systemic therapy as adjunct to cytoreductive surgery with HIPEC for colorectal peritoneal carcinomatosis. This systematic review evaluated current evidence.

**Methods:** In August 2016, a systematic search was conducted in PubMed/MEDLINE, EMBASE, and Cochrane. Timing of systemic therapy was classified as neoadjuvant, adjuvant, or perioperative. Systemic therapy regimens were classified as single agent chemotherapy, combination chemotherapy, or combination chemotherapy with targeted therapy. Outcomes were OS and severe postoperative complications.

**Results:** Thirteen observational studies, involving 1011 patients, were included. Five studies reported varying results on neoadjuvant systemic therapy and overall survival: no survival benefit (n=1), survival benefit (n=2), and superiority of combination chemotherapy with targeted therapy to combination chemotherapy (n=2). All four studies reporting on adjuvant systemic therapy did not show a significant survival benefit. Two studies reported varying results on perioperative systemic therapy and overall survival: survival benefit (n=1), and superiority of combination chemotherapy and targeted therapy to single agent chemotherapy (n=1). Five studies reported varying results on neoadjuvant systemic therapy and severe postoperative complications: no increase (n=4), and increased postoperative complications in patients receiving neoadjuvant systemic therapy with bevacizumab compared to neoadjuvant systemic therapy without bevacizumab (n=1).

**Limitations:** The low methodological quality of included studies, in which the observational design lead to a substantial risk of allocation bias, selection bias, and heterogeneity of included patients and interventions.

**Conclusions:** Currently available evidence, which is of low quality, suggests a role for neoadjuvant combination chemotherapy with targeted therapy, questions adjuvant systemic therapy as standard of care, and supports future randomised studies.

**No conflict of interest.**

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**487 POSTER**

A phase III dose finding study evaluating the safety and tolerability of cetuximab in patients with metastatic colorectal cancer deemed unsuitable for doublet/triplet chemotherapy: results of the phase I study

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**Background:** Colorectal cancer (CRC) is the 2nd most common cause of cancer death. In the UK the median age of death from CRC is 77 years with 60% of deaths occurring after the age of 75 years. Frailty and toxicity occur more frequently in older patients and consequently treatment is often limited to fluoropyrimidine monotherapy. Aflibercept (VEGF-TRAP), known as ziv-aflibercept in the United States, is a composite human decoy receptor with high affinity for VEGF-A, VEGF-B and Placental growth factor. Hence aflibercept is an attractive partner to cetuximab in the treatment of patients deemed unsuitable for doublet/triplet cytotoxic chemotherapy.

**Methods:** Eligible patients with metastatic CRC refractory to standard chemotherapy were enrolled in a 3 + 3 dose escalation cohort to identify the maximum tolerated dose (MTD). Cetuximab was administered twice daily on days 1−14 of a 21 day cycle at a dose of 825mgm2 in cohort
1 and 1000 mg/Kg in cohort 2. Aflibercept was administered at 6mg/Kg on day 1 of each cycle. The recommended phase II dose (RP2D) cohort was expanded to a total of 10 patients. CT assessment of response was performed every 12 weeks.

Results: A total of 17 patients were recruited into the study. In cohort 1, 7 patients were recruited [mean age 55.2 (range 38–80) years; 4 male, 3 female; performance status (PS) 0–2, 1–5]; 1 patient withdrew prior to the first assessment. Dose limiting toxicity (DLT) was observed in 1 patient (CTCAE Grade 3 hypotension). In cohort 2, 10 patients were recruited [mean age 65.2 (range 56–73) years; 4 male, 6 female; PS 0–4, 0–6] with DLT observed in 1 patient (CTCAE Grade 3 hypotension). The RP2D was capicabine 1000 mg/m² on days 1–14 and aflibercept 6 mg/Kg on day 1. The regimen was well tolerated with no unexpected toxicities observed. Partial response was observed in 0 (0%) patients with stable disease in 3 (17.6%) patients as best response. At the time of analysis 2 patients had died at 14 and 339 days. In the 15/17 who had not died at this analysis, median follow-up time was 182 days.

Conclusion: Administration of capicabine and aflibercept has an acceptable toxicity profile in a chemo-refractory population with encouraging activity observed. Recruitment in the phase II population of first-line treatment in frail patients unsuitable for doublet/tripllet chemotherapy is ongoing.

Conflict of interest: Advisory Board: PJR, MS, RHK, and JB participated in an advisory board for Sanofi. Other Substantive Relationships: PJR received an Educational Grant from Sanofi to support this study.

488
Evaluating the potential of dabigatran etexilate in treatment of metastatic colon cancer
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Background: Clinical observations have indicated that the coagulation system is activated in patients with colon cancer leading to generation of thrombin which can vitally contribute to the development of colon cancer. Functional thrombin receptor Protease Activated Receptor-1 is aberrantly expressed in colon cancer cells and is involved in thrombin-induced effects on proliferation and cell motility. We evaluated the effect of oral direct thrombin inhibitor dabigatran etexilate (DE) in the treatment of metastatic colon cancer in 1,2-dimethylhydrazine (DMH) induced rat colon carcinogenesis model, unexplored till date.

Materials and Methods: All animal studies were conducted after due approval by ethics committee, as per national regulations. Ninety female Sprague Dawley rats, 6–8 weeks old of weight range 160–200 gm were divided into 5 groups as per Table 1.

Table 1. Grouping and treatment

<table>
<thead>
<tr>
<th>No</th>
<th>Groups</th>
<th>Treatment</th>
<th>No. of animals</th>
<th>Sacrifice time points (End of week 8, 12 and 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Saline</td>
<td>Saline</td>
<td>18</td>
<td>6, 6 and 6</td>
</tr>
<tr>
<td>2</td>
<td>Positive control</td>
<td>DMH only</td>
<td>18</td>
<td>6, 6 and 6</td>
</tr>
<tr>
<td>3</td>
<td>DE treated</td>
<td>DMH+DE</td>
<td>18</td>
<td>6, 6 and 6</td>
</tr>
<tr>
<td>4</td>
<td>Sfu treated</td>
<td>DMH+Sfu</td>
<td>18</td>
<td>6, 6 and 6</td>
</tr>
<tr>
<td>5</td>
<td>DE+Sfu treated</td>
<td>DMH+DE+Sfu</td>
<td>18</td>
<td>6, 6 and 6</td>
</tr>
</tbody>
</table>

Pre-sacrifice parameters included measurement of body weight, food and water consumption and Fecal Occult Blood Test (FOBT). Post-sacrifice parameters included gross examination of colon, colonic edema measurement, biochemical estimations like Vascular Endothelial Growth Factor (VEGF) and Extracellular signal-regulated kinases (ERK/MAPK), Epithelial Mesenchymal Transition (EMT) parameters like E-cadherin, N-cadherin and Twist, and Mammalian target of Rapamycin (mTOR), histopathology and immunohistochemistry.

Results: DE had no effect on body weight, food and water consumption. FOBT was tested negative for all study groups. Post sacrifice, DE markedly reduced the gross carcigenogenesis changes as compared to positive control. DE significantly reduced the colonic edema as compared to Group 2. Biochemical estimations revealed that DE significantly reduced levels of VEGF and ERK/MAPK in colonic homogenates. DE treatment displayed significant increase in E-cadherin and reduction in N-cadherin. Twist and mTOR expression compared to DMH. Histopathological findings revealed that DE reduced the adenocarcinomous changes while Immunohistochemical findings showed that DE increased E-cadherin and reduced N-cadherin expression in comparison with positive control.

Conclusion: Oral administration of DE inhibits both invasion and metastasis of malignant colonic tumors, suggesting that it may be favourable in not only inhibiting thrombotic events in cancer patients, but also as adjunct therapy to treat malignant colonic tumors, subject to further clinical evaluation.

No conflict of interest.

489
Modulation of platelet levels by an anti-IL-1α antibody (MABp1) in advanced colorectal cancer patients
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Background: In a Phase III study, treatment with MABp1, an anti-IL-1α antibody, has demonstrated 76% relative increase in clinical response rate versus placebo in end-stage colorectal cancer patients. In addition to the primary end point (improved health status as measured by lean body mass and pain, fatigue and appetite), secondary measures included monitoring of pharmacodynamic parameters such as serum IL-6 levels and platelet counts. With respect to these secondary endpoints, patient receiving MABp1 treatment showed decreased serum IL-6 levels as well as platelet counts. IL-1α is known to upregulate IL-6, a known inducer of megakaryocytic topoiosis. The reduction in IL-6 and platelet counts in patients treated with IL-1α suggests that platelet-derived IL-1α may be both a target of antibody therapy and play an important role in regulation of megakaryocytosis. While the role of platelet-derived IL-1α has been established in animal models for vascular endothelial cell activation and the pathogenesis of cerebrovascular inflammation, few studies have even confirmed the expression of IL-1α on human platelets. Here we present findings to confirm the expression of platelet IL-1α on platelets within a healthy human population.

Material and Methods: Platelets from human blood were isolated on a discontinuous iodixanol density gradient. Platelets were stained with MABp1 or isotype control before and after activation with thrombin and lipopolysaccharide, and observed by confocal microscopy and flow cytometry. In addition, the isolated platelets were lysed and the membranes were isolated by ultracentrifugation. The IL-1α on the membrane was immunoprecipitated using a pro-IL-1α antibody. The membrane proteins were resolved on a SDS-PAGE and human IL-1α was detected using various antibodies. The protein was digested with trypsin, and the isolated peptides were subjected to peptide mass fingerprinting.

Results: Our work has confirmed the presence of IL-1α on the surface of platelets.

Conclusions: Based on our findings and results from previous studies, platelets appear to play an important role in the development of important conditions, including cancer. We confirm that IL-1α is present on human platelets and that this may represent an important factor in regulating platelet thrombocytosis and consequent pathology in cancer.

No conflict of interest.

490
Do microRNAs dictate response to drugs in colon cancer patients?
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Background: Using microRNA expression data and patient-derived xenograft (PDX) based drug-response information; we examined the ability of microRNAs to predict response to a series of standard cancer therapies in colon cancer.

Material and Methods: As part of the Oncotrack study (http://www.oncotrack.eu/), microRNA expression data were generated for a set of 96 colon cancers. Of these, 75 were primary colon tumours and 21 were liver metastases from the colon. Additionally, a subset of patient tumours were successfully transplanted into mice to obtain 38 PDX or patient-derived xenografts. These PDX models were treated with 14 different anti-cancer drugs including routine cancer treatments such as 5-flurouracil and irinotecan. The PDX models were classified as “responders” or “non-responders” based on a cut-off of 50% for reduction in tumour size on day ‘1’ (maximum 4 weeks) versus day ‘0’. Then, we performed a differential
expression looking for microRNAs that were significantly up or over expressed in "responders" relative to "non-responders". Where there was a significant result, microRNAs were mapped to validated (Tier 1) or predicted (Tier 2) target genes. The target list for each miR was then analysed for enrichment pathways that may impound on sustaining colorectal cancer.

**Results:** The number of responders and non-responders varied across drugs, which reduced our power to detect differentially expressed microRNAs. We found significantly up/down-regulated microRNAs in responders to 3 drugs. The drug with the most microRNA associated with response, Irinotecan, has two up- and three down-regulated miRs in responders. Of these, hsa-miR-330−3p, which is upregulated in responders to irinotecan has validated targets confirmed by three different miR-target databases (mirRecords, mirTarBase, Tarbase). The validated targets of miR-330 included genes: AGO1, CASP11, CD44, CDC42, FAM168B, HIST1H2AC, all members of the histone H3 family, NCS1, NTRK3, NUP153, PKFBX3, PKIR34, PKM, PRMT8, RPS2, RPS4X, SH3GL2, SLIT2, SNRPD3, THRA, TRRAP, TUBB, USP9X, VMA21 and ZNFM3. An enrichment analysis performed on this list of genes using DAVID functional annotation tool (https://david.ncifcrf.gov/summary.jsp) revealed a role for hsa-miR-330−3p in gene silencing, negative regulation of gene expression, nucleosome assembly and transcriptional mis-regulation in cancers. We found that irinotecan is the most effective drug in PDx models of primary and metastatic colon cancer. We hypothesise that this could be affected by the upregulation of miR-330−3p, which suppresses histones.

**No conflict of interest.**

**491 POSTER**

**ISO-005: An open-label, multiple-site, dose cohort, phase III study in patients with stage IV colorectal cancer**

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**Background:** Treatment of Colorectal Cancer, often include 5-Fluorouracil (5-FU). 5-FU is always combined with a folate, such as Leucovorin (LV), which significantly enhances the therapeutic effect of 5-FU. As LV is a prodrug and needs enzymatic activation intracellularly, treatment with the active substance would be preferable since the activation capacity shows great intra- and inter-individual variability which might lead to insufficient and unpredictable response of 5-FU based therapies in patients. [6R]-MTHF is the key metabolite of LV. The metabolism of LV to [6R]-MTHF is genetically regulated. There is a statistically significant correlation between levels of gene expression of certain folate associated genes and the rate of metabolic activation.

IV administration of the substance [6R]-MTHF-HS results in higher concentration levels of [6R]-MTHF in normal and tumour tissue compared to equimolar administration of LV. It is therefore hypothesised that administration of [6R]-MTHF-HS will result in high, and more consistent, intracellular concentrations of [6R]-MTHF in all patients (particularly in patients with low levels of folate-relevant gene expression) compared to LV administration, and will thereby improve the prognosis of mCRC patients treated with 5-FU.

**Material and Methods:** ISO-CC-005 is a multicenter phase II/III study in patients with Stage IV CRC eligible for 5-FU/LV therapy alone or in combination with oxaliplatin or irinotecan, or with without bevacizumab. 63 patients are planned for inclusion, and will receive [6R]-MTHF-HS twice every two weeks during four cycles of chemotherapy. The study is designed as a safety study, investigating the tolerability of [6R]-MTHF-HS in patients at four dose levels. Tolerability will be assessed by analyzing the number and severity of adverse events (AE;s) and Dose Limiting Toxicity.

**Results:** So far 28 patients in Gothenburg, Oslo and Skövde have been included in the study: 297 doses of [6R]-MTHF-HS have been administered. The total number of Adverse Events (AE) so far is 256 and 110 AE:s were reported to be at least possible related to [6R]-MTHF-HS since the relationship between 5-FU and [6R]-MTHF-HS is hard to distinguish and [6R]-MTHF-HS might have an enhancing effect on 5-FU. Both the frequency and number of AE:s are similar to what is reported for Stage IV CRC patients treated with 5-FU/LV in previous studies.

**Conclusions:** Since LV is a prodrug, treatment with the active substance should lead to higher intracellular concentration of [6R]-MTHF, and thereby increase the response rate in all patients treated with 5-FU regardless of folate-relevant gene expression profile.

Treatment with [6R]-MTHF-HS in combination with 5-FU in patients with Stage IV CRC has shown an acceptable safety profile. A subsequent efficacy study is planned to investigate if [6R]-MTHF-HS will improve 5-FU based CRC-treatment.

**Conflict of interest:** Ownership: Helena Taffin, minor ownership in a holding company which has a small share in Isofol Medical AB; Bengt Gustavsson, ownership in a holding company which has a small share in Isofol Medical AB. Board of Directors: Bengt Gustavsson, Isofol Medical AB. Corporate-sponsored Research: The study is sponsored by Isofol Medical AB. Other Substantive Relationships: Karin Ganløv is an employee of Isofol Medical AB.

**Proffered Papers (Monday 30 January 2017)**

**Gastrointestinal Malignancies – Upper GI**

**540 ORAL**

**Early detection of pancreatic cancer among diabetic patients: results from prescription database analyses**

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**Background:** Type 2 diabetes mellitus (T2DM) is a risk factor for pancreatic cancer (PaCa) and the relationship between these two conditions is complex. It was hypothesized that starting or changing a pharmacological treatment for T2DM could be an early sign of PaCa.

**Material and Methods:** In order to investigate the temporal relationship between diagnosis of PaCa and the first prescription of an anti-diabetic drug, prescription data from the Inter Mutualist Agency (AIM-IMA) data repositories in Belgium and prescription data of administrative nature in the Region of Lombardy (Italy) were used to identify T2DM patients. These data were linked to PaCa data from the Belgian Cancer Registry and hospital discharge databases in Lombardy. A multivariate model with time dependent variables was used to compute the hazard rates (HR) of PaCa associated with use of different diabetic treatments.

**Results:** There were 368,377 subjects including 885 cases of PaCa in Belgium (2008–2013) and 456,311 subjects including 1,872 cases of PaCa diagnosed in Lombardy (2008–2012). The proportion of pancreatic cancers diagnosed after a first prescription of any T2DM therapy drops dramatically with time: 25% in Belgium, and 18% in Lombardy. There were 372 days to switch to incretins and 315 days to switch to insulin, p <0.0001). The switch from non-insulin non-incretin anti-diabetic treatment (OAD) to incretin-based therapy or to insulin was more rapid in patients who had a PaCa during follow-up (median 372 days to switch to incretins and 437 days to switch to insulin, p <0.0001). The HR for PaCa associated with use of insulin subsequently to a prescription of OAD or incretin was 11.9 (95% CI 10.4–13.6) (in Belgium). The model with a breakdown in the timing of diagnosis found adjusted HR of PaCa among users of incretins compared to OAD that sharply and progressively decreased in time. In Belgium, the HR decreased from 3.3 (95% CI 2.0–5.5) in the 3 months immediately following the first prescription to 2.3 (95% CI 1.2–4.7) for 3 to 6 months, to 2.1 (95% CI 1.2–3.9) for 6 and 12 months, to 1.7 (95% CI: 1.1–2.8) when the first prescription was made 12 months before the diagnosis of a PaCa in Lombardy, the HR was 1.4 (95% CI 1.0–2.0) for the first 6 months of follow-up, and 1.2 (95% CI 0.8–1.7) for the follow-up period starting six months after.

**Conclusions:** Aggravation of diabetes and start of new therapies seem to be an early signal for PaCa diagnosis for some patients. Thus, use of prescription databases could help develop methodologies which could help identify patients prone to develop a pancreatic cancer in an earlier stage, and also raise awareness for clinicians about diabetes treatment patterns and their relationship with PaCa.

**No conflict of interest.**
541 ORAL

Nationwide outcomes in patients undergoing surgical exploration without resection for pancreatic cancer

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Background: Despite improved preoperative staging of pancreatic cancer, locally advanced and metastasized pancreatic cancer are still regularly detected during surgical exploration. This nationwide study investigates the incidence and outcomes of patients who had no resection during surgical exploration for pancreatic cancer.

Methods: All 10,595 patients diagnosed with primary pancreatic (adenocarcinoma between 2009 and 2013 were included from the Netherlands Cancer Registry. Predictors for unresectability, 30-day mortality and poor survival were evaluated using logistic and Cox proportional hazard regression analysis.

Results: From 2009 to 2013, the rate of patients undergoing surgical exploration increased from 20% to 27% (p <0.001). Among all 2,356 patients undergoing exploration, the resection rate increased from 62% to 71% (p <0.001), mainly due to a decrease of locally advanced pancreatic cancer (LAPC). Compared to resected patients, patients not undergoing resection had an increased 30-day mortality (7.8% vs 3.8%, p <0.001) and decreased survival (5.6 vs 17.1 months, p <0.001). Thirty-day mortality in patients with LAPC and M1 disease at surgical exploration were 4.7% versus 10.6% (p = 0.002) whereas survival was 7.2 versus 4.3 months (p <0.001) respectively. Independent predictors for unresectability at surgical exploration were older age and low hospital volume (tortile). Predictors for 30-day mortality in non-resectable cases were metastatic disease and low hospital volume, and predictors for poor survival in these patients were older age, prior cancer, metastatic disease, poor tumour differentiation, and low hospital volume.

Conclusions: Despite nationwide increasing exploration and resection rates, one-third of patients undergoing surgical exploration for pancreatic cancer did not undergo resection with doubled 30-day mortality compared to patients undergoing resection. Outcomes were significantly worse in low volume hospitals. Improving preoperative detection of LAPC and M1 may prevent unnecessary explorations and has the potential to improve outcomes.

No conflict of interest.

542 ORAL

Validation of an assessment tool for predicting overall survival following gastric cancer resection

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Introduction: Although the assessment of surgical outcomes is a major component of the process of quality improvement, evaluations of long-term surgical outcomes have rarely been attempted. Gastric cancer is the second leading cause of cancer death worldwide. We previously devised a predictive model for surgical outcomes, termed the Estimation of Postoperative Overall Survival for Gastric Cancer (EPOS-GC). EPOS-GC comprises 6 independent variables, T and N factors of UICC stage, circumferential involvement, age, American Society of Anesthesiologists physical status classification, and serum sodium level (Gastric Cancer 2015;18:138–46). This study was undertaken to validate the reproducibility of EPOS-GC in an external patient population.

Materials and Methods: Postoperative overall survival is the main outcome. The discriminative power of EPOS-GC was assessed by Harrell’s c-index, whereas calibration power by plotting Kaplan–Meier curves of observed and predicted survivals. The observed-to-expected ratio (O/E) of 5-year overall survival rates was defined as a metric of quality of care. Sample size for O/E was determined as 42 based on the hypothesis that a difference between the 5-year overall survival rates of 72% and 42% was significant. Significance of O/E was measured by chi-square test. Monotonic relationship between two continuous variables were determined by Spearman’s correlation (rs).

Results: We obtained 2045 eligible patients. EPOS-GC demonstrated a good discriminative power (c-index, 95% CI: 0.80, 0.79–0.83), but the calibration plot revealed that EPOS-GC underestimated survival rates in the high risk group. Therefore, we constructed a new model using the independent variables of EPOS-GC in the current subjects via Cox’s regression analysis. The new model demonstrated a good calibration power with reserving the high discriminative power (c-index, 95% CI: 0.80, 0.78–0.82). The O/E among hospitals determined by the new model ranged between 0.87 and 1.27 (Table 1). O/E significantly correlated with hospital volume (r=0.76, n=11, P=0.008). Five hospitals that registered <180 eligible patients had an O/E that was not significantly different from unity (0.87–1.11), whereas 5/6 hospitals registering >180 of these patients had a significantly higher O/E (1.06–1.27).

Table 1. Comparative audit of overall survival following gastric cancer resection

<table>
<thead>
<tr>
<th>Hospital</th>
<th>No. of patients</th>
<th>O/E</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>76</td>
<td>0.87</td>
<td>0.316</td>
</tr>
<tr>
<td>B</td>
<td>89</td>
<td>1.11</td>
<td>0.377</td>
</tr>
<tr>
<td>C</td>
<td>105</td>
<td>0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D</td>
<td>158</td>
<td>1.11</td>
<td>0.121</td>
</tr>
<tr>
<td>E</td>
<td>162</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>F</td>
<td>189</td>
<td>1.14</td>
<td>0.038</td>
</tr>
<tr>
<td>G</td>
<td>194</td>
<td>1.06</td>
<td>0.277</td>
</tr>
<tr>
<td>H</td>
<td>205</td>
<td>1.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>I</td>
<td>213</td>
<td>1.16</td>
<td>0.008</td>
</tr>
<tr>
<td>J</td>
<td>257</td>
<td>1.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>K</td>
<td>386</td>
<td>1.13</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: These results suggest that a minimum set of 6 variables for EPOS-GC may allow for comparative audit of overall survival in gastric cancer resection. This methodology will promote quality improvement as well as information disclosure.

No conflict of interest.

543 ORAL

Morbidity and mortality of D2 lymphadenectomy plus completed mesogastrium excision (D2+CME) versus traditional D2 lymphadenectomy in laparoscopic distal gastrectomy – an interim report of a single-centre, prospective, randomized controlled trial (NCT01978444)

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Objective: The aim of this study was to evaluate the safety of the trial (NCT01978444) with respect to its morbidity and mortality.

Background: D2 lymphadenectomy plus completed mesogastrium excision (D2+CME) has been proven to be an optimal surgical approach for advanced gastric cancer (AGC) patients. However, there is a lack of evidence regarding its oncologic safety. Here, we conducted a single-centre, prospective, randomized controlled trial comparing D2+CME with traditional D2 lymphadenectomy.

Method: Patients eligible criteria were pathologically-proven adenocarcinoma, 18 to 75 years old, cT2-4N0-3M0 at preoperative evaluation, expected curative resection via laparoscopic distal gastrectomy, no history of other cancers, chemotherapy or radiotherapy, no history of upper abdominal operation and perioperative ASA class I, II or III. The primary end-point was 3-year disease-free survival. The morbidity and mortality were compared to evaluate the safety of this trial. We hypothesized that the morbidity of this study was not significantly different from that of previous reports on laparoscopic distal gastrectomy (5.7–15.5%) [1]. This study is registered at ClinicalTrials.gov, ID number is NCT01978444.

Result: A total of 151 patients were randomized (D2+CME, 68 patients; D2, 83 patients) between October 2014 and July 2016. There were no significant differences in the age, gender, comorbidities, and ASA score. The postoperative morbidity of the D2+CME group and D2 group were 14.7% (10/68) and 18.1% (15/83), respectively (p = 0.580). Re-operation
was required in only 1 case in D2 group. The postoperative mortality was 0% in both groups.

Conclusion: There is no significant difference in the complications between D2+CLEM group and traditional D2 group. Therefore, we ensure that this trial is safe and thus ongoing.

No conflict of interest.

544

ORAL

Sarcopenia outperforms the Charlson Comorbidity Index in risk prediction in patients undergoing pancreatic resections

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Introduction: Sarcopenia is a known predictor in patients undergoing major pancreatic surgeries. We sought to combine sarcopenia with established risk predictors to improve their prognostic capacity for postoperative outcome and morbidity.

Methods: As established parameters to predict preoperative mortality risk for patients, the ASA classification and the Charlson Comorbidity Index (CCI) were used to Hounslow Units Age Calculation (HUAC) was measured to define sarcopenia in 424 patients undergoing pancreatic resections for malignancies. In patients the lowest sex-adjusted quartile for HUAC were defined as having sarcopenia (muscle wasting). Multivariable Cox regression analysis was utilized to identify preoperative risk factors associated with postoperative morbidity.

Results: Median patient age was 63 years (19–87), 47.9% patients were male, and half the cohort had multiple comorbidities (Charlson Comorbidity Index [CCI] ≥4). 30-day mortality was 10.3% and 126 (29.7%) having sarcopenia. Preoperative frailty defined by sarcopenia was associated with an increased risk for postoperative complications (OR 1.55, 95% CI 0.99–2.45, p = 0.014), and a higher 30-day mortality (HR 5.17, 95% CI 1.57–16.69, p = 0.004). With an AUC of 0.85 HUAC showed the highest predictability for 30-day mortality (95% CI 0.78–0.91, p = 0.0001). Patients with CCI ≥6 and sarcopenia defined by the HUAC had a 9.78 higher risk of dying in the immediate postoperative phase (HR 9.78, 95% CI 2.98–32, p = 0.0001).

Conclusion: Sarcopenia predicts postoperative mortality and complications best and it should be incorporated to conventional risk scores to identify high risk patients.

No conflict of interest.

Poster Session (Sunday 29 January 2017)

Gastrointestinal Malignancies – Upper GI

596

POSTER

Adjuvant HIPEC in gastric cancer patients with high risk of peritoneal carcinomatosis

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Background: The peritoneum is one of the most common site of recurrence in gastric cancer. Median survival for PC is only about four months, if untreated and the benefit of palliative systemic chemotherapy is limited. Only a quarter of patients are eligible for curative treatment, consisting of CRS/HIPEC. These clinical problems underline the need for effective adjuvant therapy in high-risk patients to minimize the risk of outgrowth of peritoneal micro metastases. Adjuvant HIPEC seems to be suitable for this purpose. Without the need for CRS, adjuvant HIPEC can be performed with a low complication rate and short hospital stay. The aim of this study is to determine the effectiveness of adjuvant HIPEC in preventing the development of PC in patients with gastric cancer at high risk of peritoneal recurrence.

Patients and Methods: This study was performed in the Georgian NCC, starting in February 2014. Eligible for inclusion are patients who underwent a curative resection for T4, CM0 stage gastric cancer. After resection of the primary tumour, 46 patients will be randomized to adjuvant HIPEC comparing with routine systemic chemotherapy only in the control arm. Different cytostatic agents were used for 60-90 min at 42–43°C. Postoperatively in both arms of the study in patients without evidence of disease based on routine follow-up using CT, CEA and CA 19-9.

Results: Morbidity and mortality were 32.8% and 3.1%, respectively, with three cases (4.68%) of peritoneal recurrence, from total number 64 patients 62% were male and 48% female. Mean age was 57.6 years, range 31 to 73 years. In the beginning of treatment, the KPS was over 80% for all patients. Median follow-up was 23 months, ranging from 7 to 52 months. 2 patients were diagnosed with a pancreatic fistulae through the identification of an abnormal discharge in a suction drain placed during surgery, and confirmed by a fluid amylase examination, no additional treatment was necessary. 2 patients had an intrabdominal abscess that required re-laparotomy.

Conclusions: Adjuvant HIPEC is assumed to reduce the expected 42% absolute risk of PC in patients with T4 GC to a risk of 14%. This reduction is likely to translate into a prolonged overall survival. In light of our experience and supported by literature data, we can affirm that HIPEC has a potential role in the prevention of gastric carcinomatosis. Certainly further studies are required on a larger scale to validate this new but promising approach.

No conflict of interest.

597

POSTER

Inhibitory effect of (−)-epigallocatechin-3-gallate and bleomycin on human pancreatic cancer MIA PaCa-2 cell growth

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Background: Human pancreatic cancer is currently one of the deadliest cancers with high mortality rate. It has been previously shown that (−)-epigallocatechin-3-gallate (EGCG), the most abundant catechin found in green tea, has shown suppressive effects on human pancreatic cancer cells. Bleomycin (BLM), an anti-cancer chemotherapeutic drug that induces DNA damage, has antitumor effects by induction of apoptosis in several cancer cell lines and also in pancreatic cancer cells. The present study investigated for the first time, the inhibitory effect of EGCG and BLM on pancreatic cancer cell growth.

Methods: Using the pancreatic cancer cell lines Mia PaCa-2 cells the efficacy and synergism of EGCG and BLM were evaluated by in vitro tests. Inhibition of cell proliferation was determined by MTT assay. Mitochondrial depolarization was performed with JC-1 probe. Viability and apoptosis was determined by Flow Cytometry with annexin V, propidium iodide staining and DNA fragmentation assay.

Results: Cell proliferation assay revealed significant additive inhibitory effects with combination of EGCG and BLM at 72 h in a dose dependent manner. The combination of EGCG and BLM induced cell cycle S-phase arrest and mitochondrial depolarization. Viability, apoptosis and DNA fragmentation assay indicated that the combination of EGCG and bleomycin potentiated apoptosis.

Conclusions: Our results indicate that EGCG and BLM have additive anti proliferative effects in vitro by induction of apoptosis of Mia PaCa-2 cells. This combination could represent a new strategy with potential advantages for treatment of pancreatic cancer. To date, this is the first report published of the inhibitory effect of EGCG and BLM on human pancreatic cancer MIA PaCa-2 cell growth.

No conflict of interest.

598

POSTER

Incidence of gastric cancer in Sri Lanka: analysis of the cancer registry data and comparison with other South Asian populations

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Background: This study aims to report the incidence of gastric carcinoma (GCa) in Sri Lanka (SL) and to compare these findings with other cancer registry data of the region and with migrant populations.

Materials and Methods: We compared the data published by the National Cancer Control Program of Sri Lanka over the last 2 decades with data from the National Cancer Registry Programme of the Indian Council of Medical Research and Karachi cancer registry. SEERstat was used to analyse the Surveillance, Epidemiology, and End Results database to analyse data on Indian migrant population.

Results: Gastric CA was the 10th most common cancer in males. The incidence of Gastric CA rises with age in both sexes, with a peak in the 70–74 year age group. There was a disproportionately higher number of GCa in the tamil population (Chi square test, p = 0.0022). The commonest type of Gastric CA in Sri Lanka was Adenomas and Adenocarcinomas, NOS (n = 175, 61.6%), followed by Cystic/mucinous/serous neoplasms second. (n = 83, 7.0%). India, Pakistan and Sri Lanka had comparable Age Adjusted Incidence (AAI) and age distribution of Gastric CA. All migrant populations had lower
incidence of Gastric CA than original population or population in their present country. Cigarette smoking is more prevalent in Sri Lankan males than females.

Conclusions: The incidence of Gastric CA and its distribution among age groups in Sri Lanka was comparable to other countries of the region. Persons of Tamil ethnicity have a higher risk of developing Gastric CA. Migrant populations had a lower incidence of Gastric CA than native populations.

No conflict of interest.
screening program from 2006 in Sichuan Province, including esophageus cancer and gastric cancer. This study aims to investigate the effectiveness of the upper gastrointestinal cancer screening program in the last 4 years.

**Material and Methods:** The targeted population are 40–69 years in rural area sampled by random cluster sampling. Esophageal and gastric endoscopy were used to detect the lesions in upper gastrointestinal tract. The esophageal precancerous lesions (mild to moderate dysplasia), cardiac and gastric precancerous lesions (severe chronic atrophic gastritis, severe intestinal metaplasia and low grade intraepithelial neoplasms) detected at baseline were followed-up in accordance with precancerous lesions screening program, and patients who diagnosed as high-grade lesion or worse were treated.

**Results:** In total, 88,825 participants were enrolled for primary screening and 2,826 were followed-up, 5,021 (5.65%) mild to moderate dysplasia cases, 1,014 (1.14%) high grade squamous intraepithelial neoplasia cases were detected in esophagus baseline screening. 60.86% esophageus mild to moderate dysplasia were detected. 70.39% enrolled in the follow-up program. The detection rate of high-grade intraepithelial neoplasia cancer were detected in gastric baseline screening. 75 (4.91%) high grade dysplasia cases were detected. 1,084 (1.22%) atrophic gastritis and low grade intestinal metaplasia and low grade intraepithelial neoplasia cases, 315 (0.35%) high-grade squamous intraepithelial neoplasia cases were detected in cardiac baseline detection. 55.92% cardiac cases were detected. 1,014 (1.14%) high gradedysplasia or preinvasive carcinoma cases were followed-up and 75 (4.91%) high grade dysplasia cases were detected. 1,084 (1.22%) atrophic gastritis and low grade intestinal metaplasia and low grade intraepithelial neoplasia lesions screening program, and patients who diagnosed as high-grade lesion or worse were treated.

**Conclusion:** The quality of the upper gastrointestinal cancer screening program is improving steadily. Improving the quality of follow-up examination could effectively improve the quality of the screening program.

**No conflict of interest.**

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603 **POSTER**

**Potential implication of SOCS-4 in pancreatic cancer development**

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**Background:** The suppressor of cytokine signalling (SOCS) family, consisting of eight family members, was identified as a negative feedback regulator of cytokine signalling. Moreover, some of the SOCS family members have been shown to be over-expressed in a wide range of cancers. In this study, we have examined the expression of SOCS-4 in different types of cancer research since a wide variety of cytokines and growth factors have been highlighted as playing key roles in cancer initiation and progression. However, studies exploring the significance of SOCS-4 in pancreatic cancer are limited. SOCS-4 over-expression has been found to be associated with the overall survival and TNM classification in breast cancer, whereas the aberrant expression of SOCS-4 gene was found in gastric cancer tissue. In an in vitro study demonstrated that the attenuation of SOCS-4 expression led to elevated thyroid cancer cell migration and invasion. Our current study explores the expression profile of SOCS-4 in the progression of pancreatic cancer, a cancer associated with very poor patient survival and prognosis.

**Materials and Methods:** SOCS-4 expression was examined throughout a clinical cohort of pancreatic cancer and normal tissue. Tissues (total n = 233 paired samples) were collected immediately following surgery performed at the Peking University Cancer Hospital. RNA was extracted following homogenisation of tissue in an RNA extraction solution and reverse transcription to generate cDNA. Subsequently SOCS-4 levels throughout the cohort were quantified using QPCR and associated with patient clinical pathological information. Median levels of SOCS-4 transcript were detected and statistical comparison was undertaken using a Mann-Whitney test.

**Results:** Significantly higher levels of SOCS-4 (p = 0.0009) were observed in pancreatic cancer tissues in comparison to normal tissues. Higher levels of SOCS-4 transcript were also detected in tumours progressed from moderately to poorly differentiated subtypes though no significant differences were observed between the groups (p > 0.05). Similar to this, lower levels of SOCS-4 transcript were again noted in node negative cancers compared to node positive cancers and in tissues from patients without detectable metastasis compared to those with metastasis, though again neither reached statistical significance.

**Conclusions:** In this initial study on SOCS-4 in pancreatic cancer, our current data suggests that SOCS-4 levels are significantly higher in tumour tissues than in normal tissues and that, in general, higher transcript expression of SOCS-4 associates with a poorer patient prognosis. Hence SOCS-4 may play a role in the progression of pancreatic cancer.

**No conflict of interest.**

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604 **POSTER**

**The impact of histological subtype on the prognosis of oesophageal adenocarcinoma**

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**Background:** The prognosis of gastric adenocarcinoma differs per histological subtype (according to the Lauren classification: intestinal, diffuse or mixed type). Patients with an intestinal type tumour have a more favourable prognosis than patients with a diffuse type tumour. In oesophageal adenocarcinomas the same histological subtypes exist, but there are no data available on the association between these subtypes and survival. This study analysed the association between histological subtype (according to Lauren) and survival after potentially curative treatment for oesophageal adenocarcinoma.

**Materials and methods:** Data were collected from all oesophageal adenocarcinoma patients who were treated with curative intent in our institute between 1998 and 2014. Treatment consisted of neoadjuvant chemoradiotherapy (36–50 Gy) followed by an oesophagectomy or definitive chemoradiotherapy (50–50.4 Gy). Radiotherapy was combined with 5-fluorouracil/cisplatin or carboplatin/paclitaxel.

Clinical data were collected from patient files. An expert pathologist re-assessed all endoscopic biopsies and surgical resection specimens to determine the histological subtype (diffuse/intestinal/mixed) and other histological variables including tumour regression grade (according to Mandar). Overall survival was calculated and compared between the subgroups using the log-rank test. The impact of histological subtype on survival was calculated with a Cox model. In surgically treated patients postoperative tumour characteristics were compared between the histological subgroups.

**Results:** Median follow-up of all oesophageal adenocarcinoma patients was 68 months (n = 160). Tumour characteristics and type of treatment (neoadjuvant chemoradiotherapy combined with surgery or definitive chemoradiotherapy) were equally distributed between patients with an intestinal (n = 121), a diffuse (n = 28) or a mixed type (n = 11) oesophageal adenocarcinoma. Overall survival (median: 29 months), was significantly different between patients with an intestinal (39 months), a diffuse (18 months) or a mixed type (25 months) tumour (log rank, p = 0.023). In multivariable analysis, the diffuse type was independently associated with a shorter survival (diffuse vs. intestinal: HR 1.99; 95% CI 1.20–3.32; p = 0.028). A pathologically complete or subtotal response was seen more often in intestinal type than in diffuse type adenocarcinomas (68% vs. 24%; p = 0.015).

**Conclusions:** Patients with a diffuse type adenocarcinoma of the oesophagus had a significantly worse prognosis than those with an intestinal type tumour. Intestinal type tumours responded considerably better to neoadjuvant chemoradiotherapy than diffuse type tumours. These differences call for a more differentiated approach in the potentially curative treatment of oesophageal adenocarcinomas.

**No conflict of interest.**

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605 **POSTER**

**Magnolol exerts chemoprotective effect by attenuating the xenobiotic, anti-oxidative enzymes and inflammatory mediator in Wistar rats**

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**Background:** This experimental study was highlight on the assessment of magnolol against diethylnitrosamine (DEN) induced hyperproliferation, inflammation oxidative stress and apoptosis tissue damage in the rats liver.

**Material and Methods:** Hegr-C2 and Huh-7 cell lines was used for the determination the effect of HEG on the inhibition of cell growth and DNA synthesis. Administration of magnolol (5, 10 and 20 mg/kg/day) was started 1 week prior to intraperitonially administration of DEN and Phenobarbital.
and continued for 22 weeks. The serum and liver tissue samples were collected and processed for biochemical and histopathological evaluation. Hepatic biochemical parameters viz., Aspartate aminotransferase (AST), Alpha feto protein (AFP), nitric oxide (NO), Alanine transaminase (ALT) and Non-hepatocellular parameter such as bilirubin, total albumin, blood urea nitrogen (BUN), total protein. We also estimated the Phase I antioxidant (NAPDH-cytochrome p450 reductase, cytochrome b5, cytochrome P420; Phase II Glutathione S-transferase and antioxidant enzymes (glutathione reductase, superoxide dismutase, catalase, glutathione peroxidase and lactate dehydrogenase) were also examined. Additionally, we also scrutinized the pro-inflammatory cytokines viz., interleukin-1, interleukin-6, tumor necrosis factor-α and nuclear factor kappa B (NF-κB), respectively.

Results: Magnolol significantly inhibited the growth of cell lines and reduced the DNA synthesis of both cell lines at dose dependent. Magnolol significantly inhibited the number of hepatic nodules and incidence of the hepatic nodules at dose dependent. DEN induced rat confirmed the significance (P < 0.0001) altered the phase I, II and antioxidant enzymes, which was significantly (P < 0.05) mitigated the park the rat liver from the cancer via alleviation of oxidative stress and inflammatory response.

No conflict of interest.

605A POSTER

Defining the individual internal gross tumor volume of hepatocellular carcinoma using 4DCT and MRI-T2 images by deformable registration

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Background: To study the feasibility of defining the individual internal gross tumor volume (IGTV) of hepatocellular carcinoma (HCC) using four-dimensional computed tomography (4DCT) imaging and T2-weighted Magnetic Resonance Imaging (MRI-T2) by deformable registration (DR).

Material and Methods: Ten HCC patients who previously received radiotherapy treatment were selected for this study. The following simulation images were acquired sequentially: 4DCT in free breathing and MRI-T2 in deep inspiration breath holding. All 4DCT images were sorted into ten phases according to breath cycle (CT00–CT90). The accuracy of DR was assessed by three methods; the maximum displacement on three dimensional directions of portal vein, the maximum displacement on three dimensional directions of the celiac trunk, and the ratio of liver overlap (P-LIVER). Gross tumor volumes (GTVs) were contoured on all CT images, and the IGTV obtained by merging the GTVs in each phase of 4DCT imaging. The GTV on the MRI-T2 image was deformably registered to each 4DCT phase image using MIM software version 6.5.6 and the results labeled as IGTV DR. The IGTV Observed (IGTV Ob) was obtained by merging the GTVs on the 4DCT images. Statistical differences in the GTVs and between the IGTV and IGTV DR were assessed by a paired t-test.

Results: The maximal displacements observed in the three dimensional directions of the portal vein were 3.6±1.2 mm along the X-axis, 5.0±1.4 mm along the Y-axis and 4.2±0.9 mm along the Z-axis. Comparatively, the maximal displacements of the celiac trunk were 2.8±1.3 mm along the X-axis, 3.0±1.7 mm along the Y-axis and 2.5±3.4 mm along the Z-axis. Furthermore, the P-LIVER was 115.4±13.8%. The edge of most lesions were identified using MRI-T2 images compared to 4DCT images. The GTVs after DR on 4DCT different phase imaging increased by an average of 8.18% (P < 0.05), whilst the volume of IGTV DR increased by an average of 9.67% compared to that of IGTV (P < 0.05).

Conclusions: The use of 4DCT imaging alone has the potential risk of missing a partial volume of the HCC. However, MRI-T2 images can carry more information than 4DCT image. As such, the combination of 4DCT and MRI-T2 images using the DR technique may improve accuracy in the delineation of HCC.

No conflict of interest.

606 POSTER

Determination of TGF-β1 polymorphism at −509 C/T promoter region in HCV patients with and without HCC

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Background: Worldwide hepatitis C virus (HCV) is a significant health problem. This virus has infected more than 170 million people worldwide and is the major cause of acute and chronic hepatitis. HCV-associated liver diseases range from chronic hepatitis to fibrosis, cirrhosis and hepatocellular carcinoma (HCC). HCV is one of the major causes of HCC. Polymorphisms of cytokines genes affect host response to viruses. Transforming growth factor-β(TGF-β1) is a multifactorial cytokine that is involved in tumor proliferation or by promoting cellular differentiation or apoptosis in the early phase of cancer development. Variations in the DNA sequence in the TGF-β1 gene may lead to altered TGF-β1 production or activity and therefore it can modulate an individual’s susceptibility to liver cancer. This study was performed, and the polymorphism in the promoter region of TGF-β1 gene that leads to development of HCC in HCV patients.

Method: It was a comparative study, comprising of 80 individuals who were divided into two groups of 40 subjects in each. Group 1 composed of chronic HCV patients while Group II had HCV patients with HCC. TGF-β1 polymorphism was determined by RFLP following conventional PCR. Data was analyzed using SPSS 20.0. Chi-square test was applied to observe association between TGF-β1 polymorphism allele and study groups.

Results: Keeping the C allele as reference in HCV and HCC patients, CT genotype frequency and percentage was detected as 11 (39.3%) and 17 (60.7%) with OR (95% CI) = 1.422 (0.457–4.427), P = 0.544, respectively. While TT genotype was found with frequency and percentage of 14 (46.7%) and 14 (46.7%) with OR (95% CI) = 1.422 (0.457–4.427), P = 0.120, respectively. These result show that there is no significant association between these polymorphisms in HCV and HCC patients but the patients possessing TT genotype or at least having 1 T allele might be at an increased risk of developing HCC due to high OR compared with CC genotype. Therefore, TGF-β1 −509 gene polymorphism might be associated with the risk of HCC in patients with chronic HCV infection in the local population.

No conflict of interest.

606A POSTER

Potential diagnostic and prognostic value of lymphocyte mitochondrial DNA deletion in relation to folic acid status in hepatocellular carcinoma

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Background and Aims: Hepatocellular carcinoma (HCC) is one of the most leading causes of death worldwide. HCV is associated with increased oxidative stress in the hepatocytes resulting in DNA changes like mitochondrial (mt) DNA deletions. In this study, we studied mtDNA deletion as diagnostic and prognostic molecular marker in relation to serum folic acid level in Egyptian patients with HCV related HCC.

Patients and Methods: The prospective case control study was conducted on ninety adult patients with HCV related chronic diseases; 50 patients with HCC, 20 with liver cirrhosis (LC) and 20 with chronic hepatitis C (CHC), in addition to 10 healthy subjects who enrolled as control group. Serum folic acid levels measured using ELISA and lymphocytic mtDNA deletions was measured using real-time PCR. HCC patients were followed up over a period of one year dating from initial presentation and the overall survival was calculated.

The diagnostic accuracy of mtDNA deletions frequency was evaluated using receiver-operating characteristic (ROC) curve analysis. Correlations between different variables were calculated using Spearman’s Correlation Coefficient. Survival analysis was analyzed with the Kaplan–Meier method. Differences in the survival rates were compared using log-rank test. P value less than 0.05 was considered statistically significant.

Results: There was a significant elevation of mtDNA deletions and a significant decrease in serum folic acid in HCC group compared to other groups (P = 0.01 and P < 0.05 respectively). Lymphocytic mtDNA deletions had a sensitivity of 82%, specificity of 60% at cut off (ΔCt) 2.65 with AUC 0.818 and 95% CI; (0.72–0.9) for HCC diagnosis.

Regarding the clinicopathological features of HCC, we found that mtDNA deletions frequency significantly correlated with HCC size (r = 0.5, P < 0.01) but none significantly with the number of HCC nodules (r = 0.0240, P = 0.8) and serum AFP level (r = 0.16, P = 0.26). Serum folate level negatively correlated with HCC size, foci number, serum AFP and lymphocytic mtDNA deletions; however, this correlation did not reach statistical significance.

Also, the median survival time for HCC patients with high mtDNA deletions (ΔCt ≥ 3.9) was significantly shorter (5.7±0.6 months) than those patients with low mtDNA deletions frequency (11.9±0.4 months).
Conclusion: This is the first study to our knowledge that explored mtDNA deletions and folate status in Egyptian patients with HCV related HCC and is the first to evaluate mtDNA deletions as diagnostic markers for HCC at a cutoff value of 2.65 (X̄) with a sensitivity of 82% and a specificity of 60%. We stipulated a causal relationship between folate deficiency and mtDNA deletions frequency among Egyptian patients with HCV related HCC. Moreover, mtDNA deletions correlated with the clinic-pathological features and poor survival in HCC patients.

No conflict of interest.

607 Naringin: a novel anticancer candidate against chemically induced hepatocellular carcinoma in rats
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Background: Naringin has been projected as a promising agent for cancer chemotherapeutics. The aim of the current study was to scrutinize the chemoprotective action and possible mechanisms Naringin against Diethylnitrosamine (DEN)-induced hepatocellular carcinoma in rats.

Material and Methods: In vivo experimental study was carried out on the cell lines such as Huh-7 and HepG2 cells. Swiss Albino Wistar rats were used in the current study. Different doses of Naringin (20, 50 and 100 mg/kg/day) was orally administered to DEN induced HCC rats via gavage. Den control rats were also macroscopically estimated the incidence of hepatic dyschromatic nodules. We determined the biochemical, antioxidant and haematological parameters. Histopathology and Immunohistochemical study were also performed. Cyclooxygenase 2, Ki-67, nuclear factor kappa B (NF-kB) and inducible nitric oxide were estimated in all group rats via immunohistochemical staining of hepatic tissue.

Result and Discussion: Cell lines study showed that the Naringin enhanced the DNA damage, caspase-3 and cell arrest and reduced the nuclear factor-Kappa B (NF-kB) activation. DEN control group rats showed the increase number and incidence of hepatic dyschromatic nodules, which was significantly reduced by the Naringin at dose dependently. Naringin also altered the biochemical and haematological parameter at dose dependently. Moreover, Naringin altered the antioxidant parameter including catalase (CAT), superoxide dismutase (SOD), glutathione-S-transferase (GST) and reduced the protein carbonyl, malondialdehyde and myeloperoxidase in the liver. Naringin Naringin also reduced the area and number of plasmatic glutathione S-transferase-positive foci in the hepatic tissue of DEN induced control rats. DEN induced control rats showed the increased activity of Cyclooxygenase 2, Ki-67, nuclear factor kappa B (NF-kB) and inducible nitric oxide, which was inhibited by the Naringin. DEN control rats demonstrated the depletion of M30 cyto-Death and number of cells positive for TUNEL (terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling), which was blocked by the Naringin.

Conclusion: It can be concluded on the basic of the result that the Naringin confirmed the chemopreventive effect against the DEN induced HCC rats via the chemopreventive action and reduction of cell proliferation or we can say that the Naringin also protected liver from the oxidative damage and inflammatory reaction.

No conflict of interest.

607A Adjuvant chemotherapy of S-1 versus gemcitabine for resected pancreatic cancer
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Background: There have been some important studies on postoperative adjuvant chemotherapy for pancreatic cancer, including CONKO-001, JASPAC 01, and ESPAC-4, during the past decade.

Study design of JASPAC 01: JASPAC 01 study is a multi-center (33 institutions in Japan), open-label, randomized phase 3 trial aiming at assessing non-inferiority of S-1 to gemcitabine as adjuvant chemotherapy for resected pancreatic cancer in terms of overall survival. Patients with resected pancreatic cancer were randomly assigned to the gemcitabine group (0.1 g/m² body surface area, daily for 5 weeks repeated at 8-week intervals) or the S-1 group (1-40 mg/m² or 60 mg/m² according to body-surface area, orally administered twice daily for 28 days, every 4 weeks up to 4 cycles) at the data center with a modified minimization method, balancing residual tumor status, nodal status and institutions. The expected hazard ratio was 0.87 (95% confidence interval of 0.66–1.16) with a non-inferiority margin of 1.25 (power 80% and one-sided type one error 2.5%).

Results: Excluding 3 ineligible patients and 5 who did not receive chemotherapy from 385 patients enrolled between April 2007 and June 2010, 190 patients in the gemcitabine group and 187 in the S-1 group constituted the full analysis set. The interim analysis on July 2012 showed that the hazard ratio for death of S-1 was 0.55 (99.8% CI, 0.36–0.84, p < 0.0001). Analysis with the follow-up data on January 2016 showed that the median survival time and 5-year survival rates were 25.5 months and 24.4% in the gemcitabine group and 46.5 months and 44.1% in the S-1 group (hazard ratio; 0.57, 95% CI, 0.44–0.72, p < 0.0001), respectively. Grade 3 or 4 adverse events including infection, leukopenia, neutropenia, thrombocytopenia, aspartate aminotransferase, alanine aminotransferase were also observed more frequently in the gemcitabine group, while amphotericin and diareea were more frequently experienced in the S-1 group.

Conclusions: JASPAC 01 study clearly showed superiority of S-1 to gemcitabine as adjuvant chemotherapy for resected pancreatic cancer. The Pancreatic Cancer Medical Guid was determined as positive usage of S-1 as the first choice for postoperative adjuvant chemotherapy.

No conflict of interest.

608 Clinical significance of D2-40 and CD31, lymphatic and blood vessel invasion markers, in gastric cancer
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Background: Lymphatic and/or blood vessel tumor invasion (LBVI) is the critical step in establishing tumor cell dissemination and metastasis in various types of cancers including gastric carcinoma (GC). Recently, the immunohistochemical detection of LBVI has been shown to have a higher sensitivity and specificity than classic staining methods.

Material and Methods: Patients with GC who underwent curative gastrectomy with standard D2 lymph node dissection in our clinic between January 2008 and July 2011 included in the study. Demographics, involvement of the lymph nodes, lymphatic and vascular invasion and overall survival were determined. Lymphovascular involvement was evaluated by using H&E as routine staining, and CD31/D2-40 as immunohistochemical markers.

Results: Fifty-two patients (32 male, 20 female) were present. Mean age was 58 (range 29–72), H&E-LBVI was determined as positive in 29 (55.8%) cases. CD31-BVI and D2-40-LVI were positive in 29 (55.8%) and 34 (65.4%) cases, respectively. There was no statistical difference between these methods using the Mc Nemar test (p > 0.05). CD31/D2-40 was positive in 39 (75%) patients, and there was a statistically significant difference between CD31±D2-40 and H&E methods (p < 0.001). All of the H&E, CD31, D2-40 and CD31+D2-40 markers were significantly associated with lymph node metastasis (p < 0.01, each). D2-40 and CD31±D2-40 markers were significantly associated with distant metastasis (p < 0.05, each). Five-year survival rate was significantly lower in lymph-node positive patients (p < 0.01).

Conclusions: In detection of vascular invasion, each of the immunomarkers CD31 and D2-40 have shown to be unsuccessful in taking better results. However, when these two immunomarkers are used together, the results are significantly paramount in showing the involvement of LBVI. In our opinion, CD31 and D2-40 should be used together while evaluating gastric resection specimens.

No conflict of interest.

608A Metformin reduces esophageal cancer risk in Taiwanese patients with type 2 diabetes
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Background: This study evaluated whether metformin might reduce esophageal cancer risk.

Materials and Methods: Patients with type 2 diabetes diagnosed during 1999–2005 were recruited from the reimbursement database of Taiwan’s National Health Insurance. A total of 16,216 ever users and 16,216 never users of metformin (matched on propensity scores) were followed until December 31, 2011. Hazard ratios were estimated by Cox regression incorporated with the inverse probability of treatment weighting using propensity score.

Results: The incidence of esophageal cancer in ever and never users was 28.49 and 50.87 per 100,000 person-years, respectively. The overall hazard ratio (95% confidence intervals) of 0.57 (0.329–0.944) suggested a significantly lower risk among metformin users. Hazard ratios comparing the first (>21.47 months), second (21.47–45.93 months) and third (>45.93 months) tertile of cumulative duration of metformin use to never users was 1.490 (0.816–2.720), 0.439 (0.185–1.040) and 0.063 (0.009–0.460), respectively.
Conclusions: Metformin reduces esophageal cancer risk when the cumulative duration is more than approximately 2 to 4 years.

No conflict of interest.

609A POSTER
Preoperative assessment of operability in pancreatic and periampullary carcinoma based on multislice computed tomography and endoscopic ultrasonography

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Background: Pancreatic malignancy has an incidence of 100 per million population while periampullary tumours have an incidence of 30 per million. Tumour with pancreatic and periampullary malignancy have metastasis on presentation or have unresectable tumours due to vascular invasion. Accurate assessment of these cases with imaging is required to confirm the diagnosis and identify resectable cases while avoiding surgery in patients with incurable disease. Studies comparing efficiency of multislice CT and endoscopic ultrasound in diagnosing and detecting curable cases have been very few. The goal of this study is preoperative assessment of endoscopic ultrasound and multislice CT in operability of pancreatic and periampullary malignancies.

Material and Methods: The study was a hospital based analytical observational study conducted in Department of Surgery, Sawai man Singh Medical College, Jaipur, from March 2015 to March 2016. A total of 52 patients with obstructive jaundice were studied prospectively.

Exclusion criteria: Patients with obstructive jaundice in whom endoscopic ultrasound and multislice CT was indicated clinically were included in study.

Conclusion: severe to verify the operability of majority of patients and adequate to plan out definitive surgical intervention.

No conflict of interest.

610A POSTER
Incidence and prognostic significance of extramural venous invasion in T3–4 esophageal cancer

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Background: Extra mural venous invasion (EMVI) is known as an adverse prognostic indicator of survival and an important predictor of systemic recurrences in colorectal carcinoma. However, the incidence and significance of EMVI in esophageal carcinoma (EC) have not been studied well. In this study we have estimated the incidence and the prognostic significance of EMVI in pathological stage T3–4 EC resection specimens without neoadjuvant chemoradiotherapy (nCRT).

Material and Methods: From a prospective maintained database we retrospectively reviewed the resected specimens of patients with an esophageal carcinoma. We only included patients without neoadjuvant chemoradiotherapy and excluded patients without previous malignancies and patients with cardio/gastroesophageal junction tumors. A total of 81 patients operated between 2000 and 2012 were included. EMVI was assessed on haematoxylin and eosin slides and for confirmation additional Elasticia van Gieson staining was performed. Disease free survival was analyzed using a multivariable logistic regression and Kaplan–Meier method.

Results: Evidence of EMVI was found in 19 patients (23.5%). The incidence of EMVI was significantly higher in squamous cell carcinomas (SCC) (p < 0.05) and among tumors located in the mid-esophagus (p = 0.05). In SCC pathological N-stage (HR 6.1, 95% CI: 1.4–27.3, p = 0.017), positive CRM (HR 9.4, 95% CI: 1.9–46.1, p = 0.006) and EMVI (HR 5.0, 95% CI: 1.0–23.8, p = 0.043) were shown to be independent prognostic factors for DFS. For OS the following factors were prognostic independent: pathological N-stage (HR 4.4, 95% CI: 1.9–9.8, p = 0.001), pathological T-stage (HR 3.4, 95% CI: 1.3–7.8, p = 0.009) and poorly differentiated tumor (HR 0.4, 95% CI: 0.2–0.9, p = 0.016). When adjusted for type of tumor pathological N-stage (HR 4.2, 95% CI: 1.3–13.7, p = 0.019), pathological T-stage (HR 3.6, 95% CI: 1.4–9.3, p = 0.008) and EMVI (HR 2.5, 95% CI: 1.1–5.6, p = 0.031) were an independent prognostic factor for OS in AC.

Conclusions: A search for EMVI may provide additional prognostic information in esophageal cancer, especially in SCC. No conflict of interest.
role in carcinogenesis through its tumor growth, invasion, angiogenesis, and metastasis-driving functions. Its expression is associated both with suppression and progression of cancer based on tumor type. Fibronectin, one of the major structural components of the basement membrane, is a strong promoter of cell adhesion, migration, differentiation, and proliferation through integrins and other cell surface receptors. Altered expression of fibronectin has been associated with pancreatic cancer risk.

In addition to its implication in cancer development, fibronectin also acts as a potent biomarker for treatment-associated resistance. We aimed to research the serum levels of caveolin-1 and fibronectin in patients with pancreatic cancer, who were not received any treatment. The results were compared with the healthy controls to investigate of serum caveolin-1 and fibronectin level as markers for pancreatic cancer patients.

Material and Methods: We measured serum caveolin-1 and fibronectin levels by enzyme-linked immunosorbent assay (ELISA) method in Oncology Institute, Cancer Biochemistry and Tumor Marker Laboratory of Istanbul University. We enrolled 43 pancreatic cancer patients with a pathological diagnosis preoperatively and 44 healthy donors in this study. Area Under Curve (AUC) was calculated using ROC (Receiver Operating Characteristics) curve analysis. The results were evaluated by the Mann–Whitney U-test using SPSS 21 (Chicago, IL, USA).

Results: The baseline serum caveolin-1 and fibronectin levels (p < 0.001 and p < 0.001, respectively) between the patients and healthy controls. The baseline serum caveolin-1 (0.474 ng/ml) and fibronectin (0.498 ng/ml) levels of the patients with pancreatic cancer were significantly higher than those in the control group (0.37 ng/ml and 0.192 ng/ml, respectively).

Conclusions: Our results revealed that serum levels of caveolin-1 and fibronectin may be useful markers in the diagnosis of pancreatic cancer.

No conflict of interest.

611 Pathological diagnosis in pancreatic cancer pre-operatively – a reality or myth?

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Background: Pancreatic cancer remains one of the deadliest cancers worldwide, and has a poor five-year survival rate of 5%. Even after complete resection of the lesion pancreatic cancer still holds very poor prognosis as the disease is always diagnosed in a late stage. With all modern modes of radiological investigations and imaging guided biopsies pancreatic tumors can be diagnosed precisely preoperatively. The aim of this study is to compare the different modes of guided biopsies in arriving at a pathological diagnosis.

Materials and Methods: A retrospective study was conducted based on the records of the Sawai Man Singh Medical College and Hospital, Department of Gastroscopy and Department of Gastroenterology which included 72 cases of pancreatic lesions who have undergone preoperative cytologies followed by laparotomies. Recent cases Usuexography (USG) guided biopsies gave positive reports in 32 cases in which 19 (59%) cases there was a need for repeating the investigation more than once. In nearly 26 cases Endoscopic ultrasound guided biopsies gave positive reports in which 8 (30%) cases were repeat biopsies. In 14 cases there was need for Computed Tomography guided cytology to get a positive report of which 5 (35%) cases underwent a second sitting. After getting a biopsy through the laparotomy, the results were compared in all the three groups in which 65% (21/32) in the USG guided biopsied group, 61% (18/29) in the EUS guided biopsied group and 71% (10/14) cases in the CT guided biopsied group had similar diagnosis. Nearly 88% of the lesion in the head and neck of the pancreas are malignant and 74% of the lesions in the body and tail are benign.

Conclusion: With the above mentioned data it is clear that the pathological diagnosis of pancreatic lesions can easily predicted and achieving a pathological diagnosis in pancreatic cancer pre-operatively needs perseverance and investigation can be repeated with the belief of getting a positive report in the second sitting if the mode of investigation is chosen accordingly. EUS guided biopsy proves to be more economic and promising for all group of patients.

No conflict of interest.

611A The close relationship between heparanase and epithelial mesenchymal transition related fibrosis in gastric signet-ring cell adenocarcinoma

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Background: Gastric signet ring cell adenocarcinoma (SRCA) is unique among gastric carcinoma characterized by remarkable fibrosis, rapid invasive progression and high frequency of metastasis to the peritoneum. SRCA is highly resistant to chemotherapy in comparison to other types of gastric cancers. Our main objective is to analyze heparanase gene expression in the disease.

Materials and Methods: Heparanase gene expression was investigated in tumoral and peritumoral tissue from patients with SRCA (n = 11) and different cancer cell lines (n = 10) including KATO-III using RT-qPCR and western blotting. Heparanase protein was also explored by ELISA from the ascites of patients with SRCA (n = 5), non-gastric SRCA (n = 3) and colic cancer (n = 6). Growth factors, EMT related molecules and ATP-binding cassette transporters expression in tumoral and peritumoral tissue from patients with SRCA (n = 8) and KATO-III cells were examined using qPCR.

Conclusions: For the first time, we found heparanase in SRCA and its role in epithelial mesenchymal transition (EMT) and malignancy as in vitro.

No conflict of interest.

612 Assessing the proportion and clinicoradiological profile of gall bladder carcinoma diagnosed in routine histopathological examinations of post cholecystectomy gall bladder (GB) specimen operated for benign GB disease

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Background: Carcinoma of gall bladder (GB) is the most common malignancy of the hepatobiliary tract and fifth most common malignancy in the gastro-intestinal tract. The prevalence of GB carcinoma parallels the occurrence of gall stone disease in a population. The rise in the number of cholecystectomy especially the laparoscopic alternative has brought a new entity, the incidental carcinoma gall bladder.

Objectives: The participants for this study were patients admitted in the Department of Surgery in SMS medical college, Jaipur planned for cholecystectomy for benign gall bladder disease. Inclusion criteria: Patients undergoing cholecystectomy, open or laparoscopic, with pre operative diagnosis of cholelithiasis, chronic cholecystitis, GB polyps and other benign GB diseases.

Exclusion criteria: Patients having pre-operative suspicious or diagnosis (radiological/pathological) of primary or metastatic carcinoma gall bladder.

Results: Out of the total 1542 cholecystectomies, 21 cases were found to have carcinomatous changes in their histopathology specimens, which makes the incidence to be 0.137%. On age distribution, mean age of incidental carcinoma gallbladder in the study was 60.33 years. On sex distribution, out of 21, 17 cases (80.95%) were females. On radiological examination, gallstone was the most consistent finding in patients included in the study with 16 out of 21 patients (76.19%), followed by GB polyp in 4 cases.
On histopathological examination, adenocarcinoma was the most dominant histological tumour in our study with 18 cases (85.71%).

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Dyspepsia</td>
<td>14</td>
<td>66.67</td>
</tr>
<tr>
<td>Right upper quadrant pain</td>
<td>12</td>
<td>57.14</td>
</tr>
<tr>
<td>Fever</td>
<td>04</td>
<td>19.05</td>
</tr>
<tr>
<td>Jaundice</td>
<td>01</td>
<td>04.76</td>
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**Conclusion:** This study thus emphasizes the importance of postoperative histopathological evaluation of all resected gall bladder specimens in routinely done cholecystectomies, in order to detect carcinoma GB at an early and potentially curable stage.

**No conflict of interest.**

**614 Disturbance of redox status enhances radiosensitivity of metastatic esophageal carcinoma**

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**Background:** High constitutive expression of Nrf2 has been found in many types of cancers, and this high level of Nrf2 also favors resistance to drugs and radiation. Here we investigate how isoliquiritigenin (ISL), a natural antioxidant, inhibits the Nrf2-dependent antioxidants pathway and enhances the radiosensitivity of HepG2 cells and HepG2 xenografts.

**Methods and Results:** Treatment of HepG2 cells with ISL for 6 h selectively enhanced transcription and expression of Keap1. Keap1 effectively induced ubiquitination and degradation of Nrf2, and inhibited translocation of Nrf2 to the nucleus. Consequently, expression of Nrf2 downstream genes was reduced, and the Nrf2-dependent antioxidant system was suppressed. Endogenous ROS was higher than before ISL treatment, causing redox imbalance and oxidative stress in HepG2 cells. Moreover, pretreatment with ISL for 6 h followed by X-ray irradiation significantly increased γ-H2AX foci and cell apoptosis, and reduced clonogenic potential compared with cells irradiated with X-rays alone. In addition, HepG2 xenografts, ISL and X-ray cotreatments induced greater apoptosis and tumor growth inhibition, when compared with X-ray treatments alone. Additionally, HepG2 xenografts, in which Nrf2 was expressed at very low levels due to ectopic expression of Keap1, showed that ISL-mediated radiosensitization was Keap1 dependent.

**Conclusion:** ISL inhibited the Nrf2-antioxidant pathway by increasing the levels of Keap1 and ultimately inducing oxidative stress via disturbance of the redox status. The antioxidant ISL possessed pro-oxidative properties, and enhanced the radiosensitivity of liver cancer cells, both in vivo and in vitro. Taken together, these results demonstrated the effectiveness of using ISL to decrease radiosistance, suggesting that ISL could be developed as an adjuvant radiosensitization drug. Disturbance of redox status could be a potential target for radiosensitization.

**No conflict of interest.**

**615 The correlation between FDG-PET parameters and hematologic parameters in patients with esophageal squamous-cell carcinoma treated with definitive chemoradiotherapy**

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**Background:** The aim of this study is to evaluate correlations between standardized uptake value (SUV), metabolic tumor volume (MTV), total lesion glycolysis (TLG) obtained from pretreatment fluorodeoxyglucose-positron emission tomography (FDG-PET/CT) and hematologic parameters [neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR)] in esophageal squamous-cell carcinoma (EC-SCC) patients treated with definitive chemoradiotherapy.

**Materials and Methods:** A total of 48 patients was analyzed. The FDG-PET/CT was delivered median 17 days before treatment and venous blood was taken within 7 days of FDG-PET/CT examination. The SUV value FDG uptake of the region greater than 2.5 was considered positive and MTV value was defined positive region. Patients were stratified by median NLR and PLR. The correlations coefficients and significance between FDG-PET parameters and hematologic parameters were calculated. The relationships between NLR and PLR, and FDG-PET parameters were analyzed.

**Results:** The median survival and follow-up time were 39.9 months (range, 31.2–69.9 months) and 16.2 months (range, 1.8–69.9 months) and, respectively. The 1- and 2-year OS and DFS rates were 62.5%, 33.3% and 43.7%, respectively.
immunosuppressive effect are complex, in which apoptosis of circulating lymphocytes induced by radiation may plays an important role. Thus we examined the relationship between the minimum of absolute lymphocyte counts (Min ALCs) during radiotherapy (RT) and clinical outcomes in the patients with hepatocellular carcinoma (HCC).

Material and Methods: A total of 69 HCC patients who had received RT were retrospectively analyzed. Peripheral blood lymphocyte was measured before, weekly during and after RT. Regression and mixed effects models were used to assess the relationship and potential predictors for overall survival (OS) and disease-free survival (DFS). Receiver operating characteristic curve analysis was used to define optimal cutoff points of continuous variables for outcomes.

Results: The average value of circulating lymphocyte counts was declined during RT (1493.19 vs. 503.46 cells/µL, P < 0.001), with the cutoff value of 450 cells/µL (sensitivity and specificity, 50% and 70.6%, respectively). The MST, 1-year OS rate and 2-year OS rate were 15 months vs 47 months, 27% vs 78% and 4% vs 71%, respectively (P < 0.001) in relatively lower Min ALCs level (<450 cells/µL) group and higher Min ALCs level (>450 cells/µL) group. Controlling for age, sex and performance status, Barcelona Clinic Liver Cancer (BCLC) score, higher serum AFP level (>400 ng/ml) before RT and a lower serum Min ALCs level (<450 cells/µL) during RT were independent negative prognostic factors for OS.

Conclusions: Radiation-related lymphopenia may act as a worse prognostic factor for HCC after RT.

No conflict of interest.

POSTER

617A Acute toxicity of the bowel after stereotactic radiotherapy for abdominalinopelvic oligometastases

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Purpose: To correlate dose-volume histogram (DVH) parameters with appearance of grade ≥2 acute gastrointestinal toxicity of stereotactic radiotherapy (SBRT) in patients with solitary or abdominopelvic oligometastatic disease.

Methods and Materials: Acute and late bowel toxicity of 84 abdominopelvic oligometastatic patients was registered. A logistic regression was performed between DVH parameters and presence of grade ≥2 acute toxicity. The odds of acute toxicity per cm³ were estimated. A Normal Tissue Complication Probability (NTCP) model was built with the most significant parameter to determine complication probabilities (CP).

Results: Thirteen of 84 patients experienced grade ≥2 acute toxicity, while 8 reported late toxicity complications. A significant relationship was found for EQD2 (V30 Gy, V40 Gy, V50 Gy and V65 Gy) and grade ≥2 acute toxicity. Dmax and D2 were not significant. According to the NTCP model, a patient irradiated volume of 10 cm³ resulted in grade ≥2 acute toxicity of less than 10%. Local control was 87% at 2 years and 82% at 5 years. Overall survival was 61% at 2 years and 32% at 5 years.

Conclusion: In SBRT for abdominopelvic oligometastases, a significant relationship was found for EQD2 (V30 Gy, V40 Gy, V50 Gy and V65 Gy) grade ≥2 acute toxicity with good local control.

No conflict of interest.
imaging studies during follow-up were assessed by a radiologist for signs of RP. RP was graded according to SWOG criteria.

Results: A total of 53 patients were included. After exclusion of patients with cervical esophageal cancers and patients with a follow-up of less than 3 months, 35 patients remained. The median VS, V10, V20, V30, V40, V50, and V60 were 57.4%, 39.6%, 19.6%, 10.9% and 10.8 Gy respectively. Grade 2 RP occurred in 2 patients (5.7%). In both patients lung doses were comparably low (VS: 30% and 36%; V20: 15% and 11%) and both patients recovered after initiating treatment with corticosteroids and antibiotics. Another 3 patients reported dyspnoea during follow-up (SWOG grade 1), that did not require intervention. None of the patients with VS >70% (n = 12) developed corticosteroid requiring pneumonitis.

Conclusion: Our data show only small prevalence of RP in patients with esophageal cancer after IMRT. We do not see a correlation of DVH parameters with the risk for RP. As grade 2 RP occurred in patients with rather low lung doses, it seems that other parameters, such as comorbidities, genetic and immunological factors could be involved in the development of RP.

No conflict of interest.

618A POSTER

Results of radical chemoradiotherapy for esophageal and junctional cancers: The Royal Marsden Hospital experience

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Background: At the Royal Marsden Hospital, the current practice guidelines for esophageal cancer are based on histology. Squamous cell carcinomas (SCC) are treated with radical chemoradiation, whereas adenocarcinomas (AC) receive peri-operative chemotherapy. Chemoradiation for patients with AC is considered for those who are ineligible for surgery. Induction chemotherapy is considered for most patients. We report the clinical outcomes of a large cohort of patients treated with radical chemoradiotherapy.

Materials and Methods: Patients with esophageal carcinomas (OC) treated with radical chemoradiation (n = 136), between January 2009 and December 2013, were retrospectively analysed. We focused on overall survival (OS), disease-free survival (DFS) and treatment response. We also looked at predictive factors for treatment outcomes. Standard statistical methods were applied.

Results: Sixty percent of patients were considered free from disease at first response assessment, 12 weeks after radical treatment. Median survival was 2.2 years. Overall survival at 2, 3 and 5 years after treatment, for SCC, was 63%, 57% and 50%, respectively. For AC, overall survival was 42%, 29% and 18%, respectively. Disease-free survival, at 2, 3 and 5 years, was 56%, 48% and 46%, respectively, for SCC, whereas it was 30%, 18% and 12% for AC. Histology, nutritional support during treatment, we lost, ≤10% at end of treatment, response to induction chemotherapy, and a break or reduction of any part of treatment were found predictive factors of response. The first three factors were also found significant predictive factors of DFS.

Conclusion: Our data support radical chemoradiation as an effective treatment strategy for esophageal cancer, achieving an OS at 5 years of 50% for SCC, and 18% for AC for those patients unsuitable for surgery. Both cohorts comprised all stages making comparison with surgical series inappropriate. Further analysis will provide outcomes for those SCC patients who could have undergone surgery had that been unit policy.

No conflict of interest.

619 POSTER

Portal lymphodissection in surgery of liver metastatic lesions

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Despite the active interest among surgeons-hepatologists a portal lymphodissection has its own limited indications and standardizedly used for primary malignant tumor of hepar. In cases of surgical treatment of metastases in hepar the lymphodissection practicability is still debated. During the period from 2014 to 2016 in Moscow Regional Cancer disansperse the portal lymphodissection was performed in 47 cases of anatomoclyl liver resections in patients with colorectal cancer with metastases in liver. Lymphodissection technique was the following: after hepatic angle of colon traction downward and further its mobilization (Kocher technique was used), for mobilization and abduction pancreato-duodenum complex medially. Then peritoneum was dissected along the common hepatic artery up to the celiac trunk and down up performed dissection of fatty tissue and lymphatic nodes and from right to left the celiac trunk vessels identification. After exposing the front surface of hepatoduodenal structures cellular tissue was abducted to the upper right angle of porta of hepar. To facilitate the mobilization of cellular tissue and limafic nodes on posterior surface Gerota's fascia was dissected on the lateral and medial edges of hepatoduodenal ligament, choleodoch and hepatic artery (were set aside with a provisory ligatures). Portal lymphodissection of posterior surface ligaments down to the level of cystic duct. Retrograde cholecystectomy with mobilized cellular tissue and lymphatic nodes as one unit were done. Morphological studying of removed lymphatic nodes allowed to identify metastases in 15 cases (31.9%).

Conclusions: Despite active interest among surgeons-hepatologists the lymphodissection of hepatoduodenal ligament determines obligerality of portal lymphodissection while morphological studying of lymphatic nodes increases the accuracy of staging by identifying extrahepatic dissemination of tumor; lymphodissection allows scrupulous distinguishing all the tubular portal structures that allows their further manipulation (evaluate anatomical variants of liver blood supplying).

No conflict of interest.

620 POSTER

Pancreatogenic complications of targeted therapy

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Significant progress in clinic oncology is inseparably linked with targeted therapy implication, wich considering the biology of the tumor process in a particular patient. Using of targeted therapy means alertness of clinical oncologists in diagnosing specific complications. Analysis was applied on 19 patients undergoing targeted therapy against whom developed an acute edematous pancreatitis from 2005 to 2015 years between the ages of 18 to 82 years. Patients included in clinical trial did not subjected to surgical intervention and had not pancreas pathology. Targeted therapy was provided with trastuzumab, bevacizuamb, sorafem. Despite on conducted conservative therapy, limited pancreatic necrosis (up to 30% of pancreas parenchyma) occurred in 2 patients, widespread pancreatic necrosis (from 30 to 50% of pancreas parenchyma) had 1 patient with subtotally-total (more than 50% of pancreas parenchyma) in 1 patient. In presence of acute aseptic parapancreatic liquid accumulations in Willis's pouch when capacity exceeding 50 ml, and in retroperitoneal cellular tissue exceeding 100 ml, as well as presence of acute pseudocyst with diameter of 3 cm and more a pancreatic punction and drainage of liquid formation were performed under the ultrasound control with a further sonography monitoring. Recurrence of clinical-instrumental effects of pancreatitis were registered in 14 cases on the background of further specific treatment. Leital outcome registered in one case of subtotal-total pancreonecrosis. In conclusion, it should be noted that an acute edematous pancreatit against the background of target therapy characterized by an aggressive course and resistance to ongoing conservative therapy, as well as recurrent course with continued specific therapy.

No conflict of interest.

621 POSTER

Prospective study on total robotic three stage esophagectomy for esophageal cancer – a single institute Indian experience

N. Naidu1, S.P. Somashekhar1. Manipal Comprehensive Cancer Centre-Manipal Hospital, Surgical Oncology, Bangalore, India

Background: Newer advances in the surgical treatment arena of Esophageal cancer is throwing great prospects of adding up to human life with lesser sufferings. Robotic surgery being one of them. Hence, a study to evaluate the safety and technical feasibility of robotic assisted three stage esophagectomy along with its short term oncological outcome was done as follows.

Material and Methods: A prospective, non-randomised study involving sixty-two consecutive histologically proven surgically resectable (T1–3, N0–1, M0) carcinoma esophagus patients at Manipal Institute, Bangalore from July 2011 to June 2016 was conducted. All undertaken total robotic assisted transhiatal and trans-peritoneal three stage esophagectomy with subsequent follow-up for 24 months.

Results: The mean age of the study group was 60 years with average hospital stay of 9 days. Histologically, 69.35% (n = 43) were diagnosed as squamous cell carcinoma and remaining adenocarcinoma 30.65% (n = 18), with lower one third of esophagus as the most common site, 61.29% (n = 38). For initial 10 cases, total docking time, thoracic docking time, total operative time, thoracic phase operative time were slightly higher followed by lesser (n=53). For subsequent cases with a mean of 33.20±1.46 min, 13.76±3.43 min, 321.13±13.75 min and 57.04±9.15 min respectively. The mean blood loss was around 256.32±17.52 ml. The mean lymph node yield was 32 and one case required conversion to open method. Major Post-op
Complications were encountered in 7 cases. Two cases required ventilator support for one day, 15 cases had an ICU stay of 1 day, 5 cases for 2 days and in one case with MI for 15 days. There was no in-hospital or 30 day mortality. All had microscopic negative resection margins. However, one patient had a local recurrence after pathological positive cervical and mediastinal lymph nodes in the follow up period. Median follow up was 24 months (2–48).

Conclusion: Robotic assisted three stage esophagectomy has the benefits of minimally invasive surgery and immediate oncological outcomes are comparable to conventional open surgery. It gives 3-dimensional, magnified view and endorist gives better dexterity with intuitive movements. These technical advantages make oncologically sound surgery. Therefore total robotic three stage esophagectomy is a safe and feasible technique for the treatment of esophageal cancer.

No conflict of interest.

622 POSTER Evaluation of hyperthermic intraperitoneal chemotherapy (HIPEC) and its peri-operative management for peritoneal surface malignancies - single institute Indian experience

N. Naidu1, S.P. Somashekhar1, 1Manipal Comprehensive Cancer Centre-Manipal Hospital, Surgical Oncology, Bangalore, India

Introduction: Peritoneal carcinomatosis is the dissemination and implantation of tumor cells throughout the peritoneal cavity, often resulting in significant morbidity without systemic metastasis having poor prognostic indicator. Inadequate drug delivery to tumour leads to treatment failure. HIPEC combines the pharmacokinetic advantage inherent to the intracavitary delivery of cytotoxic drugs, regional dose intensification along with cytotoxic effect of hyperthermia. Hence, a study to evaluate CRS and HIPEC in various peritoneal surface malignancies.

Objectives: To evaluate the outcome of the HIPEC in the peritoneal surface malignancies and to analyse the mortality and morbidity associated with the procedure. To assess perioperative management of the complications.

Methodology: A prospective observational study was done from January 2013 to June 2016, involving 106 patients. Median follow up of 18 months. Patients with colorectal and peritoneal carcinomatosis were enrolled and subjected to complete cytoreductive surgery, followed by HIPEC using FDA approved pump at 41.5 to 43.5°C over 60–90 min by open technique (uni/Bidirectional). Relevant associated factors were assessed. Data was entered in MS Excel and analysed by SPSS v.20 and subjected to descriptive statistical analysis.

Results: The median age was 54.5 years with majority being females. 74% and 75% had pre-operative chemotherapy. 46% was with serum adenocarcinoma ovary, followed by adenocarcinoma colorectum, 16%. The median peritoneal carcinomatous index was 11.95 (1–37) and the mean duration of surgery was 9.5 hrs. Majority had open technique of operating, 75% and their mean duration of hospital stay was 11.5 days. The mean gastro-intestinal recovery was seen in 5.4±1.4 days. The association of Multivisceral resection with increased infections (P = 0.039), ventilator support (p = 0.001), longer hospital stay (p = 0.002) and longer GI recovery (p = 0.015) was statistically significant and also, longer duration of surgery was associated with more adverse effects (p < 0.001). Closed method associated with more wound complications (P = 0.0001), adverse events (P = 0.0001) and ARDS (P = 0.032). Higher temperature (42.5°C to 43°C) also was associated with more adverse effects (p = 0.028), hypoalbuminemia (P = 0.044) and hypocalcemia (P = 0.014). However, only 10 days mortality was observed.

Conclusion: HIPEC is feasible with acceptable morbidity in Indian patients. It has a long learning curve & with growing experience surgical morbidity can be reduced. Morbidity can be reduced with pre-op protein supplementation, maintaining core body temperature within limits, avoiding higher perfusion temperature, expected management of electrolyte imbalances, and prompt management of infections. A dedicated team of surgeon, anesthetist, medical oncologist and intensivist is mandatory for better outcome. No conflict of interest.

624 POSTER Solid pseudo-papillary tumor of the pancreas: a single centre experience

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Background: Solid pseudopapillary tumor (SPPT) of the pancreas is a rare condition of which only about 450 cases have been reported in literature. It is known as FRAN'TZ tumor; also as solid cystic tumor; papillary epithelial neoplasia; solid and papillary epithelial neoplasia. It is characterized by a long asymptomatic course and nonspecific symptoms. One feature of this tumor is its low malignant potential.

Material and Methods: A retrospective analysis was carried out from 2004 to 2014. We studied 20 patients who underwent surgery at our centre for SPPT of the pancreas to assess different presentation, diagnostic methods and management of this rare disease. In almost all cases, primarily, an abdominal sonography showed a cystic mass which was followed by a contrast enhanced CT scan that confirmed a cystic mass in the upper abdomen, posterior to the stomach with multiple solid components and mural enhancement. Laboratory data including complete blood count, blood chemistry, serum amylase level and coagulation profiles were normal in all cases. In the follow up period, the patients were examined at planned intervals.

Results: The group consisted of 15 females and 5 males at mean age of 27.25 years. Abdominal pain and lump were the most common presenting complaints. Median size was 10 cm (range 6–17 cm). Distal pancreatectomy (11 pts) or pancreatocoduodenectomy (6 pts) were the most common surgeries performed. 2 patients were inoperable and gastrojejunostomy was done, in 1 patient only wide excision was done for tumour on ampulla. On microscopic evaluation, a low grade invasive malignant neoplasm of pancreas characterized by solid cellular sheets with papillary fronds composed of rather uniform epithelial cells arranged around small vessels and cystic spaces with fibronohyalinized borders were observed in all cases. Postoperatively patients were hospitalized for 8–14 days. In 1 patient operated for Whipples procedure, a revision gastrojejunostomy had to be done one month later because of stomal stenosis. Overall median survival after surgical resection is 90% in the long term. In our study, mean follow up was 44.4 months. 1 patient died 17 months after surgery due to unrelated cause. 3 patients were lost to follow up, the rest 16 have had an uneventful follow up.

Conclusion: SPPT of the pancreas is a rare indolent neoplasm with an unclear origin that typically occurs in young females. The diagnosis depends on histological confirmation, but its appearance on imaging is fairly characteristic. We believe that SPPT of the pancreas should be treated aggressively, with attempts made for complete resection, even if this requires metastectomy. Long-term survival can be achieved with an
aggressive approach to both the primary lesion and to the synchronous or metachronous metastatic lesion, predominantly found in the liver.

No conflict of interest.

625 POSTER
Short-term outcomes of laparoscopic distal gastrectomy (D2+CME) for obese patients with advanced gastric cancer
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Objective: This study aimed to evaluate the short-term outcomes of laparoscopic distal gastrectomy (D2+CME) for advanced gastric cancer patients with a body mass index (BMI) exceeding 27 kg/m².

Background: Although D2 gastrectomy is the standard surgical treatment for curable gastric cancer, it is difficult to be performed in overweight and obese patients. Our previous research demonstrated the existence of disseminated cancer cells in the mesogastrium, and we proposed D2 lymphadenectomy plus complete mesogastrium excision (D2+CME) as an optimal surgical approach for advanced gastric cancer (AGC) patients. By dissecting along the surgical planes and embryonic boundary of mesogastrium, D2+CME is repeatable with less blood lost and improved short-term surgical outcomes. Here, we access the feasibility and perioperative outcomes of D2+CME in AGC patients with a BMI exceeding 27 kg/m².

Method: The patients with a BMI exceeding 27 kg/m² underwent laparoscopic D2+CME with a curative R0 resection were enrolled in this study. The surgical procedure was showed in the video. Perioperative outcomes were collected.

Results: Seven obese patients between September 2014 and April 2016 were enrolled in this study. The average age of the patients was 50.4 ± 8.2 (range 40–61). The mean BMI of the patients was 29.14 ± 0.75 (range 27.64–29.76). The mean number of retrieved lymph nodes was 35.86 ± 11.63 (range 23–55). The mean volume of blood loss during laparoscopic resection was 26.1 ± 22.5 ml (range 4.0–62.0). The mean laparoscopic surgery time was 169.3 ± 22.3 min (range 130–200). The mean hospitalization time was 11.3 ± 3.1 days (range 9–18). No operative complication was observed during the hospitalization.

Conclusion: For obese AGC patients, laparoscopic D2+CME is a safe and feasible procedure, and it shows several advantages of short-term outcomes.

No conflict of interest.

626 POSTER
Factors influencing the 3-year recurrence of liver carcinoma after surgery
R. Molek1, 1P. Chatthamrak 2, P. Sukket 1, N. Saengtawee 1, D. Chuwongin 1, P. Vichitvejpaisal3.

Background: Liver carcinoma including 80% Hepatocellular carcinoma (HCC) and 20% Cholangiocarcinoma (CCA) becomes the leading causes of death in East and South-East Asia. Though hepatocarcinoma is the treatment of choice for early stage cancer, the recurrence has been reported as 30%, 62% and 79% in 1st, 3rd and 5th year respectively. Chulabhorn hospital, a cancer institute established in 2010, performed a 3-year retrospective study on the influencing factors and its correlation to liver carcinoma after surgery.

Material and Methods: After IRB approval, factors e.g. negative free margin, tumour staging, higher tumour differentiation were revised from 33 HCC and 34 CCA patients with the proportion of variables to sample size = 1:10. Data was expressed as mean and standard deviation, an analysed by using Fisher’s exact test and Cox proportion-hazards model.

Results: HCC were 22 male and 11 female aged 56.5 ± 13.8 and 53.4 ± 13.0 with the recurrence of 9 (40.9%) and 5 (45.4%) respectively. CCA were 20 male and 14 female aged 56.1 ± 9.1 and 58.3 ± 7.2 with the recurrence of 14 (70.0%) and 8 (57.1%) respectively.

Analysis regarding the recurrent factors of HCC revealed that H(t) = H0(t) · exp[6.87 (vascular invasion)], where HR = 9.17, 95% CI 2.04–41.26. This agreed with Suguru Hasegawa, et al. (2007), Hiroshi Imamura, et al. (2003) and Mitsuo Shimada, et al. (1998) concerning to factors to early recurrence of cancer.

Conclusion: H(t) = H0(t) · exp[2.42 (tumour marker CA19-9)], where HR = 2.42, 95% CI 1.04–5.65. This supported by Tae Yoo, et al. (2015) who proposed that postoperative CA19-9 change was a useful predictor of cholangiocarcinoma survival following liver resection, and Gennaro Nuzzo, et al. (2010) claimed CA19-9 as prognostic factor of CCA.

Conclusion: Vascular invasion was the recurrent factor of HCC, while the higher tumour marker CA19-9 reflected the recurrence of CCA significantly.

No conflict of interest.

627 POSTER DISCUSSION
Complete mesogastrium excision (CME) can reduce cancer leak from mesogastrium during D2 radical gastrectomy in patients with advanced gastric cancer
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Objective: This study aims to determine whether complete mesogastrium excision (CME) can reduce the “cancer leak” (intraperitoneal free cancer cells) in gastric cancer patients who underwent curative D2 gastrectomy.

Background: The mechanism underlying tumor recurrence following curative surgery remains unclear. It is believed that intraperitoneal free cancer cells (iFCC, or free intraperitoneal tumor cells, FITC) leaked or spilled into peritoneal cavity during curative surgery play an important role. In gastric cancer, new strategies should be established towards preventing leakage or spillage of cancer cells from the primary tumor involved tissues which refer to mesogastrium. Our previous research demonstrated the existence of disseminated cancer cells in the mesogastrium, and we proposed D2 lymphadenectomy plus complete mesogastrium excision (D2+CME) as an optimized surgical procedure for advanced gastric cancer (AGC). By dissecting along the surgical planes and embryonic boundary of mesogastrium, D2+CME is repeatable with less blood lost and improved short-term surgical outcomes. In this study, we further evaluated the oncological effect of D2+CME based on the detection of “cancer leak”.

Methods: Curative laparoscopic D2 gastrectomy was performed in 91 patients with AGC. The peritoneal washings were collected prior to and after tumor resection from 45 patients who underwent D2+CME (D2+CME group) and 46 patients who underwent D2 lymphadenectomy alone (D2 group). RT-PCR was used to determine the presence of cancer cell. Positive samples are defined as those with CEA mRNA level over threshold (cutoff value). Peritoneal recurrence-free survival (RFS) and peritoneal recurrence rate (RR) were examined to determine the clinical relevance of detected cancer cells.

Results: Of 91 peritoneal washing samples obtained before gastrectomy, 84 (41 in D2+CME; 43 in D2 alone) showed no presence of cancer cell. After gastrectomy, CEA positive was detected in 17 of 43 (39.5%) samples with D2 group, however, only 5 of 41 (12.2%) samples in D2+CME group detected positive CEA. Two samples in D2+CME group was also significant lower than that in D2 group after gastrectomy (p < 0.05). Presence of “cancer leak” was closely associated with pT stage and surgical procedures. The DFS of patients with CEA positive after gastrectomy was significantly poorer than that of patients with CEA negative (p < 0.005).

Conclusion: CME could reduce the leakage of free cancer cells from the envelop of mesogastrium into the peritoneal cavity during D2 radical gastrectomy, and thus, D2+CME might potentially increase the prognosis of GC patients.

No conflict of interest.
Patients and Methods: Patients with compensated cirrhosis, not candidate for LT and selected for PH or RF were prospectively included (NCT01686880). TARE was performed after a hepatic intra-arterial simulation with 99mTc-labeled albumin macroaggregates showing that selective TARE was feasible with ≤10% lung shunting. Operative morbidity was compared between patients operated after selective TARE and without preoperative TARE.

Results: Thirty-two Child A patients were included. The median tumor number was 1 (IQR: 1–4), median size 38 mm (16–160 mm). TARE was contraindicated in ten cases, due to impossibility of selective arterial approach (n = 7), lung shunting (n = 5) or technical failure (n = 1). After TARE, surgery was refused in 7 cases, due to tumor progression (n = 3), new comorbidities (n = 2), liver failure after additional portal vein embolization (n = 1) and loss of follow up (n = 1). No differences were observed in the postoperative outcome between patients operated after TARE and patients operated without TARE: median hospital stays were respectively 8 and 10 days, minor complications (Clavien < III): 60 and 60%, major complications (Clavien >III): 20 and 40% and mortality ≤5% (all NS).

Conclusion: Selective TARE followed by surgery was feasible in only <50% of the patients, mostly hampered by the impossibility of a selective arterial approach, lung shunting or post-TARE tumor progression. This therapeutic combination was safe as no additional operative morbidity was observed in patients undergoing surgery after TARE as compared with patients receiving surgery only. The potential oncological benefits of this strategy should be further evaluated.

No conflict of interest.

629 Surgical tactics in urethra resection for retroperitoneal tumors
F. Ulmasov1, M. Djuraev2, D. Egamberdiev 2.

Background: Improve the results of plastic surgery of resected urethra performed for the non organ retroperitoneal tumors.

Material and Methods: At the department of abdominal surgery National Cancer Center of Uzbekistan during the 2000–2015 years in 18 patients had resection of urethras due to the germination of retroperitoneal tumor. Restoration of the continuity of the urethra is performed after completion of the main phase of the operation. Depending on the length of the resected portion there was applied different tactics. When the defect portion to the resected urethra up to 3.0 cm continuity is restored by mobilizing the proximal and distal end of the resected urethra. When the defect was from 3.0 to 5.0 cm resected urethra ends it brought together through mobilization of resected kidneys. When the defect above 5.0 cm of right urethra, we have developed an original method of recovery of the urethra by transplantation of appendix bone. Appendectomy is performed with the resection of the distal end of the continuity of the urethra. Appendix moves to the resected portion of the urethra, urethral catheter is carried out through the distant part of the urethra appendiceal process and proximal to the urinary system. Superimposed over the catheter appendiceal-urethral anastomosis.

Results: Postoperative complications associated with plastic urethra were observed: in 1 (3.5%) patient after the formation of urethra, urethra anastomosis with the defect to 3.0, long-term period of up to 3 years in 2 (11.4%) patients had slight narrowing in the anastomosis area with the development of I-degree hydronephrosis. In the remaining patients urethral patency of anastomoses was estimated very well.

Conclusion: When the defect of the urethra was up to 3 cm, continuity can be restored through the mobilization of the distal and proximal urethra. When the defect up to 5.0 cm can be performed through the kidneys mobilization. When the defect constituting more than 5.0 cm on the right side can be used appendix with the preservation of mesentery.

No conflict of interest.

630 The impact of anaemia on survival in gastro-oesophageal cancer
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Background: Anaemia is a common in many patients diagnosed with gastric and oesophageal cancer. Blood transfusions and iron infusions are thought to increase the risk of cancer recurrence. This study aimed to detect the incidence of anaemia in this population of patients undergoing treatment, and assess the effect of anaemia on disease-free and overall survival.

Methods: A prospectively maintained database was interrogated. 193 patients who underwent curative surgery at a centralised OG unit between

Patients: 60 and 60% of the patients, mostly hampered by the impossibility of a selective arterial approach, lung shunting or post-TARE tumor progression. This therapeutic combination was safe as no additional operative morbidity was observed in patients undergoing surgery after TARE as compared with patients receiving surgery only. The potential oncological benefits of this strategy should be further evaluated.

No conflict of interest.

632 Oncological emergencies in colorectal carcinoma
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Background: The incidence of rectal cancer in India is lower than that in the western countries, and it is the eighth leading cancer in India. But still the number of colorectal malignancies which present to the emergency department (ED) are significantly higher than the west. The aim of this study is to determine the factors which play a key role in patient's profile which make them end up in ED.

Materials and Methods: A prospective study was designed based on the records of the RadhaKrishnan Biria Cancer Centre, SMS Medical College from January 2013 to December 2015 which included a total of 120 cases of colorectal cancer presented to a single unit. A thorough analysis was done on the patient's profile and their course of stay in the hospital.

Results: Of the 120 patients 38 patients were admitted through the ED which included 14 cases of intestinal perforation, 18 cases of intestinal obstruction and 6 cases of profuse bleeding per rectum (PRF) in shock. The mortality rate in their first admission was 5/14 in the perforated cases, 4/18 in the obstructed cases and 3/6 in the cases which presented as bleeding PR. The overall mortality rate was 12/38 as compared to worldwide mortality rate. 4/26 patients lost follow up after their first admission. Factors like age (mean 57 yrs), sex (female > male), literacy, religion (Hindus > muslims), dietary habits (vegetarians > non-vegetarians) and patient's residence (rural > urban) all play a significant role in deciding the type of patient's presentation to the hospital.

Conclusion: In colorectal malignancies other than the pathological stage of the disease, the mode of presentation also plays a significant role in determining the prognosis.

In developing countries like India, apart from making technical advancements, care must also be taken in educating the masses about the signs and symptoms of the disease and screening programs should be more efficiently utilized.

No conflict of interest.

633 Capecitabine, 5-fluorouracil and S-1 based regimens for previously untreated advanced esophagogastric cancer: a network meta-analysis
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Introduction: The efficacy and safety of different fluoropyrimidines [5-fluorouracil (5-FU), capecitabine and S-1] for first line treatment of patients with advanced esophagogastric cancer (AEGC) is still a matter of debate, as evidence is inconsistent or based on either Asian or Western studies. Network meta-analysis (NMA) provides both increased power to detect differences as well as cross validation among studies. Therefore, we conducted a systematic review with NMA to examine the relative efficacy
and safety of 5-FU, capecitabine and S-1 based first-line regimens of AEGC in Asian and Western patients.

**Methods:** Medline, EMBASE, CENTRAL and conferences ASCO and ESMO were searched up to January 2016 for randomized controlled trials that compared 5-FU, capecitabine or S-1 based regimens with equal chemotherapy backbones. Direct and indirect data for overall survival (OS) and progression-free-survival (PFS) were combined on the hazard ratio (HR)-scale using random-effects NMA and calculated as combined HRs and 95% credible intervals (95% CrI). Event counts for grade 1–2 and grade 3–4 adverse events were compared with pair-wise meta-analysis.

**Results:** Fifteen studies were identified wherein patients received capecitabine (n = 945), 5-FU (n = 2,132) or S-1 (n = 1,636). No significant differences were found by NMA in respective OS and PFS for capecitabine versus 5-FU (combined HR = 0.89, 95% CrI = 0.76–1.04 and HR = 0.98, 95% CrI = 0.75–1.32), for S-1 versus 5-FU (HR = 0.92, 95% CrI = 0.82–1.04 and HR = 0.88, 95% CrI = 0.70–1.11) and for S-1 versus capecitabine (HR = 1.03, 95% CrI = 0.87–1.22 and HR = 0.89, 95% CrI = 0.65–1.20). These effects were similar in Asian and Western subgroups and were not confounded by any clinicopathological baseline factor. Compared to S-1, 5-FU showed less grade 3–4 stomatitis and dehydration in both Asian and Western patients; and less grade 3–4 mucositis, febrile neutropenia and toxicity-related deaths in Western patients only. Also, S-1 showed less grade 1–2 hand-foot syndrome and grade 3–4 neutropenia compared to capecitabine in Asian patients. Conclusion: There was found no differences in OS and PFS between different fluoropyrimidines, but S-1 had the most the most favourable safety profile compared to 5-FU and capecitabine.

**Conflict of interest:** Other Substantive Relationships: This work was supported by an unrestricted grant from Nordic Pharma.

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**634 POSTER**

Targeting SHP-1–STAT3 signaling: a promising therapeutic approach for the treatment of cholangiocarcinoma

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**Background:** Sorafenib is a multiple kinase inhibitor which targets Raf kinases, VEGFR, and PDGFR and is approved for the treatment of hepatocellular carcinoma (HCC). Previously, we found that pSTAT3 is a major target of SC-43, a sorafenib derivative. In this study, we report that SC-43-induced apoptosis in cholangiocarcinoma (CCA) via a novel mechanism.

**Material and Methods:** Three CCA cell lines (HuCCT-1, KU100 and CGCCA) were treated with SC-43 to determine their sensitivity to SC-43-induced cell death and apoptosis.

**Results:** We found that SC-43 induced apoptotic cell death and activated SH2 domain-containing phosphatase 1 (SHP-1) activity, leading to p-STAT3 downregulation. Importantly, SC-43 augmented SHP-1 activity by direct binding to N-SH2 and relief of its autoinhibition. Deletion of the N-SH2 domain (dn1) or point mutation (D61A) of SHP-1 counteracted the effect of SC-43-induced SHP-1 phosphatase activation and antiproliferation ability in CCA cells. In vivo assay revealed that SC-43 exhibited xenograft tumor growth inhibition, p-STAT3 reduction and SHP-1 activity elevation.

**Conclusions:** SC-43 induced apoptosis in CCA cells through the SHP-1/STAT3 signaling pathway.

**No conflict of interest.**

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**636 POSTER**

Phospho-Akt: a potential resistance marker to chemotherapy and therapy-target to restore sensitivity in pancreatic cancer

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**Background:** Despite an aging population, data on palliative chemotherapy in elderly patients with metastatic pancreatic cancer are scarce. This study investigated the use of chemotherapy in in elderly patients with metastatic pancreatic cancer and assessed their survival.

**Methods:** From the Netherlands Cancer Registry, all 9,407 patients diagnosed with primary metastatic pancreatic adenocarcinoma between 2005 and 2013 were selected to investigate rates of chemotherapy administration by age (<70, 70–74, 75–79, >80 years), 90-day mortality, and overall survival, using logistic and Cox proportional hazard regression analyses.

**Results:** Over time, chemotherapy use in elderly patients under 80 years of age significantly increased (<70 years: from 26% to 43%, 70–74 years: 14% to 25%, 75–79 years: 5% to 13%, all p<0.001, and >80 years: 2% to 3% p=0.58). Overall survival marginally improved in younger patients (<75 years: median 11.1 to 12.5 weeks, p<0.001), but not in elderly patients (<75 years: median 6.0 to 6.1 weeks, p=0.73). With increasing age, microscopic tumour verification occurred less frequently in patients receiving chemotherapy (<70, 70–74, >75 years: 91%, 88%, 85% respectively, p=0.02), 90-day mortality increased (31%, 31%, 44%, p=0.03), and overall survival diminished (median 5.8, 6.0, 4.0 months, p=0.002). After adjustment for confounding factors, worse survival of patients (>75 years receiving chemotherapy persisted (Hazard ratio (>75 vs <70 years) = 1.27, 95% Confidence Interval 1.08–1.48, HR(70–74 vs >70 years) = 0.93, 95% CI 0.83–1.05).

**Conclusions:** Elderly patients (>75 years) who actually were treated with chemotherapy for primary metastatic pancreatic cancer exhibited a worse survival compared to younger patients who received chemotherapy.

**No conflict of interest.**
Nab paclitaxel (Nab-P) and gemcitabine (G) first line chemotherapy (CT) in metastatic pancreatic cancer (mPC) patients (pts) relapsed after adjuvant treatment (ADJT). A "real life" study

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Background: Nab-P and G represents a standard of care in first line mPC treatment. Only 5% of pts in Nab-P+G arm received ADJT in the MPACT trial. Accordingly, there is a lack of information about Nab-P + G benefit in this population. Aim of this analysis was to evaluate outcomes in mPC "real life" pts receiving first-line Nab-P + G after relapsing from ADJT. Methods: Clinical records of 330 mPC pts receiving Nab-P + G with standard schedule as first line CT were retrospectively reviewed, efficacy (Progression Free Survival, PFS and Overall Survival, OS) defined as time elapsed from the start of Nab-P + G to progression or death respectively) in pts treated with prior ADJT. Analysis was then performed in ADJT subgroup according disease free survival (DFS) cut-off (<6 vs 6−12 vs >12 months). OS and PFS were estimated with Kaplan–Meier method with 95% CI. Cox-regression model was applied to the data with univariate and multivariate approach. Results: At time of analysis 100% of the cohort (n=330) OS was 11.3 months (95% CI 9.157−13.443); mPFS 7 months (95% CI 5.827−8.173). 90 out of 330 pts (27.3%) had received G-based ADJT with mDFS of 29.2 months (95% CI 25.62−32.78). In the overall population at multivariate analysis, ADJT treatment was an independent prognostic factor related to better OS (HR 0.53, 95% CI 0.40−0.66; p < 0.001) and PFS (HR 0.69, 95% CI 0.49−0.89; p = 0.024). Median OS in ADJT pts was significantly higher than in pts who had not received ADJT (15.0 vs 10.6 months respectively; p = 0.012). This trend in mPFS was observed in ADJT versus non ADJT pts (8.6 vs 6.9 months; p = 0.06). Pts with longer DFS after ADJT showed major benefit in mOS (16.3 vs 13.1 vs 8.7 months in < 12 vs 6−12 vs >6 months DFS respectively; p < 0.001). No significant differences were observed in DFS were observed in the three subgroups (p = 0.271). Conclusions: Nab-P + G is a standard of care also in pts treated with ADJT. ADJT treatment is an independent prognostic factor related to better survival, maybe reflecting the effect of prior radical surgery. Pts who received G-based ADJT may benefit of Nab-P + G combination with an increased survival in pts with longer DFS. No conflict of interest.

Gastric cancer represents a substantial problem to health-care systems worldwide accounting for substantial patient morbidity and mortality. The interleukin 17 (IL-17) family of cytokines consists of six members (IL-17A−IL-17F). Dysregulation of members of this family have been associated with a variety of diseases and conditions, including cancer and autoimmune disorders. IL-17B and its receptor IL-17RB in gastric cancer development and progression. These molecules may be of use as biomarkers or to generate therapeutic strategies for cancer detection and treatment.

Poster Session (Sunday 29 January 2017) Gynaecological Cancer

Tumor markers in the diagnosis and monitoring of breast cancer (BC)

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Introduction: Tumor markers CA 15-3 and CEA are not highly effective markers of breast cancer, because of their low sensitivity in the early stages of the disease. Lowering the threshold standards and optimization of timing of research can improve their performance.

Methods: The study included 352 patients with breast cancer in stage T1−4N0−1M0−1 who underwent examination in Andijan regional oncologic dispensary in 2002−2010 gg. All the patients tumor markers CA 15-3 and CEA in serum were produced.

Results: On the basis of the statistical data revealed that in 28% of patients in stage T1N0−2 CA 15-3 level was higher than 40 U/ml (P < 0001). At the same time, it turned out that already at a maximum reduction of the gastric level of 30 U/ml of pure patients with elevated levels of the marker in the same stage almost doubled (53.8%). It is possible that lowering the limit adopted by the marker values (<35 ed/ml) can contribute to a correct assessment of the stage of disease and can improve the predictive value of this indicator. In the presence of metastasis markers were more informative. In 91.1% of patients in stage T1−2N1M0, T1−4N1M1, T1−4N1−2M1 set CA15−3 levels higher than 35 U/ml. High levels of CEA (considered marginal level of 3.5 ng/ml) was set in only 35.7% of patients. The findings CA15−3 marker levels after 1−2 weeks after chemotherapy in most cases fall within normal limits. CA15−3 level studies after 1−2 years after completion of treatment does not exceed the established norm only in 44% of patients. In 15% of the patients it was a “token is registered levels above 100ed/ml. The latter is an objective indicator of lack of effectiveness of existing therapies of this disease.

Conclusions: It is inappropriate to limit the definition of standards of Ca 15-3 – 30 U/ml, and a study of markers in some later date that the data reflect the true condition of the patient.

No conflict of interest.

Cervical cancer - treatment outcomes and failure

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Objective: To summarize the data and look into the various treatments offered to cervical cancer patients at Shaukat Khanum Hospital and Research Centre to highlight the most likely causes of treatment failure.

Methods: In this retrospective study, case files of all patients presenting with invasive carcinoma of uterine cervix during 1993–2002 were studied
in respect to personal profile, disease related risk factors, pathological characteristics, treatment administered and outcome in the form of tumor response and survival.

Results: Early age at marriage, multiple marriages of self or spouse, multiparty, prolonged use of contraceptives and smoking were some of the risk factors for cervical cancer in this group of patients. Out of 618 patients presenting with invasive cervical cancer, 65% presented in advanced stages II and III. Apart from advanced stage at presentation, anemia, poor nutrition, and ignorance about self-hygiene and lack of follow-up were main causes of treatment failure. Outcome of treatment was improved when chemotherapy was added to radiation.

Conclusion: Advanced stage at diagnosis and lack of follow-up were main causes of treatment failure. Implementation of screening programs on a large scale, early detection is therefore recommended.

No conflict of interest.

690
POSTER
Inspection of cervix using acetic acid — a good alternative to Pap smear in underdeveloped countries

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Objective: To determine the diagnostic accuracy of visual inspection of cervix using 3% acetic acid as a screening test for early detection of cervical cancer. Taking histopathology as the gold standard.

Methods: The cross-sectional study was conducted at Sir Ganga Ram Hospital, Lahore from January 2014 to December 2014 and comprised all sexually active women aged 19–60 years. During speculum examination 3% acetic acid was applied over the cervix with the help of cotton swab. The observations were noted as positive or negative on visual inspection of the cervix after acetic acid application according to acetowhite changes. Colposcopy-guided cervical biopsy was done in patients with positive or abnormal looking cervix. Colposcopic-directed biopsy was done to respect gold standard.

Results: There were 500 subjects with a mean age of 35.74±6.4 years. Sensitivity, specificity, positive predicted value, negative predicted value of visual inspection of the cervix after acetic acid application was 93.5%, 95.8%, 76.3%, 99%, and the diagnostic accuracy was 95.6%.

Conclusion: Visual inspection of the cervix after acetic acid application is an effective method of detecting pre-invasive phase of cervical cancer and a good alternative to cytological screening for cervical cancer in resource-poor country like Pakistan and can help us in reducing morbidity and mortality among women.

No conflict of interest.

691
POSTER
A retrospective study of cancer testis antigens MAGE-A1 and MAGE-A4 expression in high grade endometrial cancer

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Background: Cancer tests (C/T) antigens are a subgroup of tumor-associated antigens expressed in normal testis germ line cells and in various malignancies of different histological types. Biological functions of C/T genes and C/T antigens in both germ lines and tumors remain poorly understood. Due to their tumor-associated expression pattern and limited presence in normal tissues, C/T antigens appear to be valuable targets for immunotherapy of cancer as well as promising prognostic biomarkers. The aim of this study is to assess the expression of cancer tests (C/T) antigens MAGE-A1 and MAGE-A4 in high grade endometrial cancer, as well as to analyse their possible prognostic significance.

Methods: The study includes 77 patients with high grade endometrial cancers including 39 (51%), 5 (6%) and 33 (43%) with serous, clear cell and endometrioid grade 3 histology, respectively, diagnosed in University Hospital Split, Split, Croatia, between 1998 and 2011. Immunohistochemical staining was performed by using 77B (MAGE-A1) and 57B (MAGE-A4) monoclonal antibodies on archived paraffin embedded samples and was scored semiquantitatively. Survival-time and multivariate survival analyses were performed for purpose of this study. Patients were followed from the time of primary surgery until death or last follow-up till December 2014. The median follow-up time for survivors was 48 months.

Results: MAGE-A1 was found to be expressed in 93% endometrioid endometrial cancer grades 3 and 86% of serous and clear cell carcinomas. MAGE-A4 was found to be expressed in 33% of endometrioid type of endometrial cancers grade 3 and in 27% of serous and clear cell carcinomas. No correlation was found between MAGE-A1 immunohistochemical expression and patient survival. Univariate analysis showed that positive immunohistochemical staining for MAGE-A4 was associated with decreased disease free and overall survival in patients with high grade endometrial cancer. Multivariate analysis showed an association between MAGE-A4 overexpression and decreased disease free but not overall survival in high grade endometrial cancer. There was no significant correlation between MAGE-A4 and MAGE-A1 immunoperoxidase and histological subtype, FIGO stage, lymph node metastasis, muscular infiltration and lymphovascular invasion.

Conclusions: MAGE-A1 which has not been investigated in endometrial cancer so far, is highly expressed in high grade endometrial cancer, with no impact on survival. In contrast, MAGE-A4 expression appears to be of high prognostic significance, although larger numbers of patients are required to confirm this finding.

No conflict of interest.

692
POSTER
Serum CA19-9 as a tumor marker in patients with endometrial cancer

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Background: There are no potential tumor markers validated for prognosis of endometrial cancer. However, CA19-9 is one of the most widely used tumor markers in various types of cancer. Although CA19-9 expression in endometrial cancer has been investigated, its prognostic value remains controversial and no studies have investigated serum CA19-9 levels in large case series. In this study, we investigated diagnostic and prognostic applications of serum CA19-9 for endometrial cancer.

Material and Methods: This prospective study was approved by the Institutional Review Board of the institution. Between January 2006 and December 2012, serum CA19-9 levels were examined prospectively in 215 patients with endometrial cancer, and then determined during treatment and at scheduled follow-up examinations in patients with elevated baseline serum CA19-9 levels.

Results: During this period, a total of 215 patients (stage I, 142; stage II, 19; stage III, 32; stage IV, 22) were treated for endometrial cancer. The median age was 60 years (28–85), and histology types included 191 endometrioid adenocarcinoma and 24 others. Subsequently 52 patients (24.2%) relapsed at the time of the last follow-up and the median follow-up time was 62 months (1–113). Elevated serum CA19-9 levels were identified in 63 patients (29.3%) and were associated with clinical stage (p = 0.02), myometrial invasion depth (p = 0.005), lymph node metastasis (p = 0.002), distant metastasis (p = 0.04), and menopausal status (p = 0.04). Elevated serum CA19-9 levels were related to histological type, histological grade, age, body mass index (BMI), or relapse of disease. Among the 63 patients with elevated serum CA19-9 levels, 52 (82.5%) achieved remission and serum CA19-9 levels returned to the normal range in 50 cases (96.2%). Seven patients (13.5%) had relapses among these patients, and serum CA19-9 level has been elevated again in all cases.

Conclusions: Serum CA19-9 levels are a potential prognostic indicator for endometrial cancer in clinical practice.

No conflict of interest.

693
POSTER
Ca125 and hTERT in ovarian carcinoma: mutual modulation and implication of EGFR/PI3K/Akt/mTOR signaling pathway

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Background: Despite its role as a diagnostic cancer for ovarian cancer (OC), Ca125 plays a key role in advancing tumorigenesis and tumor proliferation by different mechanisms: it protects cancer cells from the immunity system, provides the first step for ovarian cancer cells invasion of the peritoneum, induces endothelial cells angiogenesis, and regulates cancer cells to drug therapy. Telomerase, an enzyme stabilizing telomerase length, is upregulated in 90% of ovarian carcinomas. The aim of our study was to investigate the possible inter-relation between...
Ca125 secretion and telomerase activity, and the possible implication of the PI3K/Akt/mTOR pathway in this modulation.

**Materials and Methods:** ovarian cancer cell lines OVCAR-3, SK-OV-3 and IGROV-1 were treated with three different telomerase inhibitors, BIBR 1532 at 5 and 10 mM and MST-312 at 1 and 2 mM, decreased the Ca125 mRNA expression and protein secretion by the three cell lines. The same pattern was obtained when cells were treated with hTERT siRNA. The activation of Akt lead to an increase in cell proliferation and motility. Interestingly, inhibition of PI3K/Akt/mTOR signaling pathway by BIBR 1532 and rapamycin lead to a decrease in Ca125 concentration suggesting the involvement of this pathway in Ca125 regulation. Moreover, an additive effect was shown when costunolide and BIBR 1532 were combined with the previous inhibitors. A decrease in telomerase expression and activity was obtained after gene silencing of Ca125 by the three cell lines, along with a decrease in EGFR, Akt and mTOR gene expression, which may explain the possible implication of this signaling pathway in the modulation of hTERT by Ca125.

**Conclusion:** Both inhibition of telomerase and PI3K/Akt/mTOR signaling pathways decreased the Ca125 secretion. A substantial role of Ca125 in cancer initiation and progression.

**No conflict of interest.**

694

Locally advanced cancer cervix: a systematic review and meta-analysis of 17 randomized trials to explore the therapeutic evidence for concurrent chemoradiotherapy over radiotherapy alone

N.R. Datta1, E. Stutz1, S. Rogers1, D. Klingbiel2, A. Siebenhüner3, S. Bodis1,4.

**Results:** The three telomerase inhibitors, costunolide and BIBR 1532 at 5 and 10 mM and MST-312 at 1 and 2 mM, decreased the Ca125 mRNA expression and protein secretion by the three cell lines. The same pattern was obtained when cells were treated with hTERT siRNA. The activation of Akt lead to an increase in telomerase activity and secretion by the three cell lines. The addition of inhibitors had an additive effect when costunolide and BIBR 1532 were combined with the previous inhibitors. A decrease in telomerase expression and activity was obtained after gene silencing of Ca125 by the three cell lines, along with a decrease in EGFR, Akt and mTOR gene expression, which may explain the possible implication of this signaling pathway in the modulation of hTERT by Ca125.

**Conclusion:** Both inhibition of telomerase and PI3K/Akt/mTOR signaling pathways decreased the Ca125 secretion. A substantial role of Ca125 in cancer initiation and progression.

**No conflict of interest.**

695

The expression of prolactin receptor and its ligands in ovarian epithelial tumours

N. Magdy1, D. Lee2, M. Masood3, S. Van Noordt4, R. Siraksa4, N. Magdy1, D. Lee2, M. Masood3, S. Van Noordt4, R. Siraksa4, M. El-Bahrawy2,1National Cancer Institute- Cairo University, Pathology, Cairo, Egypt; 2Imperial College London, Pathology, London, United Kingdom; 3Imperial College London, Medicine, London, United Kingdom; 4Kthon Kaen University, The Liver Fluke and Cholangiocarcinoma Research Center, Kthon Kaen, Thailand

**Background:** Accumulating evidence suggests a role for prolactin receptor (PRL-R) signaling in ovarian cancer and in the development of chemo-resistance. PRL-R functions as a homodimer, which may explain the possible implication of this signaling pathway in the modulation of hTERT by Ca125.

**Conclusion:** Both inhibition of telomerase and PI3K/Akt/mTOR signaling pathways decreased the Ca125 secretion. A substantial role of Ca125 in cancer initiation and progression.

**No conflict of interest.**
Background: Ovarian cancer, referred to as the 'silent killer', is often diagnosed during the later stages of the disease. Up to twenty percent of cases at time of diagnosis have evidence of metastasis. Glycogen synthase kinase-3 (GSK-3) is a protein which has been identified with a wide variety of oncogenic traits including cell cycle progression, migration and therapy resistance. ShenLingLan (SLDM) is herbal medicinal formula in which early indications show promise as an anti-cancer agent. This study therefore aimed to determine the expression levels of GSK-3 in an ovarian clinical cohort and analyse how the addition of SLDM in vitro affected ovarian cancer cell migration.

Materials and Methods: Phosphorylation changes in GSK-3 were identified using a Kinexus 

23 protein kinase array using protein lysates from immortalised ovarian cancer cells. Fresh ovarian tumours (n=113) were collected immediately after surgery and processed for histological and molecular analyses. Histopathological and clinical information including staging, differentiation and outcome were also collected and analysed against GSK-3 transcript levels using quantitative PCR (qPCR). The effects of SLDM on 3 different immortalised ovarian cell lines (SKOV-3, A2780 and COV504) and their ability to attach and migrate were evaluated using Electrical Cell-substrate Impedance Sensing (ECIS) both in the presence of SLDM and a combination of SLDM and GSK-3 small inhibitor.

Results: Significantly increased phosphorylation levels were seen in ovarian tumours which were poorly differentiated (p<0.005, vs disease free) and in those patients who had died from ovarian cancer (p<0.005, vs patients who were alive). Treatment with SLDM reduced all three ovarian cell lines’ attachment and migration in a concentration dependent manner, which was further reduced in the presence of TWS119, particularly in the SKOV-3 and A2780 cells.

Conclusions: In ovarian cancer both isomers of GSK-3 have been linked to disease, GSK-alpha in chemo-resistance and GSK3-beta with hyperthermic intraperitoneal chemotherapy for patients with recurrent ovarian cancers. Experience from MISR Cancer Center G. Amira1, A. Sherif2, I. Sallam3, M. Sherif1, K. Diab1, A. Saber1,2. MISR Cancer Center, Surgical Oncology, Giza, Egypt; 2MISR International Hospital, General and GIT Surgery, Cairo, Egypt; 3MISR Cancer Center, Medical Oncology, Giza, Egypt

Background: Most patients with primary ovarian cancer develop a recurrence that is associated with a poor prognosis. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have a promising results in patients with Recurrent Ovarian Cancer (ROC). Pathologic complete response (pCR) after HIPEC is an important prognosticator in the management of ROC. As rates of obesity is high among Egyptian Females, in this study it is clear that body mass index (BMI) affects the likelihood of achieving pCR and complete CRS. We describe an analysis of the relationship between BMI at diagnosis and pCR (absence of residual or recurrent disease) in ROC cases. With unfavorable levels of complete CRS, another important predictor of management outcomes in patients with ROC.

Methods: 39 Study participants were ROC presented to our center from 7/2012 to 11/2015 of which 28 patients underwent the primary surgery at MISR Cancer Center and 11 are referred from other centers. As part of a prospective trial on residual tumor and whose postoperative pathological review definitively described pCR. Clinical characteristics potentially associated with pCR including BMI, age, race, residual tumor size/biomarkers, nodal status, morbidity issues(fistulas and Chest complications) and the presence of extra-pelvic metastasis were examined, as were the relationships between BMI, pCR, and residual tumors. We reported proportions, adjusted odds ratios (OR), and 95% confidence intervals (CI) significant at 2-tailed p<0.05.

Results: Of 39 patients, 24 (61%) had pCR; 27 (69%) were obese BMI >30, and 15 (38%) had residual tumor. There was a difference between obese and non-obese (BMI 30 patients’ pCR rates(61% [24/39] vs. 38% [15/39], p = 0.69) or residual tumor(38% [15/39] vs. 61% [24/39].
IFN-gamma showed that in healthy women is 1:4, and in patients with IFN-gamma and TNF-alpha in the blood of patients with malignant tumors, which revealed a significant increase using test systems "Vector-Best", 2007.

Conclusions: BMI have a significant impact on pCR attainment or residual tumors after CRS plus HIPEC, but the significance of both prognosticators in obese patients warrants further investigation.

No conflict of interest.

**700** POSTER

**Analysis of prostaglandin-endoperoxide synthase (PTGS)-2 gene polymorphisms and risk of cervical cancer in an eastern Indian population: a case control study**

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Background: The Prostaglandin-Endoperoxide Synthase (PTGS)-2 gene appears to act largely as a suppressor of cell proliferation, cell differentiation. Based on the above, the aim of this study was to study the presence of imbalance cytokines in patients with malignancies.

Methods: We enrolled 200 histo-pathologically confirmed patients with cervical cancer (age 18–60 years) (cases) and their corresponding sex and age matched 200 normal individuals (controls). To identify genetic variants responsible for cervical cancer, we performed sequence analysis of PTGS-2 genes. Questionnaire survey was conducted to comprehend the demographic data, smoking status, and cancer stage of patients.

Results: PTGS-2 genotype rs898466: −1195A/G, a functional variant of PTGS-2 gene is strongly associated with cervical cancer disease in our study population. The genotype frequency of rs898466 polymorphism was significantly different between case and control groups (p < 0.001). Compared with the wild type genotype AA, the variant genotype GG was associated with 20 fold increased risk (p < 0.001; Odds ratio = 20.76; 95% CI: 2.86–160.73) for cancer patients. The rs5275: exon1+837T>C polymorphism was not associated with cancer risk although this allele was correlated with decreased risk (p = 0.701; Odds ratio = 0.71; 95% CI: 0.26–1.90). CC genotype was more frequently found in controls as compared with cases and showed an inverse association with the development of cervical cancer, thus suggesting a possible protective effect.

Conclusions: PTGS-2 genotype rs898466: −1195A/G gene polymorphism demonstrated strongly associated with cervical cancer disease. But exon1+837T>C polymorphism was not associated with cancer risk in East Indian women. Further studies evaluating the role of PTGS-2 gene polymorphisms in ethnically diverse populations and a larger cohort may help in understanding the etiopathogenesis of cervical cancer in women worldwide.

No conflict of interest.

**701** POSTER

**Study of the basic balance of cytokines in the blood of ovarian cancer patients**

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Background: The pathogenesis of many diseases may be caused by an imbalance in cytokine system, including processes and cancer. It is known that the range of physiological properties greatly cytokines is involved in cell proliferation, cell differentiation. Based on the above, the aim of this work was to study the presence of imbalance cytokines in patients with malignancies.

Material and Methods: We investigated serum samples of 65 patients with histologically verified malignant ovarian tumors, aged from 32.6±1.5 that had hospital treatment in the Tashkent Maternal Complex N 6 in department of Gynecology and in the City Oncology Dispensary have been investigated. The control consisted of 20 healthy women of similar age and gender. The concentration of cytokines determined by IFN using test systems "Vector-Best", 2007.

Results of the study: We studied the concentration of IFN-gamma, IL-4, TNF-alpha in peripheral blood serum, which revealed a significant increase in IFN-gamma and TNF-alpha in the blood of patients with malignant neoplasm reliable background suppression on IL-4. Study of IL-4 ratio to IFN-gamma showed that in healthy women is 1:4, and in patients with malignancies 1:18. To date, the imbalance between Th1 and Th2 order is considered as the basic unit, which determines the immunopathogenesis of neoplasm.

**Table 1. Levels of IL-6 and TNF-alpha in patients with ovary tumours**

<table>
<thead>
<tr>
<th>Group of examinees</th>
<th>Level (M±m pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF-α IL-4</td>
<td></td>
</tr>
<tr>
<td>Malignant ovary tumour (n = 65)</td>
<td>16.5±4.8^</td>
</tr>
<tr>
<td>Control group (n = 20)</td>
<td>5.45±1.6</td>
</tr>
</tbody>
</table>

Conclusions: 1. All the types of ovary tumours have reliably high indices of IL-4 and NF-α as compared with control group. Malignant neoplasm’s of ovary were accompanied by a more lower content of IL-4 and TNF-α in blood serum than in malignant tumours.

2. Results obtained by us allow consider a high level of IL-4 and NF-α in malignant ovary neoplasms as marker of aggression and malignancy of a course of disease.

No conflict of interest.

**702** POSTER

**Analysis of expression of microRNA in cytological smears as a new method for the diagnosis and prognosis of preinvasive cervical carcinoma**

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Background: Cervical cancer remains the leading cause of death among women of reproductive age, even in countries with existing cytology screening program. Testing for HPV suggested integrate in cytological screening program to increase the effectiveness of early diagnosis of cervical intraepithelial neoplasia (CIN, LSIL, HSIL). In recent years it was shown that infection with HPV, development and progression of dysplasia of cervical epithelium are accompanied by changes of microRNA expression profile of epithelial cells. Evaluation of these changes may have diagnostic value in doubtful cytological data (ASCUS) and prognostic value in identifying of LSIL and HSIL that was the aim of this study of this study.

Material and Methods: Study enrolled patients in whom cytology study revealed changes corresponding to cervical cancer (n = 33), intraepithelial neoplasia of high (HSIL, n = 28) and low grade (LSIL, n = 34) and healthy women (n = 20). Diagnosis of cervical cancer and HSIL was confirmed by subsequent histological examination. On the basis of cytology data analysis, we have selected 18 miRNAs that are likely involved in process of neoplasia of cervicalepithelium. RNA was isolated by original method from material of cytological smears, dried on glasses; miRNAexpression analysis was performed by semi-quantitative RT-PCR. Also in all cases it was carried out research of fifteen HPV types of high oncogenic risk, viral load and genotyping.

Results: Statistically significant difference of expression level in the test groups was identified for a number of molecules microRNA: miR-375, miR-20a, miR-196b, miR-192, miR145 and miR-126. It was found that progression of the neoplastic process was accompanied by increased expression of miR-20a and decreased expression of miR-375. It was developed the classifier that allows by assessing expression of the three microRNAs to confidently differentiate cervical cancer from dysplasia (AUC = 0.876), or divide norm from group with neoplastic changes of the squamous epithelium (cervical cancer). H5IL that implies further thorough control group examination (AUC = 0.94). The observed changes in microRNA expression correlated with presence of HPV, but not correlated with the viral load. Samples of the LSIL group were characterized by the most heterogeneous profiles ofmicroRNA expression, which may indicate the heterogeneity of this category of patients in regard to the risk of cervical cancer development.

Conclusion: Expression profile of studied microRNAs reflects staging of cervical cancer development and suggests a high effectiveness of the

No conflict of interest.

702A POSTER
Comparison of MRI, PET-CT, and frozen biopsy in the evaluation of lymph node status before fertility-sparing radical trachelectomy in early stage cervical cancer

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Background: To compare the accuracy of magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT) and frozen biopsy before fertility-sparing radical trachelectomy in early stage cervical cancer.

Materials and Methods: This was a retrospective study including 73 young women with early stage cervical cancer who tried fertility-sparing laparoscopic or robotic radical trachelectomy. All patients underwent preoperative MRI and PET-CT. Comprehensive lymph node dissection was performed during surgery, and all retrieved lymph nodes were sent to frozen biopsies before final diagnosis and excluding radical trachelectomy. The diagnostic accuracy of MRI, PET-CT, and frozen biopsy was compared using McNemar test and logistic regression using generalized estimating equation. The final pathologic report on lymph nodes was the gold standard for diagnosis.

Results: A total number of retrieved lymph nodes was 1448, and mean some retrieved lymph nodes was 20 (range 2–61). Sixteen lymph node areas were positive in 11 patients (15.1%). There was no significant difference in sensitivity (27.27% versus 54.55%, P = 0.18), specificity (80.36% versus 76.79%, P = 0.41), accuracy (71.64% versus 73.13%, P = 0.76) of MRI versus PET-CT. There was significant difference in sensitivity (100% vs. 27.27%, P = 0.005), specificity (100% vs. 80.36%, P = 0.001), accuracy (100% vs. 71.64%, P < 0.001) of frozen biopsy versus MRI. There was significant difference in sensitivity (100% vs. 54.55%, P = 0.026), specificity (80.36% versus 76.79%, P = 0.001), accuracy (100% vs. 73.13%, P < 0.001) of frozen biopsy versus PET-CT.

Conclusions: Frozen biopsy of all retrieved lymph nodes during surgery is still the best way to evaluate lymph node status before fertility-sparing radical trachelectomy.

No conflict of interest.

703 POSTER
Prognostic impact of primary tumor SUVmax on preoperative 18F FDG PET/CT in local advanced cervical cancer

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Background: The purpose of this study was to evaluate the prognostic value of pretreatment 18F-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (18F FDG PET-CT) in patients with locally advanced cervical cancer.

Materials and Methods: Ninety-two patients with histological diagnosis of cervical cancer, underwent 18F FDG PET-CT in addition to routine protocol including International Federation of Obstetrics and Gynecology (FIGO) staging and Magnetic Resonance Imaging (MRI).

Results: The 18F FDG PET-CT identified the presence of para-aortic lymph node metastases in 17 patients (18%), who were treated with extended field irradiation. The high primary tumor SUVmax showed a significant negative impact on disease-free survival and overall survival (p = 0.02; p = 0.01; p = 0.01) respectively and 18F FDG PET-CT positive para-aortic lymph nodes and advanced FIGO stage were predictive of worse disease-free survival (p = 0.01; p = 0.001) respectively.

Conclusions: High primary tumor SUVmax showed a significant prognostic impact in this large patients cohort. Furthermore, 18F FDG PET-CT modified the radiotherapy planning in 18% of patients.

No conflict of interest.

704 POSTER
The treatment of acute and late vaginal toxicity after adjuvant high dose rate [HDR] vaginal brachytherapy in patients with intermediate risk endometrial cancer: Is local therapy with hyaluronic acid of clinical benefit?

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Background: The aim of the present study was to evaluate the effectiveness of hyaluronic acid (HA) in the prevention of acute and late vaginal toxicities in patients with intermediate risk endometrial cancer who received adjuvant high dose rate (HDR) vaginal brachytherapy (BT).

Material and Methods: We retrospectively analyzed 126 patients with endometrial cancer who underwent extracavitary hysterectomy with or without lymphadenectomy and adjuvant HDR-vaginal BT +/- adjuvant chemotherapy, between January 2011 an January 2015. Target delineation was contoured according to American Brachytherapy Society Consensus Guidelines. The total dose prescription was 21 Gy in 3 fractions (one
fraction for week). Vaginal oozes containing 5 mg of HA were given for whole duration of vaginal BT and for the two following weeks. This treatment was administered once a day in asymptomatic patients and twice daily in those with vaginal symptoms. Acute and late toxicities were evaluated according to late toxicity criteria of RTOG v. 4.03.

Results: The median age of patients was 67 years. Histologically, 100 tumors (79.4%) were type 1 endometrioid carcinomas. According to the revised FIGO 2009 classification, most tumors were in stage IA (30.9%) and in stage IB (27.9%). Thirty-three patients (26.2%) received adjuvant chemotherapy before vaginal BT. Five year disease-free survival (DFS) and five-year overall survival (OS) were 88% and 93%, respectively. The most common acute toxicities were grade 1−2 vaginal inflammation (18 patients, 14.3%) and grade 1−2 dyspareunia (7 patients, 5.5%). Two patients (1.6%) had more than one toxicity. Late toxicity occurred in 20 patients (15.3%). The most common late toxicities were grade 1−2 fibrosis (14 patients, 11.1%) and grade 1−2 telangectasias (7 patients, 5.5%). Six patients (4.8%) had more than one late toxicity. No grade 3 acute or late toxicities were observed. Seventeen patients (13.5%) had both acute and late toxicities.

Conclusions: These results appear to suggest that the local therapy with HA is of clinical benefit for intermediate risk endometrial cancer patients who received adjuvant HA treatment in 10 mm in AP direction. Use of CBCT during the course of IGRT and comparing HA treatment versus no local treatment in this clinical setting is warranted to further evaluate the efficacy of HA in preventing vaginal BT-related vaginal toxicity.

No conflict of interest.

704A

Poster Session, Sunday 29 January 2017 Abstracts S93

Uterine motion associated with strict bladder filling protocol during imaging-guided radiation therapy (IGRT) of carcinoma cervix - do we need to redefine internal target volume (ITV) margins?

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Background: The Internal Target Volume (ITV) margins of the uterus and cervix take into account the interfraction motion (IFM) of uterus occurring mainly due to variations in bladder volumes over the course of radiotherapy. Traditionally, the ITV margins are 15 mm in Antero-Posterior (AP) and Supero-Inferior (SI) axes and 7 mm in lateral axes. The aim of this study was to assess whether the ITV margins need to be redefined when a strict bladder filling protocol is followed.

Material and Methods: Fifteen patients of carcinoma cervix, who were treated with Image-guided Radiotherapy (IGRT) (to a dose of 46 Gy in 23 fractions over 4.5 weeks) from February, 2016 to July, 2016 were recruited. During the course of IGRT, cone beam computed tomographic scans (CBCT), were acquired thrice in the first week of treatment and then weekly for the remaining 3.5 weeks, following our institutional protocol. Patients were asked to empty their bladder 1 hour prior to radiotherapy followed by 500 ml water intake in the first 30 minutes. Empty rectum was also ensured prior to radiotherapy. The Varian Eclipse Offline review v 11.0 was used to match the uterine contours of CBCTs with that in planning CT scan in all three axes – AP, SI and lateral. The median values of these corrections obtained with matching gave an estimate of the IFM and hence ITV margins.

Results: The median values with standard deviations (SD) of IFM are as follows: Supero-Inferior (SI) = 1.9 mm (SD 3.39), Antero-Posterior (AP) = 2.6 mm (SD 4.64) and Lateral = 0.5 mm (SD 2.10). So, the IFM(AP) is 2.6 ± (4.64 ± 2) = −6.68 to +11.88 mm = 18.56 mm, IFM(SI) is 1.9 ± (2.33) = −4.88 to +8.66 = 13.56 mm and the IFM(lateral) is 0.5 ± (2.12) = −3.7 mm to +4.7 mm = 8.4 mm. Hence ITV expansions should be 9.28 mm (AP), 6.78 mm (SI) and 4.2 mm (lateral).

Conclusions: The median values of the IFM in all three axes were found to be within acceptable limits as compared to the traditional margins. The decision of redefining the ITV margins needs to be taken with caution considering the sample size of this study.

No conflict of interest.

705

The importance of prognostic nutritional index in cervical cancer patients treated with concomitant chemoradiotherapy

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Background: We investigated the prognostic value of nutrition-related index (PNI) in locally-advanced cervical cancer (LACC) patients treated with definitive concomitant chemoradiotherapy (CCRT).

Material and Methods: This retrospective study included 109 LACC patients treated with 50.4 Gy/28fx (range: 50–55.8 Gy) radiotherapy (RT) and 4×7 Gy brachytherapy. 104 (95%) patients also had concurrent cisplatin-based chemoradiotherapy concurrent with RT. The PNI was measured weekly, that was calculated by utilizing pre-CRT blood data and during the treatment (PNI = 10− serum albumin in g/dL + 0.005× total lymphocyte count per μL) for each patient. The primary endpoint was the impact of PNI changing on overall survival (OS) and progression free survival (PFS).

Secondary endpoint was to define a cut-off value for PNI in this patient population. Kaplan–Meier analysis and the log-rank test were utilized for survival analysis. We also performed receiver operator characteristic (ROC) curve analysis to determine the PNI cut-off value for this patient population.

Results: Median follow-up and age for entire cohort were 29.9 months (range 3.7–111.9 months) and 57 years (range 23–82 years), respectively. The mean tumor size was 5.5±1.9 cm (range 1.5–13.1 cm). The histopathology was squamous cell carcinoma in 98 patients (90%) and adenocarcinoma in 19 patients (10%). According to distribution of FIGO staging; 8 patients (8%) had stage IB, 4 patients (4%) had stage IIA, 55 patients (51%) had stage IIB, 10 patients (9%) had stage IIA, 26 patients had stage IIIB, and 6 patients (6%) had stage IVA disease. 63 patients (58%) had pelvic ± paraaortic lymph node (LN) metastasis. At last follow-up, 63 patients (58%) were alive (55 alive no evidence disease, 8 alive with disease) and 39 patients (36%) were died with disease. A PNI cut-off value of 49 was identified by using ROC analysis. In univariate analysis, early stage (<IIB), small tumor (<4 cm) and absence of LN metastasis were associated with significantly longer OS and PFS. However PNI cut-off value was not significant prognostic factor for OS and PFS. In multivariate analysis, weekly for PNI change was independent significant factor for OS and PFS (p = 0.002, p = 0.01, respectively).

Conclusions: We found that calculated PNI changes a useful tool in prognostic stratification LACC patients treated with definitive CCRT.

Therefore, as an adjunct to other prognostic factors, we recommend the inclusion of PNI in routine pretreatment assessment of LARC patients planned to be treated curatively.

No conflict of interest.

705A

Feasibility of knowledge-based IMRT planning automatic optimization for cervical cancer

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Background: To compare the dosimetric differences of the planning target volume (PTV) and the organ at risk (OAR) for postoperative patients with cervical cancer on knowledge-based radiation therapy (KBRT) and conventional intensity-modulated radiation therapy (C-IMRT).

Material and Methods: Ten postoperative patients with cervical cancer were chosen, CT scan, PTV and OAR contouring were obtained. KBRT plan and C-IMRT plan were performed for each CT image respectively with Eclipse 13.0 system. Under the condition of 95% volume of PTV of prescription dose, DVH of two treatment plans, conformal dose of target volume (PTV) and OARs, HI, CI and planning time were compared.

Results: The KBRT plan compared with C-IMRT planning, dose of PTV, HI and CI had no big differences. Nine of the ten patients had less or equal dose to the bladder. Eight of the ten patients respectively had less or equal dose to the rectum, left and right femoral head. Planning time of KBRT reduced obviously.

Conclusions: KBRT plans, keeping with C-IMRT plans in dose distribution of the target, reduced the dose of OARs, improved the quality of the IMRT plans and consistency, shortened the time of planning, provided a train of thought for online adaptive radiation therapy.

No conflict of interest.

705B

Evaluation of a knowledge-based planning solution for cervical cancer

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Background: Comparison of 20 cases of patients with cervical cancer after surgery (target and bladder and rectum overlap) dosimetric differences between K-IMRT IMRT and C-IMRT IMRT plan automatic optimization were evaluated.

Material and Methods: 110 patients with cervical cancer were selected from 2014–05–01 to 2015–07–01 in Shandong provincial cancer hospital.10 cases with overlapping volume of target area and endager organs were used as the experimental group E1, and the other patients as
model group were automatically optimized model. In the model group, 10 cases were selected as the experimental group, and cases were selected as the experimental group. E1, E2 group using the automatic generation optimization model K-IMRT IMRT plan. The dosimetric differences were compared between the two groups.

**Results:** The dose parameters of the two groups were compared with the maximum dose of K-IMRT plan, the CI was significantly better than that of E2 group, and the difference was statistically significant (P<0.05). There was no significant difference in the dose parameters of E1 group and the minimal dose of E2 group (P>0.05), and there was no significant difference between the HI group and the group. The two group parameters in E1 group organs at risk, rectal V20, left and right femoral head V15, V20, V25, V30, E2 group of bladder V35, D50, V20, V30, rectum, left and right femoral head, V15 V20 ± 20 K-IMRT plan dose was significantly reduced compared to C-IMRT plan dose and the difference was statistically significant (P<0.05). MU and plans to optimize the time K-IMRT was significantly reduced.

**Conclusions:** The automatic optimization of the intensity modulated radiation therapy plan is feasible in patients with overlapping cervical cancer target areas and the overlapping of the organs.

**No conflict of interest.**

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**Poster 706**

**Results of treatment of patients with ovarian cancer initial stage**

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**Objective:** To determine the role of organ-preserving treatment for patients with malignant tumors of the ovary initial stages and morphological factors determining the course of the disease made it possible to improve the method of treatment of this category of patients. During the operation, carried out surgical staging if the stage of the disease was responsible for the TNM T1aN0M0 graduation, served only one-sided salpingo-oophorectomy at the side of the lesion and biopsy of the contralateral ovary, omentum resection with intraoperative morphological study.

**Results:** The use of organ-preserving treatment for patients with malignant tumors of the ovary IA stage of puberty reproductive age allowed to keep their reproductive function and prevent the development of a surgical menopause, and the rate of 5-year survival with this approach did not differ from the figures after performing standard operations (panhysterectomy, omentectomy) and amounted to 89.2±9.9% and 86.3±5.5%, respectively (p>0.05).

**Conclusions:** Fifteen patients of reproductive age, who underwent conserving therapy – sided adnexectomy, became pregnant (12-one, and in two 3). In 8 patients with normal pregnancy ended in childbirth. The remaining patients for their desire was conducted artificial abortion in a period of 6 to 11 weeks. All patients after delivery under surveillance without evidence of recurrent disease.

**No conflict of interest.**

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**Poster 709**

**The prognostic impact of the pathological response to neoadjuvant dose-dense therapy for ovarian carcinoma**

E. Takahiro1, M. Yunokawa2, H. Yoshida3, S. Bun4, T. Shimoi4, A. Shimomura4, E. Noguchi5, M. Kodaira5, K. Yonemori5, C. Shimizu2, Y. Fujinara4, T. Kato1, K. Tamura1. 1Graduate school of medicine- Chiba University, medical oncology, Chiba, Japan; 2National Cancer Center Hospital, Breast and Medical Oncology, Chiba, Japan; 3National Cancer Center Hospital, Breast and Medical Oncology, Chiba, Japan; 4National Cancer Center Hospital, Breast and Medical Oncology, Chiba, Japan; 5National Cancer Center Hospital, Breast and Medical Oncology, Chiba, Japan; Tokyo-104–0045, Japan

**Purpose:** To determine the pathological response to neoadjuvant dose-dense therapy for ovarian carcinoma. This study investigated the pathological response of 53 patients with p53, bcl-2, and bcl-6 oncoprotein expression in non-epithelial ovarian tumors among the child and adolescent patients who had early recurrence and metastases, which demanded recurrent aggressive chemotherapy.

**Conclusions:** p53 gene suppressor and bcl-2 oncoprotein expression in non-epithelial ovarian tumors among the child and adolescent patients were characterized with high and low rates, which enables to use this rate determination for given pathology hormone progesterone identification.

**No conflict of interest.**
Material and Methods: We retrospectively investigated patients with advanced epithelial ovarian, tubal, or peritoneal carcinoma treated at our hospital from July 2004 to October 2014. Patients received dd-TIC (area under the curve-based dosing of carboplatin 6 mg/ml/m² on day 1 and paclitaxel on days 1, 8, and 15, every 3 weeks) therapy as NAC followed by IDS. We divided the pathological response into four groups as follows: no response (Grade 0); mild response, more than two-thirds of the cancer cells were alive (Grade 1); moderate response, less than two-thirds but more than one-third of cancer cells were alive (Grade 2a); good response, less than one-third of cancer cells were alive (Grade 2b); and complete pathological response (Grade 3); in all the resected specimens with IDS.

Results: Sixty-four patients were enrolled. Median age was 60 years and 29 patients (45.3%) were at stage IV. Most patients (82.8%) were diagnosed with high-grade serous carcinoma. The median cycle of NAC was 3 (range 2–6) and 48 patients (75.0%) achieved complete resection at IDS. For pathological response, 6 (9.4%) patients were classified as Grade 0, 17 (26.6%) as Grade 1, 14 (21.9%) as Grade 2b, 4 (6.3%) as Grade 3 (complete pathological response). In multivariate analysis, Grade 2b and 3 pathological response was a significant favorable prognostic factor (p = 0.047, HR 0.52, 95% CI 0.28–0.99) for PFS (A1). Disease stage was also a significant unfavorable prognostic factor (p = 0.003, HR 2.77, 95% CI, 1.04–7.15) as was poor performance status, and complete resection were not significant factors.

Conclusions: Complete pathological response and good response to NAC might be favorable prognostic factors for PFS in patients with advanced ovarian cancer.

710 POSTER

Integrated efficacy and safety analysis of the poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib in patients (pts) with high-grade ovarian carcinoma (HGOC)


Integrated efficacy and safety analysis of the poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib in patients (pts) with high-grade ovarian carcinoma (HGOC). Safety was assessed in pts with HGOC who were diagnosed with high-grade serous carcinoma. The median cycle of NAC was (range 2–6) and 48 patients (75.0%) achieved complete resection at IDS. For pathological response, 6 (9.4%) patients were classified as Grade 0, 17 (26.6%) as Grade 1, 14 (21.9%) as Grade 2b, 4 (6.3%) as Grade 3 (complete pathological response). In multivariate analysis, Grade 2b and 3 pathological response was a significant favorable prognostic factor (p = 0.047, HR 0.52, 95% CI 0.28–0.99) for PFS (A1). Disease stage was also a significant unfavorable prognostic factor (p = 0.003, HR 2.77, 95% CI, 1.04–7.15) as was poor performance status, and complete resection were not significant factors.

Conclusions: Complete pathological response and good response to NAC might be favorable prognostic factors for PFS in patients with advanced ovarian cancer.

712 POSTER

Prevalence of human papillomavirus in saliva of women with HPV genital lesions in Albania

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Background: The human papillomavirus (HPVs) are DNA viruses associated with benign and malignant lesions of skin and mucous membranes. The HPVs has been implicated as the cause of virtually all cervical cancers worldwide but studies showed that these viruses can cause numerous cancers in several tissues including Oral Squamous Cell Carcinoma (OSCC). The aim of this study was to estimate the prevalence of HPV-DNA in saliva samples collected from women in which it has been previously established the HPV infection of the cervix with relative genotyping and, then, to study the possible correlation.

Methods: Saliva samples were collected from 100 women with HPV cervical lesions, aged between 22 and 52 years old, and 25 healthy women with normal cytology (control group), aged between 20 and 49 years old. PCR assay was used to detect HPV DNA.

Results: The prevalence of oral HPV infection in saliva samples was 24% in women with HPV cervical lesions while in the control group was 8%. It has been demonstrated a strong association between high grade squamous intraepithelial lesion and oral infection due to HPV16 and 18, that are the most frequently detected HPV genotypes.

Conclusion: This study shows that patients with genital HPV infection are at risk for oral infection and hence, for the development of OSCC.

No conflict of interest.
713 POSTER Pharmacokinetic (PK) profile of quisinostat in combination with gemcitabine and cisplatin in patients (pts) with non-small cell lung cancer (NSCLC) or paclitaxel and carboplatin in pts with NSCLC or epithelial ovarian cancer

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Background: The purpose of this work was to determine PK parameters of multiple drugs in plasma of non-small cell lung cancer patients to assess the safety and efficacy of BEP chemotherapy in MOGCT.

Material and Method: Quisinostat was administered at escalated doses (8, 10 and 12 mg) orally each week on Day 1 and on Day 7 of the 1st cycle and evaluate potential PK interactions of quisinostat and chemotherapy (CT) drugs in pts with relapsed NSCLC and ovarian cancer in phase I study.

Results: The half-life of quisinostat was 2.7-fold increased 2.6-fold higher than the CT drugs. The mean value increased from 5.0 to 3.0 (p < 0.05). No significant change of PK parameters were observed in the gemcitabine + cisplatin group on Day 7 compared to Day 1 (p > 0.05).

Conclusions: There was a modest effect of co-administration of paclitaxel + carboplatin on the quisinostat disposition but not in combination with gemcitabine + cisplatin.

Conflict of interest: Advisory Board. Mikhail Fedyanin is a medical adviser of NewVac, LLC. Corporate-sponsored Research: Andrew Cakana, Charles Phelps and Sergey Baranovsky.

714 POSTER The safety and efficacy of bleomycin, etoposide and cisplatin (BEP) chemotherapy in patients with malignant ovarian germ cell tumor

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Background: Malignant ovarian germ cell tumor (MOGCT) is the rare malignancy and occurs in young or adolescent patients. Standard treatment is made of surgery followed by bleomycin, etoposide, and cisplatin (BEP) chemotherapy. It is sensitive to platinum-based chemotherapy with excellent cure rate. However, it needs skillful experience in administration and toxicity management to maintain optimal dose. The aim of our study was to evaluate safety and efficacy of BEP chemotherapy in MOGCT patients.

Material and Methods: This report is retrospectively recorded cases that were treated at Asan Medical Center (Seoul, Korea). From 1992 to 2015, 154 patients with 1 to IV MOGCTs underwent BEP chemotherapy. In the BEP chemo treatment, patients received 3–6 cycles regimen every three weeks per cycle. The safety of BEP was evaluated by Common Terminology Criteria for Adverse Events (CTCAE) v 4.03 and efficacy were determined overall survival (OS) by the Kaplan–Meier method.

Results: Moderate adverse events with BEP chemotherapy was observed 37.6% (n = 58). Severe to life-threatening was reported 22.1% (n = 34). Mean frequency in the moderate adverse event was 1.12 times. Severe adverse events mean frequency was 1.12 times, and life threatening was one case. About 1% (n = 14) patients recurred and disease-free survival was 10.3 months. Overall survival rate was evaluated 94.8%.

Conclusions: BEP regimen has good activity and acceptable toxicity in patients with MOGCT. The updated and expanded results confirm a low relapse rate following BEP chemotherapy in MOGCT. Fertility-sparing surgery was possible in the early stage of cases.

716 POSTER A preclinical evaluation of niraparib efficacy as monotherapy, maintenance and after olaparib treatment (PARP inhibitor after PARP inhibitor) in patient-derived ovarian xenograft tumor models

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Background: Niraparib is an investigational oral, once daily, highly-selective poly (ADP-ribose) polymerase (PARP)-1/-2 inhibitor being developed for use in ovarian and other cancers. Preclinical efficacy of niraparib was evaluated as monotherapy in ovarian cancer patient-derived xenograft (PDX) models and as maintenance therapy after platinum treatment. This preclinical study also assessed the relative efficacy and exposure of niraparib and olaparib in tumor bearing mice.

Materials and Methods: Mice bearing PDX tumors were administered test articles during cycles after tumors initiated growth and were monitored biweekly. For monotherapy studies niraparib or olaparib was dosed daily at 50 mg/kg or 75 mg/kg, respectively. For maintenance treatment, a single 30 mg/kg carboplatin dose was given on day one, followed on day eight by daily niraparib at 50 mg/kg. Some mice receiving olaparib were switched to niraparib on day 44 of treatment. Each tumor was tested for homologous recombination DNA repair deficiency using the Myriad myChoiceHRD test to evaluate the potential utility of using this tumor classifier to identify patients that may benefit from niraparib therapy.

The concentrations of niraparib and olaparib in tumors and plasma were determined at steady state in tumor bearing mice. Terminal blood samples were collected via cardiac puncture at 6 hours post final dose. After euthanasia, the tumor was collected from each animal. Plasma, tumor, and dose formulation samples were analyzed for niraparib and olaparib by LC-MS/MS.

Results: Single-agent niraparib caused tumor regression in 9 of 30 ovarian PDX models overall (30%), and in 9 of 19 HRD positive models (47%). In addition, five (four HRD negative) models responded with 50% or greater tumor growth inhibition. Niraparib maintenance therapy resulted in complete regressions in 2 of 3 models evaluated, including one model that was refractory to platinum. In one BRCA2 mutant platinum-sensitive PDX model niraparib caused tumor regression, while olaparib achieved only tumor growth inhibition. In addition, when the olaparib treatment was switched to niraparib, tumors progressed. Plasma and tumor exposures of niraparib at the 50 mg/kg dose were >12-fold higher than those of olaparib at the 75 mg/kg dose (Table).

Table: Plasma and tumor exposures 6 h post final dose

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Plasma (ng/mL)</th>
<th>Tumor (ng/mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib</td>
<td>168±87</td>
<td>123±32</td>
</tr>
<tr>
<td>Niraparib</td>
<td>2150±681</td>
<td>4567±3250</td>
</tr>
</tbody>
</table>

Conclusions: In a preclinical evaluation, niraparib is highly efficacious as monotherapy causing tumor regression in HRD+ ovarian PDX models. In addition, niraparib shows significant growth inhibition in tumor models regardless of HRD status. Niraparib demonstrated durable remissions as maintenance therapy in both platinum-sensitive and platinum-refractory tumor models. Finally, niraparib caused complete tumor regression in a PDX model whose best response to olaparib was stable disease.

Conflict of interest: Corporate-sponsored Research: S.J. Weroha reports grants from Tesaro, Inc. and AstraZeneca. Other Substantive Relationships: K. Mikule, S. Wang, and K. Wlicoxen are employees of Tesaro, Inc.; S.J. Weroha has a patent with Mayo Medical Ventures with royalties paid.
The state of cancer care for the uterine body and the ways of its improvement in the Republic of North Ossetia-Alania in 1990–2014

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Introduction: Attention to the problem of diagnosis and treatment of endometrial cancer (EC) is due to the increasing incidence of this tumor. Materials and Methods: Forms No. 7, No. 35, No. 5 (table C51), table 2 PH. Results: Over 25 years in the Republican oncological dispensary (ROD) for treatment was 1700 patients with EC, which is 6.9% of tumors of all sites in women and 39.4% of tumors of the reproductive organs. The women's average age 57.8 years. The absolute number of patients by age: 20–24 years: 4 (0.2%); 25–29: 1 (0.05%); 30–34: 10 (0.6%); 35–39: 29 (1.7%); 40–44: 56 (3.3%); 45–49: 110 (6.5%); 50–54: 187 (11.0%); 55–59: 277 (16.3%); 60–64: 316 (18.6%); 65–69: 298 (17.5%); 70–74: 235 (13.8%); 75–79: 111 (6.5%); 80–84: 40 (2.3%); >85: 26 (1.5%). “Crude” incidence rate per 100,000 women had an average of 18.6; at 20–24 years was 0.6, 25–29: 0.2; 30–34: 1.5; 35–39: 4.4; 40–44: 8.9; 45–49: 18.5; 50–54: 55.4; 55–59: 54.6; 60–64: 65.7; 65–69: 67.6; 70–74: 51.9; 75–79: 37.6; 80–84: 19.1; >85: 21.3. The peak incidence was in the group of 60–69 years. The average 5-year-old “gross” the rate of incidence in 1990–1994 was 12.8; 1995–1999: 18.3; 2000–2004: 17.0; 2005–2009: 21.7; 2010–2014: 22.4; that is, it increased 1.8 times. The growth rate of 75%. The cumulative risk of EB is 1.6%. Standardized rate per 100,000 women (world standard) in 1990–1994 was 9.1; 1995–1999: 12.9; 2000–2004: 11.9; 2005–2009: 14.3; and 2010–2014: 14.0; that is, it increased 1.5 times. Growth rate was 33%. Active cancer is found only in 7.8% of patients. Morphologically verified diagnosis of 97.6%. In the early (I–II) stage was 77.6%, stage III 17.4% and stage IV 5.0%. Mortality in the first year was 6%. The relationship between mortality and stage IV disease high is 1.8 and indicates the mistakes made in the definition of tumor extension. Consists on the account during the observation of 82.5 per 100,000 population. 5 years or more is observed in up to 71%. The index of accumulation was 11.4. Conclusion: Mortality and morbidity from EC rose. Mistakes in determining the extent of tumor. Active detection and survival in patients with low. The necessary screening of women at risk for EC. The use of CT and MRI in the diagnosis of tumor extension. No conflict of interest.


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Introduction: Cancer of the cervix (CC) is a global health problem worldwide. Materials and Methods: Forms No. 7, No. 35, No. 5 (table C51), table 2 PH. Results: From 1990 to 2014 in the Republican oncological dispensary (ROD) 1446 hospitalized patients with CC accounting for 5.8% in the structure of all malignancies in women and 33.5% of tumors of the reproductive organs. A mean age of 55.5 years, median age of 54.2 years. Age-specific HIV incidence per 100,000 women: 20–24 years: 0.9; 25–29: 2.6; 30–34: 10.2; 35–39: 18.3; 40–44: 24.8; 45–49: 32.3; 50–54: 33.2; 55–59: 33.0; 60–64: 33.4; 65–69: 26.1; 70–74: 31.9; 75–79: 39.2; 80–84: 18.3; and >85: 11.5. The peak incidence was in the group of 75–79 years. “Gross” rate of incidence per time of observation amounted to an average of 15.9 per 100,000 female population. The average 5-year incidence rate in 1990–1994 was 12.5; 1995–1999: 13.5; 2000–2004: 12.5; 2005–2009: 14.2; and 2010–2014: 13.5; that is, it increased in 1.1 times. The growth rate was 8%. The cumulative risk of developing OC was 1.05%. Standardized (world standard) incidence rate per 100,000 female population for the entire period of observation was on average 9.1. In 1990–1994: 9.0; 1995–1999: 9.8; 2000–2004: 8.4; 2005–2009: 9.5; 2010–2014: 8.9; that is, it has not changed. RYA actively identified only 2.8%. Morphological verification of the diagnosis in 87%. In the early-stage (I–II) disease is diagnosed in 25.4%, stage III in 29.2% and stage IV in 45.4%. Mortality at 1 year was 35.2%. The ratio of mortality to stage IV disease is 0.9. Consists on the account during the follow-up of 31.1 per 100,000 population. Of 5 years or more 49.5%. The index of accumulation is 4.6. Special treatment received 44.4%. Only surgical − 13.1%, combined or comprehensive − 85.9%, drug only − 0.6%, chemoradiation − 0.4%. Conclusion: The incidence of cervical cancer is not reduced. At a high percentage of neglect and mortality. Active revealing of patients and the survival rate of 5 years and lower. The state of medical diagnostic care to patients are not satisfactory. Screening of women at risk for ovarian cancer is extremely important. No conflict of interest.

Diagnostic accuracy comparison between preoperative imaging study and sentinel lymph node biopsy during robotic or laparoscopic surgery in the detection of endometrial and cervical cancer regional lymph node metastasis

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Background: Endometrial and cervical cancer metastasize mainly lymphatic pathway. Lymph node status is the most important prognostic factor. If lymph node metastases are present at the time of primary surgery, 5-year survival drops from 85% to 50%. More than 90% of the removed lymph nodes are free of metastatic disease. Patients could be preserved from potential morbidity. Sentinel lymph node biopsy (SLNB) concept might be applicable in endometrial and cervical cancer. Materials and Methods: Performed a retrospective review of patients with cervical cancer and endometrial cancer who diagnosed and treated at a single institute (Asan Medical Center, Seoul, Korea). All cases underwent preoperative PET/CT or MRI followed by definitive robotic (da Vinci®) or laparoscopic surgical therapy including SLNB with Indocyanine green (ICG) fluorescence detection using Firefly® and NIRICG.
Results: The 89 patients underwent intraoperative sentinel nodes mapping. The age range of the patients was 29–72 years and the median age was 49 years. Deposition of ICG into at least one lymph node was observed in 100% of studied cases. Sentinel node detection and frozen biopsy were performed on all 78 subjects. On permanent pathology, 20.2% (18/89) of studied women had positive lymph node metastasis and 88.9% (16/18) of them had positive metastasis in SLN frozen biopsy. Most common detected lymph node metastasis locations in SLNB were obturator area 50% (9/18). And 35.6% obturator lymph node metastasis was found in all lymph node metastasis. Tumor size was not related with SLNB positive. Sensitivity, specificity, positive predictive value and negative predictive value were evaluated among preoperative PET/CT, preoperative MRI and sentinel lymph node node frozen biopsy. In three variables (PET/CT, MRI, SLNB), Overall detection sensitivity were 50.0%, 31.3%, 81.3%. Specificity were 98.0%, 94.0%, 99.3%. Positive predictive value were 72.7%, 35.7%, 92.9%. Negative predictive value were 94.8%, 92.8%, 96.0%. False positive rate were 2.0%, 6.0%, 0.7%. False negative rate was 50.0%, 68.7%, 18.7%.

Conclusions: Individualized treatment to reduce therapy-associated morbidity is an important consideration in the surgical treatment. SLNB with ICG mapping is more accurate method than conventional imaging tools. SLNB has gained more acceptance and may offer an alternative to complete pelvic lymphadenectomy in the future.

No conflict of interest.

Poster Session (Saturday 28 January 2017)

Haematological Malignancies

763

Low dose palliative radiotherapy for refractory aggressive lymphoma

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Purpose: There are few reports on the administration of palliative radiotherapy to patients with aggressive lymphoma. To determine the efficacy of low-dose palliative radiotherapy in patients with refractory aggressive lymphoma in this study.

Materials and Methods: The present study included 11 patients with 30 sites of aggressive lymphoma (diffuse large cell lymphoma, n = 7; mantle cell lymphoma, n = 2; follicular large cell lymphoma, n = 1; and peripheral T cell lymphoma, n = 1). The patients received local palliative radiotherapy after receiving a median of 4 chemotherapy regimens. The radiotherapy doses, administered to the 30 sites were as follows: 8 Gy, single fraction (n = 27); 6 Gy, single fraction (n = 1); 4 Gy, single fraction (n = 1); and 4 Gy, 2 fractions (n = 1).

Results: The complete response rate was 45% (6/11); the partial response rate was 36% (4/11). Toxicity occurred at one irradiated site (the mandibular), which showed temporal acute gingivitis; however, medication was not required. Retreatment was required for 3 sites on the head (parotid, face and mandible) due to persistent discomfort. None of the other sites (27/30) required retreatment. A patient with refractory DLBCL underwent radiotherapy (4 Gy, single fraction) for hepatic hilar lymph node involvement but did not recover from jaundice and died of DLBCL.

Conclusion: Eight Gray single fraction radiotherapy was one of meaningful for the treatment of refractory aggressive lymphoma in terms of its efficacy and the incidence of adverse events. The use of 8 Gy single fraction radiotherapy is therefore recommended for achieving local control in patients with refractory aggressive lymphoma.

No conflict of interest.

764

Anti-cancer effect of Toxoplasma gondii-derived protein, profilin-like protein as a TLR agonist

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Background: Immunotherapy is the one of cancer therapies and its availability has been expanded by self-cancer vaccine trials using tumor-associated antigens (TAs) which are isolated from self-cancer tissues. However, the antigenicity of TAs is not enough for inducing a strong immune response, and accordingly, vaccine adjuvants are needed to improve the efficacy. Accordingly, the present study investigated on the role of a new TLR agonist, profilin-like protein (TGPRF-1) for a vaccine adjuvant.

Material and Methods: TGPRF-1 was prepared using bacterial expression system and confirmed that TGPRF-1 increased IL-12 production through MyD88 signalling pathway.

Results: Treatment of TGPRF-1 protein on bone marrow-derived macrophage (BMM) especially induced IL-12 (231%) and several chemokines (CCL12 (592.9%), XCL1 (330.9%), CCL5 (267.3%)), and increased antigen-presenting markers (MHC class I & II and B7.1 & B7.2). The treatment of TGPRF-1 increased IL-12- and IFN-γ-levels in mouse sera. At this time, IL-12 and IFN-γ were increased in four groups of TLA, TGPRF-1, ACV+TLA, and ACV+TGPRF-1 except ACV alone. suggested that ACV alone has no role in inducing IL-12 and IFN-γ. In particular, ACV+TGPRF-1 group induced more IFN-γ production than ACV+TLA group.

Conclusion: The present study strongly suggests that TGPRF-1 is a new candidate of vaccine adjuvant for enhancing IL-12-dominant innate immunity.

No conflict of interest.

765

POSTER

ATP promotes immunosuppressive MSCs inhibiting lymphocyte proliferation and expressing indoleamine dioxidegenase

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Background: Mesenchymal stromal cells (MSCs) act as immunosuppressive cells, partially due to the expression of the enzyme indoleamine dioxygenase (IDO) which converts tryptophan to kynurenine. Decreased concentration of tryptophan and increased kynurenine, both inhibit lymphocyte proliferation. Accumulation of MSCs within tumor tissue is associated with tumor progression. Necrotic cell death with release of damage associated molecular patterns (DAMPs) is a characteristic feature of advanced solid tumors. ATP is a DAMP family member. Hence, unphysiologically increased concentrations of ATP is found around stressed and necrotic (tumor) tissue.

Material and Methods: MSCs were generated from bone marrow of healthy donors. Fibroblastoid-shaped adherent cells with capacity for chondrogenic, osteogenic, and lipogenic differentiation and positive for CD73, CD90, CD105 and HLA-A, B, C and negative for CD34, CD3, CD45 were referred to as MSCs. In the presence of ATP at concentrations between 62 to 2000 μM, MSCs were cultured for 4 days in DMEM containing 10% human serum and 100 μg tryptophan/ml. Supernatants were tested for kynurenine in a colorometric assay, as well as for their capacity to inhibit lymphocyte proliferation. Metabolism was assessed by measuring WST-1 cleavage. MSC proliferation was measured by using CyQuanti detecting DNA-content. Intracellular expression of IDO in MSCs was assessed by FACS.

Results: ATP increased dose dependently the expression of IDO in MSCs with subsequent increased kynurenine concentration within the supernatant at about 60%. This effect could be abolished completely in the presence of ATP degrading enzyme (apryase) or when MSCs were pretreated with a P2X7-receptor antagonist (AZ 11645373). Consistently, supernatants from MSCs stimulated with ATP inhibited lymphocyte proliferation from 65% to 16%. Of note, ATP intensely enhanced MSC metabolism without having any influence on their proliferation.

Conclusion: We characterized ATP as a DAMP family member responsible for necrosis-induced immunomodulation. Given the increased concentration of DAMPs within tumor tissue and the fact that necrotic material/DAMPs can act as chemotacticians to MSCs, our results have implications for therapeutic strategies targeting the tumor microenvironment.

No conflict of interest.

766

POSTER

Down regulation of PDGFβre gene is associated with imatinib induced thrombocytopenia in chronic myeloid leukaemia

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Background: Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by the expansion of a clone of hematopoietic stem cells that carry the Philadelphia chromosome (Ph). Ph chromosome results from reciprocal translocation between chromosomes 9 and 22 ([t(9;22)]) and results in BCR-ABL gene, encoding a constitutively active protein tyrosine kinase. Imatinib is the first line treatment for CML, which specifically targets BCR-ABL tyrosine kinase. However, a significant number of CML patients treated with Imatinib develop drug resistance and/or some side effects like thrombocytopenia amongst others, the mechanisms of which in most
cases are unknown. Platelet-Derived Growth Factor Receptor (PDGFR) is involved in the regulation of hematopoiesis. Imatinib mesylate, a platelet-derived growth factor receptor inhibitor, induces thrombocytopenia in a significant proportion of patients with chronic myeloid leukemia.

**Material and Methods:** PDGFRα gene promoter polymorphism (+909CA) and PDGFRβ gene expression were characterized in 50 CML patients at different clinical stages, with respect to 50 age and sex matched healthy controls. DNA and RNA was extracted and RNA was then converted to cDNA. qRT-PCR was performed using SYBR Green based qPCR. PDGFRα gene expression was found to be upregulated in CML patients. 1.26 fold higher, as compared to healthy controls. Patients in chronic phase and accelerated phase had higher PDGFRβ gene expression (median fold change 1.21 and 2.19 respectively) as compared to patients in blast crises (median fold change 0.65). However, this difference did not reach statistical significance (p value 0.20) as well as stages of CML disease (p value 0.47). However, a statistically significant correlation was found between thrombocytopenia and nonthrombocytopenic CML patients (p value 0.002).

**Conclusion:** The AA genotype of +909CA promoter polymorphism is associated with down regulation PDGFRα expression and may be causally related to thrombocytopenia observed in imatinib treated CML patients.

**No conflict of interest.**

**767**

**RIZ1 gene promoter hypermethylation is responsible for downregulation of its expression with progression of chronic myeloid leukemia to advanced phases**

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**Background:** Chronic myeloid leukemia (CML) is a clonal disorder with Philadelphia (Ph) chromosome as the sole genetic abnormality. The heterogeneity of CML is due to additional genetic aberrations which may include SNPs, mutations, epigenetic alterations of various tumor suppressor or cell cycle regulatory genes and even their aberrant expression pattern. Epigenetic changes like histone/DNA methylation, histone acetylation, microRNA expression have an important role in disease progression of CML. Promoter hypermethylation of various genes are the key targets of promoter hypermethylation in cancer. The role of DNA methylation on progression of CML and response to drug therapy has not been elucidated completely. We studied 100 CML patients in different clinical phases (50 CP, 25 AP and 25 BC) and 100 healthy controls to elucidate the role of RIZ1 gene in chronic myeloid leukemia (CML).

**Materials and Methods:** We characterized RIZ1 gene promoter methylation and expression in 100 CML patients (50 Chronic phase, 25 Accelerated phase and 25 Blast crisis) recruited from Lok Nayak Hospital, Maulana Azad Medical College, New Delhi, with respect to 100 age and sex matched healthy controls. RIZ1 promoter methylation was studied by methylation specific PCR (M-PCR). RIZ1 gene expression study was performed using SYBR green based qRTPCR and the results were expressed as mean fold change.

**Results:** In this study, it was found that RIZ1 gene promoter methylation significantly (p = 0.009) increases with CML disease progression to advanced phases. Also, RIZ1 promoter methylation was also found to be significantly associated with haematological (p < 0.001) and molecular (p = 0.0033) response of patients to Imatinib. Patients with RIZ1 promoter methylation showed a higher survival (12.66±2.14 months) in comparison to patients without RIZ1 promoter methylation (40.75±2.11 months) with a statistically significant p value of 0.0007. The RIZ1 gene expression was found to decrease progressively during the progression of CML disease with 0.16, 0.6 and 1.5 fold decreased expression in CP, AP and BC phases respectively. Moreover, patients with RIZ1 promoter methylation had a lower RIZ1 gene expression pattern as compared to patients without RIZ1 promoter methylation (p = 0.0008).

**Conclusion:** Thus, it may be concluded that RIZ1 gene promoter methylation increases and its expression decreases progressively during CML disease advancement. Hence, this may be cause among other for poor drug response of some CML patients to Imatinib therapy.

**No conflict of interest.**

**768**

**POSTER**

**Does IGF2BP1 (insulin like growth factor 2 binding protein 1) drive ETV6-RUNX1 positive B-acute lymphoblastic leukemia?**

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**Background:** Acute lymphoblastic leukemia/lymphoma (ALL) is the commonest childhood hematological neoplasm. Around 85% of ALL is of B-cell origin, 50% of which exhibit genetic rearrangements among which ETV6-RUNX1 is the commonest. The presence of translocation has been demonstrated prenatally ‘in utero’. RNA binding proteins (RBPs) represent one mechanism of controlling gene expression post-transcriptionally. IGF2BP1 is an oncopetal protein overexpressed in multiple epithelial tumors.

**Materials and Methods:** The patient cohort consisted of 127B-ALL patients admitted to the Pediatric Oncologic Department at the University of Padua. Microarray was done using an Agilent 8x60k chip. Data analysis was done using R statistical package.

**Results:** Microarray from cDNA of 44 cases of B-ALL with three different common translocations: REH (ETV6-RUNX1 translocation), RS 4; 11 (MLL-AF4), 697 (E2A-PBX1) and NALM6 (no known translocations involving DLL). IGF2BP1 was among the top RBPs whose expression was highest in ETV6-RUNX1 translocation positive B-ALL. This was validated by qPCR on a large cohort of B-ALL patient-derived bone marrow samples(n = 127).

**Conclusion:** IGF2BP1 overexpression in the mouse bone marrow led to a significant increase in the WBC (white blood corpuscles) count in the peripheral blood. There was also a relative increase in the percentage of B-lymphocytes when compared to T-lymphocytes and myeloid cells. However, IGF2BP1 expression alone was insufficient to transform the hematopoietic progenitors and cause B-ALL.

In vitro, real-time PCR showed significant expression of IGF2BP1 only in REH/REH and NALM6 cell lines. The absence of expression in 697 and NALM6 suggests that IGF2BP1 might be directly downstream of ET6V-RUNX1 fusion protein. Lentiviral vectors (pHAGE6 based) have been created to knock down (using mirRNA 155 formatted siRNA) or overexpress human IGF2BP1 and have been validated. Further work involves characterization of these cell lines resistance in CML. The role of function studies of IGF2BP1 may include SNPs, mutations, epigenetic alterations of various tumor suppressor or cell cycle regulatory genes and even their aberrant expression pattern. Epigenetic changes like histone/DNA methylation, histone acetylation, microRNA expression have an important role in disease progression of CML. The role of DNA methylation on progression of CML and response to drug therapy has not been elucidated completely.

**Conclusions:** B-ALL is a significant clinical problem worldwide. The role of RBPs in leukemia is not well defined. Our study has uncovered a role for one RBP, IGF2BP1, in the pathogenesis of ET6V-RUNX1 positive B-ALL. Since the translocation alone is insufficient for leukemic transformation of B cells, it will be important to understand the role of IGF2BP1 in leukemic transformation of B cells. Once proven conclusively, IGF2BP1 can be used as a novel therapeutic target as well as a prognostic biomarker.

**No conflict of interest.**

**769**

**POSTER SPOTLIGHT**

**Novel therapies in chronic lymphocytic leukemia (CLL): quantifying the impact on patient relevant outcome measures**

**M. Singh1, S. Mealing1, S. Cote2, S. Baculea3. 1ICON PLC, Health Economics and Epidemiology, Abingdon, United Kingdom; 2Janssen-Cilag Ltd., Health Economics- Market Access and Reimbursement- Oncology, High Wycombe, United Kingdom**

**Background:** CLL is an orphan disease that primarily affects the elderly. Of the diagnosed patients, 34% are symptomatic and eligible for 1st line (1L) therapy but the majority of these (56%) are unfit for chemotherapy. Historical treatment options for these patients include chlorambucil (Chl), Bendamustine/Rituximab (BR) and ChlR combination. Recent guidelines also recommend the use of novel agents such as ibritinib (ibr) in this patient group.

Due to limited follow-up in the clinical trials of 1L novel agents for CLL, the long-term benefit to patients of using these products rather than historical therapies is unknown. We therefore developed a Microsoft Excel®...
based model to generate treatment specific lifetime undiscounted estimates of Overall Survival (OS) and Quality Adjusted Life Years (QALYs) for treatment with BR, Chl, ChlR and Ibr. Two scenarios were generated representing worlds without and with novel agents for treating CLL: one using traditional therapies both in 1L and at relapse; one using Ibr in 1L and Physicians Choice (PC) including ideasilib in addition with rituximab (IR) at relapse.

Materials and Methods: The model was based on health states relating to 1L Progression Free Survival (PFS), second-line PFS, Post-Progression Survival (PPS) and death. PFS data for 1L and Relapsed/Refractory (RR) therapy came from RESONATE and RESONATE2. Mortality during 1L PFS, and 2L PFS and PPS were based on RESONATE2, and RESONATE, respectively. The composition of RR/PC was based on IMS Oncology analyser data and assumptions (35% BR, 32% FCR-Lite, 33% R). For the scenario with novel agents use, assumption of 30% use of IR after Ibr was made; usage of R and FCR-Lite was reduced by 15% each. Baseline Health Related Quality of Life (HRQoL) and the impact of Ibr on HRQoL were based on RESONATE2 EQ-SD data. Additional HRQoL and adverse event values were taken either from a recent UK reimbursement submission or literature.

Table 1. Results

<table>
<thead>
<tr>
<th>Scenario</th>
<th>No novel agent use to treat CLL</th>
<th>Novel agent use to treat CLL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L treatment</td>
<td>BR</td>
<td>CN</td>
</tr>
<tr>
<td>OS (years, undiscounted)</td>
<td>8.5</td>
<td>5.4</td>
</tr>
<tr>
<td>QALYs (undiscounted)</td>
<td>6.1</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Results: Mean OS where novel agents were not used ranged from 5.4 to 8.5 years and QALYs from 3.5 to 6.1 (Table 1). Mean OS with novel agents was 10.0 years, corresponding to 7.6 QALYs. Ibr use in 1L followed by PC including novel agent at relapse resulted in projected increase in OS of between 18% (1.5 years) and 86% (4.6 years), corresponding to 25% to 117% increase in QALYs, compared with traditional therapies.

Conclusions: In an elderly and unfit CLL patient population, with a relatively short life expectancy, the use of novel agents such as Ibr yields substantive predicted lifetime patient related benefit compared to historical therapies.

Conflict of interest: Corporate-sponsored Research: This study was funded by Janssen-Cilag Ltd., who commissioned ICON plc to conduct the work. Moushmi Singh and Stuart Mealing are the employees of ICON. Simona Baculea and Sarah Cote are the employees of Janssen-Cilag Ltd.

772

Assessment of BCR-ABL1 transcript levels at 3 months is the major determinant for outcome in patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors

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Background: Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder of the hematopoietic stem cell and is associated with an acquired genetic abnormality known as Philadelphia chromosome in >90% of patients as a result of a rearrangement between the BCR and ABL1 genes (BCR-ABL1). In CML patients BCR-ABL1 transcript level >10% on the international reporting scale at 3 months correlates with significantly unfavorable overall survival and progression-free survival as well as lower molecular and cytogenetic responses. The purpose of this study was to analyse 214 first-line imatinib-treated patients to determine whether patients with the poorest outcome can be better stratified at 3 months which affects the further treatment decisions based on the molecular response.

Material and Methods: A total of 288 patients with CML were treated with daily dose of imatinib 400 mg (n = 112, 38.8%), imatinib 600 mg (n = 92, 31.5%) and imatinib 800 mg (n = 74, 25.6%) and were monitored by peripheral blood molecular analysis. A switch to nilotinib occurred in 79 patients (median month of switch was 9, range 5–71 months), dasatinib in 11 (3.8%) patients, and ponatinib in 7 (2.4%). We used the Polymerase chain reaction based qualitative and quantitative tests to detect and measure the BCR-ABL1 gene in leukemia cells taken from bone marrow samples. The study was approved by the local ethics committee and was conducted according to the Declaration of Helsinki.

Results: The therapy responses were significantly superior for patients with BCR-ABL1 values <10% (n = 236, 81.9% of all patients) compared with those with >10% (n = 41, 18.6% of all patients). The poorest outcomes among the 41 patients with BCR-ABL1 >10% at 3 months were identified by the rate of BCR-ABL1 decline from baseline, assessed by estimating the number of days over which BCR-ABL1 halved. Patients with BCR-ABL1 halving time <92 days (n = 29, 70.7%) had significantly superior outcomes compared with patients whose BCR-ABL1 values did not halve by 92 days (n = 12, 29.3), p < 0.0001.

Conclusions: A single measurement of BCR-ABL1 transcription level assessed at 3 months is the best way to identify patients that will have poor outcomes. This results could help improve clinical recommendations and treatment decisions among the patients with CML.

No conflict of interest.

773

Combination of pomalidomide/dexamethasone in the treatment of relapsed/refractory multiple myeloma in patients with del(17p), t(4;14) and t(14;16) chromosome aberrations

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Background: Over the last decades, significant improvement in myeloma therapy has been observed mainly as a result of the use of new anti-myeloma agents. Pomalidomide is a potent immunomodulatory agent with direct antiproliferative, pro-apoptotic, and antiangiogenic effects, as well as modulatory effects on the immune system. Many authors had shown that chromosome aberrations del(17p), t(4;14) and t(14;16) among myeloma patients are associated with poor survival. The aim of this study was to correlate the response to combination therapy of pomalidomide with dexamethasone and existence of del(17p), t(4;14) and t(14;16) chromosome aberrations in advanced myeloma patients. The second aim was to analyse whether the fail of therapy response was related to the end-stage feature or the adverse genetic profile.

Material and Methods: Patients were eligible to enter into the study if they had relapsed/refractory multiple myeloma following at least 4 prior regimens of treatment. The FISH cytogenetic analysis of del(17p), t(4;14) and t(14;16) was performed on bone marrow plasma cells. A total of 152 patients (72 patients with loss of 17p (32.3%) and/or t(4;14) (21.7%) and t(14;16) (46.8%) (median age 67, range, 39–84 years) and 63 patients (median age 69, range, 48–86 years) without mentioned genetic abnormalities were enrolled in the study. The study was approved by the local ethics committee and was conducted according to the Declaration of Helsinki.

Results: The therapy responses were significantly superior for patients without del(17p), t(4;14) and t(14;16) chromosome aberrations. The median follow-up was 9 months. Among all patients, 82 patients (54%) had discontinued treatment because of disease progression or pomalidomide-related toxicity (12% and 17% of patients had pomalidomide dose reduction and interruption). A total of 129 (84.8%) patients clearly...
responded, and 62% had stable disease. The ORR according to presence of del(17p), t(4;14) and t(14;16) showed a difference compared with the ORR in cohort without molecular abnormalities. The median duration of response was 5.5 months with 49% of patients maintaining response beyond 8 months.

Conclusions: Our study showed that combination of Pomalidomide/Dexamethasone is an effective doublet immunomodulatory drug-based regimen for advanced myeloma patients including patients with risk-related cytogenetic features and adverse FISH such as del(17p), t(4;14) and t(14;16) who are characterized by a rapid disease progression. The subjects characterized with del(17p), t(4;14) and t(14;16) karyotype did not show prolonged OR. Future studies will determine the underlying mechanisms of molecular abnormalities using genetical markers to guide the optimal choice of therapy which would improve the long-term remissions and survival of myeloma patients.

No conflict of interest.

Proffered Papers, Saturday 28 January 2017

Head and Neck Cancer

ORAL

A tailored multidisciplinary head and neck cancer rehabilitation program compared to usual supportive care for patients treated with concomitant chemoradiotherapy: The design of an "assessment of effectiveness" controlled cost-effectiveness in a multicenter prospective observational study

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Background: Since 2011 a personalized, multidisciplinary head and neck cancer rehabilitation (HNR) program is offered to advanced head and neck cancer (HNC) patients in the Netherlands Cancer Institute (NKI). This program is developed to restore and improve patients' functioning, and to optimize health related quality of life (HRQoL). Results from a prospective observational feasibility study show a significant, clinically relevant improvement in HRQoL of patients supported by HNR. In addition, an earlier preventive (swallowing) exercise program (PREP), which is part of HNR, was found cost-effective compared to usual care in advanced head and neck cancer patients treated with concomitant chemoradiotherapy (cCRT).

The aim of the current study is to assess the added value, in terms of effectiveness and cost-effectiveness, of the complete HNR compared to usual supportive care (USC) provided to advanced HNC patients treated with cCRT.

Methods: We will perform a multicenter prospective observational study comparing (cost-)effectiveness of the HNR program to USC for advanced HNC patients treated with cCRT. Primary outcome is HRQoL, which will be assessed using EORTC(QLQ-C30 questionnaire. Functional HRQoL, cost-effectiveness, return to work (RTW), participation, unmet needs (UN) and clinical outcomes are secondary outcomes. Functional improvement will be assessed using the EORTC QLQ-H&N35 questionnaire. Participation will be determined by the Utrecht Scale for Evaluation of clinical Rehabilitation (USER-P) questionnaire. Study-specific questions will be used to assess RTW, UN and for cost-effectiveness purposes (e.g. medical consumption).

Results from the EQ5D-5L will enable the assessment of utilities necessary for cost-effectiveness analysis. Both patient groups will be asked to complete the questionnaires at: diagnosis (t=0), 3 months (t=1), 6 months (t=2), 9 months (t=3) and 12 months (t=4) follow-up after start of cCRT.

Differences in primary and secondary outcomes between the intervention and control group will be analyzed using linear mixed effect models. In addition, a cost-effectiveness analysis (CEA) will be performed by means of a Markov decision model. The CEA will be performed using a societal perspective of the Netherlands.

Results: Final results are expected in 2018.

Conclusion/Discussion: To develop an institutional infrastructure enabling tailored multidisciplinary rehabilitation for specific tumor groups is challenging; multi(inter)disciplinary collaboration must be ensured and adequate financing must be secured. Multidisciplinary rehabilitation is not yet implemented as usual care in all centers, which offers the opportunity for a controlled clinical study. In this way practical and ethical problems related to randomization and blinding are avoided, while a valid estimate of effect can be obtained nonetheless.

No conflict of interest.

823

What is the most effective treatment for head and neck squamous cell carcinoma? An individual patient data network meta-analysis from the MACH-NC and MARCH collaborative groups

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Background: Randomized trials (RCTs) and meta-analyses have demonstrated the survival benefit of concomitant chemoradiation (CRT) or altered fractionation radiotherapy in the treatment of locally advanced head and neck cancer (LAHNC). However the relative efficacy of these treatments is unknown. This study aimed to perform a network meta-analysis of LAHNC treatments to define if one treatment was superior to the other.

Material and Methods: Individual data of 2 meta-analyses evaluating the role of chemortherapy (MACH-NC) and of altered fractionation radiotherapy (MARCH) were used. Network meta-analysis was done under a frequentist approach. A random effect model was used. The log-rank test, stratified by trial, was used. Overall survival (OS) was the primary endpoint. Homogeneity and consistency were assessed by a global Cochran Q statistic. P-score (P-s) was used to rank treatments.

Table: OS results for selected comparisons in the network meta-analysis

<table>
<thead>
<tr>
<th>Treatment comparison</th>
<th>HR</th>
<th>95% CI</th>
<th>Number of trials per comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compared to platinum-based CRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFCRT</td>
<td>1</td>
<td>0.80</td>
<td>[0.65–0.99]</td>
</tr>
<tr>
<td>IC (TaxPF) followed by LRT</td>
<td>2</td>
<td>0.90</td>
<td>[0.73–1.12]</td>
</tr>
<tr>
<td>ACR</td>
<td>3</td>
<td>0.97</td>
<td>[0.86–1.10]</td>
</tr>
<tr>
<td>IC (TaxPF) followed by CRT</td>
<td>4</td>
<td>0.98</td>
<td>[0.80–1.21]</td>
</tr>
<tr>
<td>Compared to LRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFCRT</td>
<td>1</td>
<td>0.62</td>
<td>[0.51–0.76]</td>
</tr>
<tr>
<td>IC (TaxPF) followed by LRT</td>
<td>2</td>
<td>0.70</td>
<td>[0.57–0.86]</td>
</tr>
<tr>
<td>ACR</td>
<td>3</td>
<td>0.75</td>
<td>[0.67–0.85]</td>
</tr>
<tr>
<td>IC (TaxPF) followed by CRT</td>
<td>4</td>
<td>0.76</td>
<td>[0.62–0.94]</td>
</tr>
<tr>
<td>Platinum-based CRT</td>
<td>5</td>
<td>0.77</td>
<td>[0.72–0.83]</td>
</tr>
</tbody>
</table>

TaxPF: taxane, platinum and S-forouracel.

Results: Data of 117 RCTs were analyzed, corresponding to 150 comparisons. They included 28,804 patients with 19,131 deaths and 20,586 progression events. Efficacy of 16 modalities of treatment was evaluated by 35 types of direct comparisons. Hyperfractionated radiotherapy with concomitant chemotherapy (HF-CRT) was ranked as the best treatment in all analyses; the hazard ratio (HR) of HF-CRT compared to platinum-based CRT was 0.80 [95% Confidence interval (CI) 0.65–0.99] for OS (P-s 0.97) and 0.77 [95% CI: 0.62–0.96] for progression-free survival (P-s 0.98). The table summarizes the comparison of the best treatments
with platinum-based CRT and loco-regional treatment (LRT) alone. The superiority of HF CRT was robust to sensitivity analyses. Three other modalities of treatment had a better P-score than platinum-based CRT (P=0.78) but their HR for death were not significantly different: induction chemoradiotherapy (TaxPF) followed by CRT (IC-LRT, P=0.89), accelerated radiotherapy with concomitant chemotherapy (ACRT, P=0.62) and induction chemotherapy (TaxPF) followed by CRT (IC-CRT, P=0.79).

Conclusion: The results of this network meta-analysis suggest the superiority of HF CRT for the treatment of LHN. Although toxicity is not addressed, these results, which ideally need to be confirmed by RCTs, could be clinically useful in advanced diseases with a high risk of locoregional failure, as represented by the patients in these meta-analyses.

No conflict of interest.

824

Improving radiotherapy of squamous cell carcinoma of the head and neck (HNSCC) through a continuous process of biological based clinical trials: Talisman to 40 years experience from the Danish Head and Neck Cancer Group - DAHANCA

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Background: DAHANCA, The Danish Head and Neck Cancer Group, has since 1976 coordinated and organized a national population based treatment of HNSCC in Denmark. In addition has a national database with more than 35,000 HNSCC patients been established. The treatment has been based on national guidelines originated in a large number (>30) of clinical trials. These trials are typically large unbiased population based controlled clinical studies including all eligible patients with the country, (and represents some of the World’s largest randomized trials in HNSCC - see www.dahanca.dk).

Methods: The most pivotal of the studies have focused on improving the efficacy of radiotherapy in advanced HNSCC on a biological basis, by exploring in successive and additive order the role of hypoxia modification with nimorazole, accelerated fractionation with 6 fx per week, chemoradiotherapy with weekly cisplatin and EGFr inhibition by Zalutumumab. The present study is an analysis of these trials (DAHANCA 5, 6, 7, 10, 18, 19) conducted in the years 1985 to 2013. Although the radiotherapy technique may have changed over time is the definition of the tumor target comparable among the studies. All patients were treated with RT only without any additional (nodal) surgery.

Results: During the years has the number of HPVpositive oropharyngeal tumors been increasing, and HPV+16 status was obtained pro- or retrospectively from oropharynx SCC trials. A multivariate analysis corrected for HPV positive in oropharyngeal tumors (HR: 0.47 [0.37–0.60], 95% cft.), large T-size (HR: 1.58 [1.33–1.87]) and N-positivity (HR: 1.99 [1.63–2.44]) showed independent benefit of hypoxia modification (HR: 0.64 [0.52–0.80]); accelerated fractionation (HR: 0.63 [0.53–0.77]) and chemoradiotherapy (HR: 0.46 [0.35–0.59]); but with no benefit of EGFr-inhibition (p=0.17). Similar effects were found when using death from cancer as endpoint. All gained benefits have been included in current national guidelines (www.dahanca.dk).

Conclusion: By an more than 3 times increase of the long-term curability of HNSCC, has this national population based series of prospective clinical trials conducted over a long time period shows the importance of HNSCC, has this national population based series of prospective clinical trials conducted over a long time period shows the importance of the Dutch Society of Radiation Oncology, and is engaged in regulating and improving RT for HNC. One of the objectives of the LPRHHT is to evaluate the variation in treatment plan (TP) objectives and possibly improve treatment planning by increased organ at risk (OAR) sparing and reduction of variation between institutes.

Materials and Methods: A survey was conducted in all 14 Dutch RT centers treating HNC to identify how a typical TP for oropharynx cancer was judged in terms of PTV coverage, dosimetry requirements and OAR sparing. To do this, a CT-scan of an oropharynx cancer patient with creation of PTVs and OAR doses was sent to each department. Planning aims were low mean doses of individual salivary glands, swallowing structures and oral cavity, with PTVboost/elective coverage V95 >98%. Prescription dose was 70 Gy/35 fractions for the boost, 54.25 Gy for PTV/ elective, using a simultaneously integrated boost. Results were presented anonymously, and the 4 centers with lowest OAR doses were asked to share planning tips and tricks with other centers. Centers were asked to undertake a second attempt to lower the OAR dose, using the suggestions of the other centers. In step 3, after evaluating the results, all centers were asked to plan a new case, using their improved planning protocol.

Results: Five different intensity modulated planning systems/techniques were used. The initial variation in OAR dose was high, with a mean dose range of 20–46 Gy for combined swallowing structures and 18–49 Gy for the submandibular gland (step 1). Using the suggestions significantly improved the plan quality and reduced the variation in step 2 by loss of PTV coverage. For instance, the submandibular gland mean dose ±SD reduced from 35.4 ±9.3 to 28.0 ±7.6 Gy. The SD is a measure of variation between institutes. Average combined salivary/swallowing mean doses ±(SD) decreased from 30.3 ±5.3 to 18.5 ±4.3 Gy. The more consistent OAR sparing was confirmed by the low SDs in the plans for the comparison for the new patient in step 3.

No conflict of interest.

832

Parallel assessment of hypoxia in tumor and LN metastases increases prognostic value of hypoxia-specific PET imaging in locally advanced head-and-neck cancer – secondary analysis of the DDFMISO trial

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Background: Primary tumor (T) hypoxia based on hypoxia-specific PET imaging is a known prognostic parameter for locally-advanced head-and-
neck cancer patients. A secondary analysis of the prospective clinical trial on repeated pre- and per-treatment [18F]fluoromisonidazole (FMISO) PET/CT imaging aimed to assess whether parallel evaluation of the oxygenation status in lymph node metastases (LN) and the Tu increases its prognostic value.

**Patients and Methods:** Patients with LN-positive disease from the trial (NCT00180180, Zips et al. 2012, Seidzit et al. 2015) were included in this analysis (n = 45). The patients were treated with curatively intended radiochemotherapy (RCT). The imaging protocol consisted of FMISO PET/CT at four time points: baseline, week 1, 2 and 5. The Tu and LN was based on pre-treatment FDG PET/CT. Qualitative hypoxia analysis was performed for each Tu and LN using a visual binary scale: hypoxic or normoxic being FMISO uptake higher than or equal to background respectively. Based on this scale two prognostic parameters were defined: Tu-hypoxia (patients with a hypoxic Tu, independently of LN oxygenation status) and synchronous Tu- and LN-hypoxia (Tu&LN-hypoxia). In the patients with a large LN (n = 15) a quantitative analysis of FMISO PET/CT was performed to validate the qualitative hypoxia scale. The log-rank test and multivariate Cox-regression were used to evaluate the prognostic impact of hypoxia on loco-regional control (LC) and loco-regional control (LRC).

Table 1. Prognostic value of the hypoxia parameters – p value of log rank test

<table>
<thead>
<tr>
<th>FMISO-PET/CT-sets</th>
<th>Baseline</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 5</th>
</tr>
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<tr>
<td>Local control</td>
<td>n = 45</td>
<td>n = 40</td>
<td>n = 44</td>
<td>n = 45</td>
</tr>
<tr>
<td>Tu-hypoxia</td>
<td>0.133</td>
<td>0.090</td>
<td>0.001</td>
<td>0.004</td>
</tr>
<tr>
<td>Tu&amp;LN-hypoxia</td>
<td>0.001</td>
<td>0.011</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Loco-regional control</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tu-hypoxia</td>
<td>0.129</td>
<td>0.084</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Tu&amp;LN-hypoxia</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Results:** Qualitative FMISO assessment (Table 1) confirmed poor LC in patients with Tu-hypoxia in week 2 and 5. Detection of synchronous Tu- and LN-hypoxia had a strong negative impact on LC and LRC at all measured time-points. These results were supported by multivariate analysis (for LRC: HR = 14.8, p = 0.016; HR = 8.3, p = 0.003 and HR = 5.5, p = 0.005 at baseline, week 2 and week 5, respectively). Moreover, there was a significant correlation between the qualitative and quantitative FMISO PET/CT parameters (p < 0001; R = 0.6–0.8).

**Conclusions:** Parallel evaluation of tumor and LN hypoxia improved the prognostic information in comparison to primary tumor assessment alone, based on secondary analysis of the Dresden FMISO PET/CT trial. If this prognostic value of synchronous tumor- and LN-hypoxia is confirmed in ongoing prospective clinical trials and show to outperform tumor assessment only, it may become a powerful decision-making parameter useful for dose escalation or combined modality trials.

No conflict of interest.

Poster Session (Sunday 29 January 2017)

**Poster 877**

**Head and Neck Cancer**

**Diagnostic usefulness of galectin 3 as surrogate biomarker for differentiating benign from malignant thyroid lesions**

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**Introduction:** Better and accurate diagnosis of thyroid cancer offers better treatment. However, the preoperative diagnosis of thyroid lesions is not only the serious existing challenge that needs to be addressed by pathologist, but also very often, establishing the differential diagnosis between benign and malignancy of a thyroid nodule, based only on the histopathological exam, can be quite difficult. Outstandingly, galectin 3 expression among different thyroid lesions, has recently gained momentum and has been extensively studied as an immunohistochemical marker of thyroid malignancy, and a high diagnostic accuracy has been reported even for difficult pathological diagnoses, such as minimal invasive follicular carcinoma.

**Objectives:** The present study aimed at evaluating the diagnostic utility of galectin 3 expression among different thyroid lesions.

**Materials and Methods:** This is a descriptive, retrospective, hospital-based study conducted at Soba Teaching Hospital, Total Lab care Clinic, and Faculty of Medical laboratory sciences, University of Khartoum during a period from January 2016 till July 2016. We retrieved 60 archived formalin-fixed paraffin-embedded blocks from patients with thyroid lesions and stained them using immunohistochemistry for galectin 3.

**Results:** Immunoreactivity of galectin 3 was observed in 12 (20%) thyroid lesions. Our current study shows that 100% of Graves’ disease were found to be negative and 100% of medullary carcinoma [di] were found negative for the marker. Intriguingly, about 33.4% of multinodular goiters were found positive for the marker, along with 27.8% of follicular carcinomas were found positive. Furthermore, 18.75% of papillary carcinoma was positive also for the marker, and 100% of Hurthle cell carcinoma was positive.

**Conclusion:** Galectin-3 expression is a valuable evidence of malignancy in cases where cytomorphological features are not conclusive, however it should not be used alone in thyroid panel therefore the search for other molecular markers must continue in order to enhance this diagnostic accuracy since the results found still show a persistency of false-negative and false-positive tests.

No conflict of interest.
Methods: This study was carried out on 60 consecutive patients with a histologically proven non-cutaneous Head and Neck Squamous Cell Carcinoma (HNSCC). Every patient was subjected to clinical examination for cervical lymph nodes, CT scan on the neck with intravenous contrast and was correlated with results of Cytological evaluation.

Results: Clinical palpation for cervical lymph nodes had a sensitivity of 82.9%, specificity 69.2%, Positive predictive value 90.6% and Negative predictive value 52.9%. The sensitivity of CT scan in detection of cervical lymph node metastasis in our study is 97.8%, the specificity is 94.6%, the positive predictive value is 95.6%, while negative predictive value is 91.6%. CT scan was better than clinical palpation.

Conclusion: CT increases the accuracy of lymph node metastasis detection. CT is better than clinical palpation.

No conflict of interest.

881 POSTER
Postoperative radiotherapy versus surgery alone for T1N1 and T2N0 oropharyngeal squamous cell carcinoma: a nationwide and retrospective study

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Background: Postoperative radiotherapy is a well-established treatment regimen for patients with locoregionally advanced oropharyngeal carcinoma and is associated with improved overall and disease-free survival. Consenting of patients with an intermediary stage disease (T1N1 and T2N0) is a much more precarious task. This is a result of insufficient availability of data about postoperative radiotherapy due to this relatively uncommon stage. The aim of this study is to evaluate the effects of postoperative radiotherapy for patients with intermediary stage oropharyngeal carcinoma.

Materials and Methods: This retrospective analysis was conducted at 9 Austrian institutions. A total of 91 patients with oropharyngeal squamous cell carcinoma were included and underwent surgery of whom 43 patients received postoperative radiotherapy. It was possible to determine p16 status in 52 patients. Rates of overall and disease-free survival were calculated by means of Kaplan–Meier.

Results: Postoperative radiotherapy showed no benefit in regard to overall survival (p = 0.0052). Moreover, we evaluated the influence of p16 status on survival. In patients with p16 staining it was not possible to detect any difference in disease-free survival (p = 0.002), whereas p16 negative patients showed an improved disease free survival after postoperative radiotherapy. However, these results remained not significant due to the currently small sample size of p16 negative patients (p = 0.0448).

Conclusion: Although we could not observe any difference in overall survival our data suggest that postoperative radiotherapy is able to prolong disease free survival in patients with intermediary stage oropharyngeal squamous cell carcinoma. In particular, patients with p16 negative tumors may profit from postoperative radiotherapy. It is planned to determine p16 in all patients in order to make a concise statement for this subgroup.

No conflict of interest.

882 POSTER
Head and neck cancer in a developing country - a hospital based retrospective study across 10 years from Pakistan

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Background: Head and neck cancers are among the most common cancers in developing countries, especially in South East Asia. Oral cavity is the most commonly affected site. The risk factors are tobacco, betel nut and alcohol. The dimensions of the disease are quite different in developing countries than the western world. Poor socioeconomic status, poverty, lack of health care facilities and illiteracy are the factors that pose a major challenge to the management of the disease.

Aims: The aim of this study is to analyze the prospectively maintained database that has been collected over the period of 10 years showing the trends of the disease and the management outcome of these individuals.

Materials and Methods: All patients diagnosed with head and neck cancer from 2004–2014 from Cancer registry database of Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH & RC) have been retrospectively analyzed.

Results: A total of 5027 patients were studied with a mean age of 58.33 ± 20.54. Overall prevalence of head and neck cancer is approximately twice (3292 (65.6%) in males. Overall 29.1% patients had history of smoking. Betel nut as a risk factor was approximately 3 times more common in males. Oral cavity was the most commonly involved (42.6%) site followed by larynx 13%, Skin malignancies 11.6% and salivary glands 6.9%. Squamous cell carcinoma was the most common histological type 69.2%. A significant number of patients have been accepted with the intent to cure the disease (81.1%) while only few (11.7%) have been treated with palliative intent. Majority of patients presented in advance disease; 43.4% in stage IV disease. Response to chemo-radiation, whether neo-adjuvant or adjuvant was complete in 1899 (37.6%) patients.

Conclusion: There is a huge burden of the head and neck cancer on the health care system in Pakistan. Smoking and betel nut appeared as a major risk factor for these cancers. There is a need to limit the use of these risk factors and there is a need to train people in the specialty and develop National Cancer Control Program in for better monitoring and disease control.

No conflict of interest.

883 POSTER
Incidence and histologic patterns of thyroid cancer in Sri Lanka 2001–2010

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Background: The increasing incidence of thyroid cancer in many developed countries is well documented. In general, increasing cancer incidence is typically interpreted as an increase in the true occurrence of disease which may also reflect better reporting or increased diagnostic scrutiny. We conducted this study to examine trends in thyroid cancer incidence and histological patterns in a developing country, Sri Lanka.

Materials and Methods: A retrospective cohort evaluation of patients with thyroid cancer during 2001–2010 was performed using population based data from the Sri Lanka National Cancer Registry. Trends in incidence and histological patterns were analyzed by age group and gender.

Results: The age standardized incidence of thyroid cancer increased from 3.2 per 100,000 in 2001 to 4.8 per 100,000 in 2010 – a 1.5-fold increase (95% confidence interval [CI] 1.26–1.78; p < 0.001 for trend). A greater part of this increase is attributable to an increase in incidence of papillary thyroid cancer, which increased from 2.2 to 3.4 per 100,000; a 1.55-fold increase (95% CI, 1.36–1.78, p = 0.002 for trend). Follicular cancer showed a much smaller increase from 0.72 to 0.87 per 100,000 (p = 0.045), while other less common varieties of thyroid cancer showed no significant increases in incidence over this period.

Conclusion: Incidence of papillary carcinoma was not different between females, (from 3.58 to 5.21 per 100,000, a 1.43-fold increase) and males (0.88 to 1.47 per 100,000, a 1.67-fold increase, p = 0.675). Highest incidence of papillary carcinoma was observed in 30 to 39-year age group, which has increased from 5.56 to 12.9 per 100,000, a 2.32-fold increase, p < 0.001 for trend).

Conclusions: The increasing incidence of thyroid cancer in Sri Lanka is predominantly due to the increasing incidence of papillary cancers. As many other countries, these trends are more likely to be due to increased detection and better reporting of thyroid cancer, although an inherent increase in the incidence cannot be excluded. Further studies including tumour size and thyroid cancer mortality may help answer these questions.

No conflict of interest.

884 POSTER
Retrospective study of rare cutaneous malignant adnexal tumors of head and neck in a tertiary care cancer hospital

M. Faisal1, O. Waqas1, A. Amjad2, I. Haider1, R. Hussain1, A. Jamshed2, 1Shaukat Khanum Memorial Cancer Hospital and Research Center, Surgical Oncology, Lahore, Pakistan, 2Shaukat Khanum Memorial Cancer Hospital and Research Center, Pathology, Lahore, Pakistan; 3Shaukat Khanum Memorial Cancer Hospital and Research Center, Radiation Oncology, Lahore, Pakistan

Background: Skin adnexal tumors (SAT) are a large and diverse group of benign and malignant neoplasms, which exhibit morphological variation towards one of the different types of adnexal epithelium present in normal skin and pose diagnostic challenge. The purpose of this study is to share our experience with these rare but aggressive tumors at a tertiary care cancer hospital in a developing country.
Materials and Methods: Retrospective review of 11 patients diagnosed with rare adrenal tumors and its variants from January 2005 to December 2014, treated either surgically or non-surgically, was performed to describe the clinic-pathological characteristics and outcome of the disease.

Results: A total of 11 patients were diagnosed with adrenal carcinoma and its variants. Male to female ratio was 1:2.1. The histological variations included sebaceous differentiation (n=3), micro cystic adnexal carcinoma (n=4), trichilemmal carcinoma (n=1), pilomatrix carcinoma (n=1) and hidradenocarcinoma (n=1). The mean age at presentation was 49 years (Range: 34–75). Primary subsite of involvement was scalp in 9 patients followed by eyelids in 2 patients. Surgery stayed as primary treatment modality in almost all patients while post-operative radiotherapy was offered to 6 patients. Median dose of radiation was 45 Grey to the primary site. Indications for radiotherapy included close margins (n=2), positive margins (n=1), high grade histology (n=3) and multifocal disease (n=1). On follow up, 1 patient (n=1) developed loco-regional recurrence and 2 patients (n=2) developed distant metastasis.

Conclusion: Adenocarcinoma are rare tumors with diverse histological patterns and a tendency for loco-regional and distant metastasis. Surgery should be the mainstay of treatment reserving radiotherapy for adjuvant, palliative and re-treatment scenarios.

No conflict of interest.

885 POSTER
Tumor circulating microemboli as poor prognosis factor in patients with locally advanced head and neck squamous cell carcinoma under treatment

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Currently, there are some options of treatment for locally advanced head and neck squamous cell carcinoma (LAHNSCC) patients, such as upfront surgery followed by radiotherapy (RT), RT with chemotherapy (CT) or cetuximab preceded or not by induction CT (ICT). Despite efforts, there are no predictive biomarkers to guide this choice. Our objective was to determine the prognostic role of circulating tumor microemboli (CTM) in LAHNSCC patients treated in two treatment scenarios and to correlate them with progression free survival (PFS) and overall survival (OS).

Material and Methods: Blood samples of non-metastatic LAHNSCC patients, stages III/IV, were analysed for CTM (Rarecells, France). The ISET membrane has 10 spots with million pores of 8 μm. It is well establish that 4 spots of ISET membrane are enough to count CTCs per mL of blood (Krebs et al., 2012). So, we used 4 spots to make immunocytochemistry for CD45 to exclude leucocytes and analyse CTCs/CTMs. Patients were eligible in two scenarios: induction chemotherapy plus RT + CT (n=7) and adjuvant treatment (RT + CT; n=38). Patients were evaluated in two moments: before the beginning of chemotherapy (baseline) and after approximately two months (first follow-up).

Results: There were included 45 patients, 8 women and 37 men, with median age of 60.4 years (42.21–76.8 years). Patients under induction chemotherapy showed more presence of CTM (66.7%) than those under adjuvant treatment (33.3%; p = 0.028). The median follow-up was 12.6 months (1.74–27.4 months). The median number of CTCs at baseline was 3.0 CTCs/mL (0–7 CTCs/mL) and at first follow-up it was 2.0 CTCs/mL (0–11 CTCs/mL, n = 37). There was a correlation between the number of CTCs and the presence of CTM only at baseline (p = 0.015). The presence of CTM at baseline (4.4%) was not determinant for DFS (p = 0.3) and OS (p = 0.4), however, at first follow-up (6.7%), the presence of CTM was statistically significant for both, DFS (p = 0.028) and OS (p = 0.036). Patients with CTM had a DFS of 10 months and OS of 16.2 months versus 20.7 and 33.3 months respectively for those without CTM.

Conclusions: The presence of CTMs after treatment were statistically correlated to worse DFS and OS in LAHNSCC, probably due to selection of resistant tumor clones. No conflict of interest.

886 POSTER SPOTLIGHT
Concurrent chemoradiation (CCRT) or radiotherapy with anti-EGFR directed monoclonal antibody (anti-EGFR) or CCRT + anti-EGFR in locoregionally advanced head-and-neck squamous cell carcinoma (LAHNSCC): a comprehensive review of randomized data

P. Specenier¹, K. Janssens², J.B. Vermorken¹. ¹Antwerp University Hospital, Oncology, Edegem, Belgium; ²Antwerp University, Faculty of Medicine and Health Sciences, Wilrijk, Belgium

Introduction: Several randomized trials on the relative role of CCRT and RT with anti-EGFR were recently published/presented.

Aim: To summarize the existing literature on the role of anti-EGFR directed antibodies as compared to or in association with CCRT.

Results: We retrieved 8 randomized trials from the literature and major congresses (table).

Table (abstract 886).

<table>
<thead>
<tr>
<th>Study author</th>
<th>Phase</th>
<th>N</th>
<th>RT dose and n</th>
<th>Study arms</th>
<th>LRC</th>
<th>OS</th>
<th>PFS</th>
<th>SAE</th>
<th>Grade 3–4 toxicities</th>
<th>Dysphagia</th>
<th>Myocutis</th>
<th>Dermatitis</th>
<th>Interruption &gt;10days</th>
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<tr>
<td>Concert-2</td>
<td>II</td>
<td>61</td>
<td>70–72 Gy, in 30–32 days</td>
<td>cis 100 mg/m² × 2</td>
<td>61%*</td>
<td>40%</td>
<td>32%</td>
<td>40%</td>
<td>11%</td>
<td>0%</td>
<td>32%**</td>
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<td>20</td>
<td>51%*</td>
<td>34%</td>
<td>40%</td>
<td>42%</td>
<td>24%</td>
<td>7%</td>
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<td>35</td>
<td>70 Gy, cis 40 mg/m²/week</td>
<td>80%</td>
<td>9%*</td>
<td>53%</td>
<td>21%</td>
<td>0%*</td>
<td>53%*</td>
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<td>78%*</td>
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<td>75.8%**</td>
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<td>RT + anti-EGFR or CCRT + anti-EGFR</td>
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<td>54%</td>
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<td>78.4%**</td>
<td>50.8%</td>
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<td>GORTEC 2007–02 II</td>
<td>179</td>
<td>70 Gy, cis 100 mg/m² × 2</td>
<td>58.9%</td>
<td>61%</td>
<td>17%</td>
<td>0%*</td>
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N, number of patients; LCR, locoregional control rate; cis, cisplatin; pan, panitumab; cet, cetuximab; n, number of fractions; Gy, Gray; RT, radiotherapy; NS, not significant; CCRT, chemoradiation; SAE, serious adverse events; carbo/5-FU, carboplatin 70 mg/m² × 5-fluouracil 600 mg/m²/day, day 1–4; cis/5-FU, cisplatin 20 mg/m²/day and day 5–FU 400 mg/m²/day day 1–4.

*Co-primary endpoint.
**Modifications in cisplatin dose.
***Interruption >7 days/permanent discontinuation.
** Intensification/substitution/predictive toxic adverse events.
# RT completed 70 Gy.
* Co-primary endpoint.
** Modifications in cisplatin dose.
*** Interruption >7 days/permanent discontinuation.
** Intensification/substitution/predictive toxic adverse events.
# RT completed 70 Gy.

No conflict of interest.
Conclusions: CCRT is superior to RT + anti-EGFR. CCRT + anti-EGFR is superior to RT plus anti-EGFR, CCRT + anti-EGFR is not superior to CCRT, AFX (accelerated fractionation RT) + anti-EGFR is not superior to CCRT and non-inferiority has not been demonstrated. CCRT is still the standard of care in locoregionally advanced patients with LA-HNSCC present mostly at the end of treatment (n=46, 92.0%) smears. Statistically present mostly at the end of treatment (n=46, 92.0%) smears. Statistically significant (p<0.000) increase in all nuclear abnormalities at different days of CCRT was observed i.e. karyolysis, karyorrhexis, binucleation, micronucleation, prominent nucleoli and multinucleation.

Conclusion: A direct dose-response association exists among the frequencies of various nuclear changes and CCRT in peritumoral area of OSCC patients. Further studies are required to evaluate the role of these changes in predicting peritumoral area chemo-radiosensitivity. No conflict of interest.

887
Dose response relationship of nuclear changes with fractionated concomitant chemoradiotherapy in assessing chemo-radiosensitivity of peritumoral area in oral squamous cell carcinoma patients
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Introduction: Globally, oral cancer is the eighth most common cause of cancer-related deaths, although many people are unaware of its presence. Of these oral cancers, more than 90% are oral squamous cell carcinomas (OSCC) arising in the mucous membranes of the oral cavity and oropharynx. The early OSCC are usually treated with surgery and radiation therapy, whereas patients with advanced OSCC may undergo combination of treatments i.e. radiation therapy, chemotherapy and concomitant chemoradiotherapy (CCRT). A CCRT regimen represents the most excellent current standard therapy for many patients with regionally advanced solid tumours, and improves the likelihood of cure. The clinical goal of administering chemotherapy and radiation concurrently is to develop both locoregional and systemic tumour control.

Objectives: To establish the relationship among various nuclear changes and days of concomitant chemoradiotherapy and to explore the possibility of utilizing them as an assay to predict peritumour response to concomitant chemoradiotherapy.

Study design: Study group consisted of 50 patients with histologically confirmed OSCC treated by fractionated radiotherapy, receiving a total of 60-Gy to 90-Gy of external beam radiation in 30 to 33 fractions of 2-Gy each given daily. Patients were also given 4-6 cycles of chemotherapy. Serial scrape smears were collected from the peritumoral area before the start of treatment and after immediate exposure to radiation, at 17th day and end of treatment. Staining with haematoxylin and eosin and May-Grünwald Giemsa stains was done to assess nuclear abnormalities like micronucleation, nuclear budding, binucleation, and multinucleation.

Results: Karyolysis and karyorrhexis both were present in smears at the 17th day and end of day of therapy. Binucleation was observed in n = 163 (32.5%) smears and it was mostly seen at the end of treatment, followed by 17th day of treatment. Micronucleation was observed in n = 144 (72%). It was predominantly seen at the end of treatment (n = 50, 100%) smears. Prominent nucleoli were noted in n = 187 (93.7%) smears and were observed in 100% smears obtained on the 17th day and at the end of treatment. Multinucleation was noted in 32.5% of smears and it was present mostly at the end of treatment (n = 46, 92.0%) smears. Statistically significant (p<0.000) increase in all nuclear abnormalities at different days of CCRT was observed i.e. karyolysis, karyorrhexis, binucleation, micronucleation, prominent nucleoli and multinucleation.

Conclusion: A direct dose-response association exists among the frequencies of various nuclear changes and CCRT in peritumoral area of OSCC patients. Further studies are required to evaluate the role of these changes in predicting peritumoral area chemo-radiosensitivity. No conflict of interest.

888
Neoadjuvant metronomic chemotherapy in locally advanced head and neck cancers – feasibility study
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Background: A large majority of oral cancer patients in developing countries present in an advanced stage with borderline resectable/ inoperable stage to busy resource constrained tertiary cancer centres. Conventional chemotherapy protocols are associated with issues like toxicity, tolerance, cost and compliance. The present study was conducted to assess feasibility of low cost home based chemotherapy option.

Material and Methods: Single Arm feasibility study was done in borderline resectable/inoperable oral cancer patients. Home based metronomic regimen consisting of oral methotrexate 15 mg/m2 once a week and oral celecoxib 200 mg twice daily for eight weeks was used. RECIST Criteria 1.1 was used to assess response to therapy.

Results: Study included 60 patients. Mean age was 51.98 years with male predominance (80%), 55 patients adhered to the treatment, compliance rate being 91.60%. Affordability (Rs 700 per month) and tolerance to therapy was 100% and no grade III or IV toxicity was seen. Overall 18 patients had stable disease (32.73%), partial response was seen in 15 patients (27.27%) and disease progressed in 22 patients (40%). At the end of 9 weeks 26 (43.3%) patients were deemed resectable.

Conclusions: Neoadjuvant low cost, home based metronomic chemother-apy using oral methotrexate and celecoxib seems to be a viable option in managing advanced oral cancer in resource constrained set ups. No conflict of interest.

889
Retrospective analysis of definitive chemoradiotherapy with either high-dose or weekly cisplatin in patients with locally advanced squamous cell head and neck cancer: 2-year outcome
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Background: Radical radiotherapy with concurrent high-dose cisplatin (100 mg/m2/3 weeks) (HDC) chemotherapy is standard of care in the non-surgical management of locally advanced head and neck squamous cell carcinoma (HNSCC). However, many patients are not eligible to receive this regimen due to poor performance status or medical co-morbidities. Low-dose cisplatin (40 mg/m2/week) (LDC) is an alternative, but as robust data is still lacking, it is not known if LDC is as effective as HDC. We aimed to add insight to this matter, by reviewing our experience in treating unresectable locally advanced HNSCC. We presented intermediate results at ESMO 2015 Congress in Vienna: the 1-year overall survival (OS) was improved with HDC compared to LDC. We present the final results with the 2-year disease-free survival (DFS) and OS of these patients.

Methods: Patients with locally advanced HNSCC who received radical radiotherapy associated with either HDC or LDC between December 2008 and December 2013 were retrospectively reviewed. Patients who did not complete their radiotherapy course and those who received chemoradiotherapy in adjuvant setting were excluded.

Results: 72 patients were analyzed (42 in HDC regimen and 30 in LDC regimen). Most patients had carcinoma of the hypo- and oropharynx (75%). Median age was similar in the two regimens (57 years), as well as median performance status ( Karnofsky index of 90%). The median number of administered cycle in the HDC and the LDC was 2 (range 1-3) and 5 (range 3-7), respectively. The estimated median DFS was 16 months in HDC compared to 15.0±11.6 months in LDC regimen (P=0.159); the estimated 2-year DFS was 50.0% and 43.3%, respectively. The estimated median OS was 84.0±34.1 months in HDC compared to 24.0±6.1 months in LDC regimen (P=0.042); the estimated 2-year OS was 64.3% and 50.0%, respectively. Grade 3 hematologic toxicities were observed at the same frequency (16%) in the two regimens, as well as grade 3 mucitis (34% in HDC versus 30% in LDC).

Conclusion: This limited retrospective monocentric analysis showed an improvement of median overall survival with HDC compared to LDC in patients with locally advanced HNSCC treated with definitive chemoradiotherapy. Toxicities appeared similar between the two groups. No conflict of interest.
prognosis with median overall survival of 2−12 months. To improve loco-regional control and to allow functional reconstruction after ablative surgery, neoadjuvant protocols have been developed implementing radiochemotherapy prior to definitive surgery. Our aim was to assess whether neoadjuvant radiochemotherapy regimen improves overall outcomes and operability rates in such patients.

**Material and Methods:** 144 patients were enrolled in this trial during the period from May 2014 to May 2016 and received four cycles concurrent cisplatin (40 mg/m²) with conventional radiotherapy (40 Gy in 20 weeks). Cobalt-60. This was followed within 4−6 weeks with resection of the primary tumor and the regional neck nodes with appropriate reconstruction.

**Results:** 132 patients were evaluable for toxicity and response. Twelve patients defaulted while on neoadjuvant therapy. Complete clinical response was seen in 54 of 132 patients (CFR = 40.9%), and partial response in 63 of 132 patients (PR = 47.7%). In 60 of the 132 patients complete pathological response (cPR = 45%) was documented in the resected specimen. Resseractability was achieved in 144 of the 132 patients Tookal Grade (Grade III toxicity).

**Conclusions:** Neoadjuvant radiochemotherapy has been very effective in downstaging locally advanced technically unresactable oral cavity cancers in almost 86.6% (117/132) patients. It was also associated with excellent clinical and pathological response rates and acceptable side effects (Grade III toxicity).

**No conflict of interest.**

**Poster Session, Sunday 29 January 2017 Abstracts S107**

892

**POSTER**

**Hypothyroidism following adjuvant radiation in oral cavity carcinoma: a study of 60 cases at tertiary care institute**

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**Background and Introduction:** Thyroid is one of the important endocrine gland of the body responsible for growth and development and is situated in the anterior midline of neck. Oral cavity cancers are the commonest in head and neck cancers. The treatment of choice is radiotherapy. We did a non-randomized study of 60 oral cavity cancer patients who were subjected to adjuvant external beam radiotherapy after surgery and effect of radiation on thyroid function was measured.

**Materials and Methods:** A prospective study was carried out on 60 patients of carcinoma oral cavity in the age group of 30−70 years. Following surgery, all patients were subjected to adjuvant external beam radiotherapy and the target volume included a part or whole of the thyroid gland. All patients received a dose of 60 Gy in 30 fractions. All patients underwent thyroid function tests (after proper consent) at the start of the radiotherapy which were within normal limits. In the follow-up period, thyroid function of all patients was measured at the end of 3 months and then 6 months of the treatment. Follow-up ranged from 3 to 20 months (median: 11.5 months).

**Results:** Out of 60 patients, 44 were males (73.3%) and 16 were females (26.6%). All patients received radiation to the neck to a dose of 60 Gy in 30 fractions post surgery. Sixteen of 60 patients (26.6%) were found to have clinical hypothyroidism and seven patients (11.6%) were found to have subclinical hypothyroidism. Thus, a total of 23 patients (38.33%) developed radiation induced hypothyroidism. Mean time for development to hypothyroidism was 4.5 months. Nine of 16 patients (56.25%) with clinical hypothyroidism were in the age group of 51−60 years. Prior surgery for oral cavity carcinoma in all patients had no effect on the development of the hypothyroidism.

**Conclusions:** Hypothyroidism is commonly unrecognized sequelae of external beam radiation in patients of head and neck carcinoma but it is easily treatable if detected during the follow-up procedures. Although our study has a short follow up period and relatively small sample size, serial repeat testing of thyroid functions in post radiated patients of head and neck carcinoma is recommended.

**No conflict of interest.**

893

**POSTER**

**Multimodality treatment in operable sinonasal cancer: single center experience**

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**Background:** We report the outcome of patients affected by operable sinonasal cancer (SNC) treated with multimodality management at our Institution.

**Material and Methods:** We reviewed 63 consecutive patients treated between May 2000 and January 2015. In all cases, surgery was the primary modality followed by adjuvant radiotherapy (RT), alone or with concurrent chemotherapy (CT). The type of surgery depended upon primary site, extent of disease, cosmetic considerations and discretion of the surgical team; surgery was always aimed at obtaining a gross total resection (GTR). Patients undergoing primary induction CT due to locally advanced disease or with different histotypes were excluded from the analysis. In all patients, Kaplan−Meier statistics, univariate analysis, multivariate analysis, and log-rank test were performed.

**Results:** The median age of patients’ population was 70 (range 32−92), with a male prevalence (44 patients, 69.8%). The median age of patients was 70 (range 32−92), with a male prevalence (44 patients, 69.8%). Primary location of disease was nasal fossae in 36 patients (57.1%) while paramosal localization was present in 27 patients (42.9%). The most frequent histotype was squamous cell carcinoma in 28 (44.4%), followed by intestinal type adenocarcinoma in 28 (44.4%) and primary neuroendocrine lesions in 7 (11.2%) patients, respectively. RT total dose was 60−66 Gy given in 30−33 fractions over 6 weeks. Systemic therapy consisted of cisplatin, given either in a weekly or 3-week schedule at 40 mg/m² or 100 mg/m², respectively. 3D conformal RT was delivered in 36 pts (57.1%), while intensity-modulated radiotherapy (IMRT) was performed in the remaining 27 patients (42.9%). Concurrent cisplatin-based CT was employed in 14 patients (22.2%) with a median of 4 cycles (range 1−6). At a median follow-up of 25 months (range 3−194), 21 patients (33.3%) are alive. In terms of disease progression, 27 patients developed disease and 11 distant failures were observed, respectively. The resulting 2-year loco-regional control was 76.2% and the 2-year distant metastases-free survival was 85.7%. Overall, the 2-year progression-free survival (PFS) was 61.9% and the
2-year overall survival (OS) was 66.7%. At univariate and multivariate analyses, age, disease subsite, histotype, RT technique and administration of CT were not statistically significant in terms of influence on outcome measures or prediction of better outcome.

Conclusions: Operable sinonasal cancer represents a rare but curable miscellaneous group of diseases. A strong need of better prognosticators is required in order to better select and intensify treatment (through induction chemotherapy, accelerated RT, concomitant chemo-radiation) for those cases that recur despite multimodal approach. Prospective validation consisting of patients' cohorts with adequate power and identification of molecular factors to guide treatment are warranted. No conflict of interest.

894 POSTER
Wnt signaling pathway in the diagnosis of papillary thyroid cancer
J. Nascimento dos Santos1, L.C.S. Carvalho1, S.K. Santos Batista1, E.A. Ribeiro1, M.J. Chagas1, A. Abrahamo Martin1, R. Canavari1, 2UNIVAP, Instituto de Pesquisa e Desenvolvimento, Sao Jose dos Campos, Brazil

Background: Thyroid tumours are the most common endocrine malignancy in the world population and are considered a public health problem. The diagnosis of these tumours may present inconclusive results, requiring the application of techniques that provide an understanding of the molecular biology of tumour. Considering the importance of Wnt pathway in thyroid carcinogenesis and high frequency of papillary carcinoma in the world population, the aim of this study was evaluate the expression of genes involved in WNT pathway in order to identify diagnostic molecular markers that differerentiate the subtypes classic and variant of papillary thyroid carcinoma.

Material and Methods: Papillary thyroid cancer samples were investigated by quantitative real time PCR using Human Wnt Signaling Pathway RT-Profiler PCR Array, containing 84 Wnt-related genes.

Results: Specific genes showed differential expression, up or down regulation, between the two tumor groups analyzed.

Conclusions: These results indicate that expression analysis of genes belonging to this pathway may be an important tool in the discovery of tumor markers for diagnosis and contribute further for more effective treatment of patients affected by papillary thyroid tumors. No conflict of interest.

894A POSTER
Systematic review: Is there any evidence for utilisation of selective intra-arterial (IA) chemoradiotherapy in external auditory canal (EAC) tumours over conventional therapy?
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Background: Current guidelines from the Pittsburgh staging system recommend a combination of surgery and radiotherapy (RT) for treatment of external auditory canal (EAC) tumours. The majority of these therapies include postoperative complications and toxic systemic effects. Selective Intra-arterial chemoradiotherapy (IACRT) poses as a compelling alternative as it largely avoids side effects associated with conventional therapy. IACRT has played a large role in therapy of head and neck cancers due to the susceptibility of such cancers to regional chemoradiotherapy. However the efficacy of IACRT over conventional therapy for the treatment of early EAC tumours has not been systematically proven. The objective of this review is to analyse studies involving IACRT and comparing them to studies with conventional treatment modalities and perform a pooled analysis on the relative efficacy of IACRT.

Methods: Systematic searches were performed to identify studies reporting treatment of EAC tumours. A search of electronic databases, i.e., Web of Science, Medline, SCOPUS, Cochrane using broad search terms was done. All studies involving IACRT and conventional treatments were included. Parameters analysed were overall survival and/or disease free survival.

Results: Broad search on EAC tumours yielded 349 abstracts. The literature was refined to generate 4 studies on super-selective IACRT, and 14 studies on conventional treatment methods. There were a total of 38 patients treated with IACRT based on 4 studies. The results from these studies showed comparable overall survival rate for treatment with IACRT when compared to conventional therapy, based on Kaplan–Meier method. The positive overall survival rates are applicable for both early and late EAC tumours, in all studies except for one done by Sagawa. This study compared survival rates from 29 patients who were treated with conventional surgery (13 patients) versus patients who were treated with IACRT (16 patients). It showed a 50% survival rate of IACRT patients compared to a 91.7% survival rate with surgery. Nevertheless, this study was confounded by selection bias as the patients that were treated with surgery had earlier (T1/T2) tumours and patients that received IACRT were largely made up of patients who had advanced (T3/T4) tumours.

Conclusion: In view of the largely promising results and increasing popularity of targeted therapy it is necessary perform more clinical studies to confirm the postulated benefit and efficacy of IACRT. This is because there has only been 4 documented studies on IACRT for treatment of EAC tumours and all 4 of these studies have been performed in Japan, which raises questions regarding the global applicability of this treatment. No conflict of interest.

895 POSTER
Intraoral stent reduces set-up errors in image guided radiotherapy for head and neck cancer patients
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Background: Intensity-modulated radiotherapy (IMRT) techniques could minimize radiation dose to normal structures such as parotid glands without compromising tumour dose in head and neck cancer treatment. This requires accurate delivery daily targeting throughout the entire course of IMRT. The set-up errors have been investigated using several modalities, including computer computed tomography. Intraoral stent (IOS) has been reported to reduce the radiation doses to normal tissues and the affection from scattered radiation. However, the role of IOS for set-up is still unclear. The purpose of this study was to investigate the usefulness of IOS in external beam radiation therapy of head and neck cancer.

Material and Methods: This was an institutional review board-approved, retrospective study (approval number 2378). We analyzed a total of 152 set-up data in five consecutive patients who underwent image-guided radiotherapy (IGRT) for head and neck cancer using at our institution between January 2015 and May 2016 (the IOS group) and a total of 127 set-up data in two patients who underwent IGRT for head and neck cancer without the use of IOS between October 2014 and August 2015 (the non-IOS group). Between the two groups, patients were matched with regarding to all immobilization equipment except for the use of IOS. The absolute values were used for statistic analysis. In the each patient, mean value and standard deviation (SD) was calculated and compared between the two groups.

Results: Among all available data, median set-up error was 0.10 and 0.080 in x-axis (P = 0.93), 0.15 and 0.18 (P = 0.040) in y-axis, and 0.060 and 0.16 (P < 0.0010) in the IOS and non-IOS groups, respectively. Among the patients using mean values, median set-up error was 0.11 and 0.10 in x-axis (P = 0.83), 0.14 and 0.18 (P = 0.46) in y-axis, and 0.082 and 0.15 (P = 0.0016) in the IOS and non-IOS groups, respectively. Median SD of set-up error was 0.067 and 0.082 in x-axis (P = 0.41), 0.074 and 0.11 (P = 0.11) in y-axis, and 0.073 and 0.11 (P = 0.0323) in the IOS and non-IOS groups, respectively.

Conclusions: In each patient, dispersion and SD were significantly reduced in Z-axis by use of IOS. IOS can improve the precision of radiotherapy in head and neck cancer patients with reduction of random set-up errors during the course of radiotherapy.

No conflict of interest.

896 POSTER
Prognostic value of 18F-fluorodeoxyglucose positron emission tomography (FDG PET) before and during radiotherapy of head and neck cancer
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Background: The purpose of this study is to evaluate the prognostic value of metabolic parameters obtained from FDG PET before and during radiotherapy in patients with head and neck cancer.

Material and Methods: Nineteen patients with primary head and neck cancer were included in this study. Six patients had oropharyngeal cancer, 10 patients hypopharyngeal cancer and 3 patients laryngeal cancer. Sixteen patients (84%) received concurrent cisplatin (14 patients) or cetuximab (2 patients) chemotherapy. FDG PET-CT was taken...
before radiotherapy and between the third and fourth week of radiotherapy. The maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV) and total lesional glycolysis (TLG) of primary tumor were analyzed. MTV was defined using threshold of 50% SUVmax and TLG was the product of MTV and mean SUV within the volume. Median follow-up period was 36 months. Three-year overall (OS) and progression-free survival (PFS) rates were calculated using Kaplan–Meier method. The log-rank test was used to compare clinical and metabolic parameters in univariate analysis. Cox proportional hazards model was used for multivariate analysis.

**Results:** In univariate analysis, the 3-year PFS rate of patients with TLG >30 during radiotherapy were lower than those with TLG <30 during radiotherapy (33% vs. 85%, p = 0.019). The 3-year OS rate of patients with TLG >30 during radiotherapy were also lower than those with TLG <30 during radiotherapy (50% vs. 100%, p = 0.015). TLG during radiotherapy was associated with both PFS (p = 0.036; hazard ratio 8.055; 95% confidence interval 1.146–57.061) and OS (p = 0.045; hazard ratio 10.586; 95% confidence interval 1.049–106.869) in multivariate analyses.

**Conclusions:** A high TLG during radiotherapy was a worse prognostic factor in head and neck cancer patients. **No conflict of interest.**

**Poster 898**

**Locoregionally recurrent head and neck squamous cell carcinoma: incidence, survival, prognostic factors, and treatment outcomes**

**S-Y Wu** 1, Taipei Medical University – Wan Fang Medical Center, Department of Radiation Oncology, Taipei, Taiwan

**Purpose:** For locoregionally recurrent head and neck squamous cell carcinoma (HNSCC), appropriate therapeutic decisions and prognostic factors remain unclear.

**Patients and Methods:** The enrolled 4,839 patients were categorized into four groups: Group 1 comprised those undergoing chemotherapy (CT) alone; Group 2 comprised those receiving reirradiation (re-RT) alone (total radiation dose >60 Gy through intensity modulation radiation therapy [IMRT]); Group 3 comprised those receiving concurrent chemoradiotherapy (CCRT) alone (irradiation total dose >60 Gy through IMRT); and Group 4 comprised those receiving salvage surgery with or without RT or CT.

**Results:** Age ≥65 years, Charlson comorbidity index (CCI) score >6, clinical stage III–IV at first diagnosis, and recurrence-free interval <1 year were significant independent prognostic risk factors for overall survival as per univariate and multivariate Cox regression analyses. After adjusting, adjusted hazard ratios (aHRs; 95% confidence intervals [CIs]) for overall mortality in recurrent clinical stages I and II were 0.63 (0.45–0.89, p = 0.009); 0.65 (0.52–0.83, p < 0.001), and 0.32 (0.26–0.40, p < 0.001) in Groups 2, 3, and 4, respectively, whereas they were 1.23 (0.99–1.52, p = 0.062), 0.69 (0.60–0.79, p < 0.001), and 0.39 (0.34–0.44, p < 0.001) for Groups 2, 3, and 4, respectively, for overall mortality in recurrent clinical stages III and IV.

**Conclusions:** Salvage surgery is the recommended first treatment choice for recurrent oral cavity and pharyngeal cancers. Re-RT alone and CCRT are more suitable for inoperable recurrent stage I–II oral and nonoral cavity malignancies. **No conflict of interest.**
Clinical outcomes of endoscopic resection for head and neck cancer invading the subepithelial layer

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Background: Recent developments in endoscopic diagnosis have enabled gastrointestinal endoscopists to detect head and neck cancers at an early stage. Patients with such early lesions can be treated using endoscopic resection with minimal invasiveness. Endoscopic resection has been used for head and neck cancers, but the curability of this treatment is unclear, particularly for lesions invading the subepithelial layer. This study aimed to evaluate the curative potential of endoscopic resection for head and neck cancers invading the subepithelial layer.

Material and Methods: Between June 2003 and June 2016, 33 patients with head and neck cancers invading the subepithelial layer underwent endoscopic resection at the Hokkaido University Hospital. Among them, five patients with locally recurrent lesions after chemoradiotherapy were excluded; in total, 28 patients with 30 lesions were finally included in the study. Endoscopic resection was performed by a gastrointestinal endoscopist. A head and neck surgeon assisted during the procedure. All procedures were performed under general anesthesia.

Results: The mean patient age was 68.4 years (range, 47–80 years; 28 males). The mean tumour thickness was 790 µm (range, 190–4000 µm). During a median follow-up of 28.5 months (range, 2–143 months), no local tumour recurrence was detected and lymph node metastasis was found in one patient (3.6%). This patient underwent neck lymph node dissection with organ preservation. At the end of 2016, 18 among the 28 patients had died. Causes of death were as follows: esophageal squamous cell carcinoma (two patients), lung cancer (two patients), hepato-pancreatic cancer (one patient), unknown cancer (one patient), and suicide (one patient). Nine patients (32.1%) were followed up for >5 years, and the 3-year overall and cause-specific survival rates were 74.1% and 100.0%, respectively. The 5-year overall and cause-specific survival rates were 66.7% and 100.0%, respectively.

Conclusions: Our results suggest that the curative potential of endoscopic resection for head and neck cancers invading the subepithelial layer is promising in other organs, including primary head and neck cancers, and is important for prognostic factors.

No conflict of interest.

S110 Abstracts Poster Session, Sunday 29 January 2017
Poster Session, Sunday 29 January 2017

Abstracts S111

G1 26%, G2 10%, multifocality: G1 20%, G2 10%. Microcarcinomas (0.3–1 cm): G1 57%, G2 60%, lymph node involvement: G1 40%, G2 30%. Distant metastasis: G1 5%, G2 10%. In Group I 51% of patients with Pt1 have a capsule invasion. In 9% of patients of Group I stage T1–T2 was changed to pT after postoperative histology. Only capsule invasion has demonstrated the correlation with the mutation activity level (p < 0.05), whereas the association with lymph node involvement was not significant (p > 0.05).

Conclusions: Capsular invasion shows the strongest correlation with the presence of mutation, thus a more aggressive local surgery management in patients with PTC might be advisable (e.g. thyreoidectomy instead of hemithyroidectomy).

No conflict of interest.

905 POSTER Surgical management of invasive and metastatic thyroid cancer

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Background: It is known that 4.2–9% of patients with thyroid cancer have a distant metastasis. There are multiple approaches to treating thyroid malignancy, however it still remains unclear which one is superior.

Materials and Methods: The prospective study included 314 patients, recruited between 2000 and 2016 with thyroid malignancy with local and distant metastases. They were all managed with various surgical approaches. Histologically papillary, follicular and medullary types of malignancy were identified. Group I (n = 101) had patients with T4N0M0; Group II (n = 120) had patients with regional metastasis of thyroid cancer (T3N1a–bM0; T4N1aM0; T4N1bM0). Group III (n = 73) had patients with contralateral regional metastasis, mediastinal metastasis and regional recurrences (T3N1a–bM0–1, T4a–b N1a–bM0–1). Group IV (n = 20) had patients with distant metastasis to various anatomical sites. (T3N1a–bM1, T4a–b N1a–bM1).

Results: Paresis of recurrent laryngeal nerve was noticed in 10.7% of cases, parathyroid insufficiency in 1.7%, post-operative death in 0.84%, the 10-years follow up was: Group I – 85.7% of patients; Group II – 80.1%; Group III – 83.3% and Group IV – 49.0%. The 5- and 10-years overall survival were 86.3% and 80.5% respectively.

Conclusions: Surgical management of regional and distant metastasis except lungs metastasis improved 5 and 10-years surveillance and makes possible additional treatment. The assessment of oncological risk factors and prognosis is a main point in planning of huge operations in patients with thyroid cancer.

No conflict of interest.

906 POSTER Microsurgical reconstruction in patients with oropharyngeal cancer

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Background: The management of patients after total or subtotal glossectomy is particularly difficult due to the high disability and the need for further reconstructive steps. Radical extent surgery is associated with impaired respiration, speech, and nutrition that is reflected in low-quality of life and the necessity for further special rehabilitation of such patients.

Materials and Methods: 16 patients underwent primary tongue microvascular reconstruction after total and subtotal glossectomy. All patients were observed with primary tongue cancer. Tumor stage was T3 in 6 patients and T2 in 10 patients. Simultaneously with the resection stage, microsurgical reconstruction of the tongue has been performed. As the reconstructive material have been used free flap: colon-omentum flap (4), radial forearm flap (6) and thoracodorsal flap (3), TRAM-flap (2), chimeric flap with the inclusion of the serratus anterior muscle (1). Flaps revascularization was performed with branches of the external carotid artery and internal jugular vein. Reinforcement of the flap between the graft nerve and the lingual nerve was performed in 4 cases by forming micro-neural anastomoses, simultaneously with vascular graft revascularization.

Results: Postoperatively, significant complications from donor tissue grafts studied cases of necrosis were not noted. Natural nutrition has been restored in all patients. In all the patients the speech function was considered satisfactory.

Conclusions: The results of the data analysis of patients undergoing total or subtotal glossectomy followed by microsurgical free flap reconstruction, confirm the effectiveness of reconstructive surgery as a method of treatment for advanced stage of oral cancer.

No conflict of interest.

907 POSTER Is it feasible to perform sentinel lymph node biopsy with only blue dye in early oral cancer? A large cancer center experience

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Background: Oral cavity squamous cell carcinoma is one of the most common cancers in south Asia. Sentinel lymph node biopsy has a good accuracy using combination of lymphoscintigraphy and blue dye technique in early cancer; however, the limited availability of lymphoscintigraphy facilities in many developing countries requires exploration of alternative techniques. The need for the present study was to evaluate the feasibility and role of sentinel lymph node biopsy in identifying the occult lymph node metastasis using methylene blue dye alone.

Materials and Methods: We conducted a prospective study in 94 patients with early oral cancer (cT1, T2 and cN0) in a high volume tertiary care cancer centre in India from 2013 to 2016. Patients having negative neck nodes on clinical examination and ultrasound were included in study. Intra operatively, one ml of methylene blue dye was injected at the interface of tumor and palpable normal tissue in four quadrants. After 10–15 minutes incision in neck was given and any visualized blue nodes were dissected and sent for frozen section, routine histopathology and immunohistochemistry (IHC) for cytokeratin. Elective neck dissection was done in all patients as per institutional protocol.

Results: A total of 94 patients (79.8% male and 20.2% female) with mean age of 46.23 years (range 20–77 years) were included in this study. Smokeless tobacco was the commonest risk factor. Tumor subsites were tongue (45.7%), buccal mucosa (38.3%), and lip (16%). Mean follow up was 14.20 ± 6.7 months (range 2–17 months). Identification rate of sentinel lymph node was 96.1%, 100%, 93.9% and 95.5% respectively. IHC detected two micrometastases and one isolated tumor cells. Occult lymph node metastasis was seen in 27.6% cases. The lymph node distribution was as level IA (5.7%), IB (48.6%), IIA (37.1%), and III (6.8%). None of the patient had lymph metastasis to level IV or V. Majority of the patients (57.4%) had pathological T2 disease. We did not encounter anaphylactic or allergic reactions to methylene blue dye alone. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy for frozen section and histopathology were 84.6%, 100%, 100%, 93.9% and 95.5% respectively. IHC detected two micrometastases and one isolated tumor cells. Occult lymph node metastasis was seen in 27.6% cases. The lymph node distribution was as level IA (5.7%), IB (48.6%), IIA (37.1%), and III (6.8%). None of the patient had lymph metastasis to level IV or V. Majority of the patients (57.4%) had pathological T2 disease. We did not encounter anaphylactic or allergic reactions to methylene blue dye alone. The lymph node distribution was as level IA (5.7%), IB (48.6%), IIA (37.1%), and III (6.8%). None of the patient had lymph metastasis to level IV or V. Majority of the patients (57.4%) had pathological T2 disease.

Conclusion: Thus we conclude that SLNB with blue dye alone in early oral cancer is feasible. It can be used successfully with good sensitivity and negative predictive value in limited resource countries like India. Immunohistochemistry contributes to SLNB increasing sensitivity and negative predictive value to improve diagnostic value.

No conflict of interest.

908 POSTER The incidence of occult level VI lymph node metastasis in cN0 thyroid papillary carcinoma

A. Ozpek1, E. Unal1, T. Canbak1, A. Acar1, M. Ozbagriçak1, 1Health Sciences University Umraniye Training and Research Hospital, Department of General Surgery, Istanbul, Turkey.

Background: Cervical lymph node metastases in papillary thyroid cancer (PTC) are common. Although central neck dissection is indicated in clinically nodal-positive disease, it remains controversial in patients with no clinical evidence of nodal metastasis. The aim of this retrospective study was to determine the incidence of central lymph node involvement in clinically lymph node-negative patients with papillary thyroid cancer who underwent total thyroidectomy.

Materials and Methods: We reviewed the records of patients who had undergone surgical treatment for PTC at our institution between
2012 and 2016. Patients with 1 cm and larger PTC, who underwent total thyroidectomy and prophylactic ipsilateral central lymph node dissection (CLND, level VI) were enrolled. Papillary microcarcinoma of the thyroid as an incidental finding in patients treated surgically for presumably benign thyroid disease and clinically or radiologically-evident lymph node positive patients treated with total thyroidectomy and therapeutic CLND were excluded.

Results: All of the patients had fine needle aspiration cytologies proving PTC before surgery, and all underwent total thyroidectomy in conformity with our clinics’ algorithm. Thirty-one patients were documented to have PTC before surgery, and all underwent total thyroidectomy in conformity with our clinics’ algorithm. Data regarding patients’ demographics, pathology findings, management and outcomes were retrieved. Patients with a preoperative diagnosis of thyroid cancer were excluded from this study.

Results: The mean age of these patients was 42 ± 1.48 years and 258 (81.9%) were female. Thirty-two patients with PTCM were diagnosed incidentally following thyroid surgery for presumably benign thyroid disease (32/315 or 10.1%) were presented. Mean diameter of PTCM was 4.4 ± 2.7 mm. In 14 patients (43.7%) the tumor was multifocal and in about half of them tumor foci were found in both thyroid lobes. In two patients the tumor infiltrated the thyroid capsule. Interestingly, in 5 patients (5/315 or 1.5%), macrotumor/papillary thyroid carcinoma (mean 1.2 ± 0.4 cm) were detected as well, reflecting a total number of 37 patients (11.7%). There was no need for completion thyroidectomy in our series. All patients received suppression therapy and all of them were destined to radioactive iodine ablative therapy and brings forth clinically closer follow-ups. Follow-up (mean 2 years, range 4–48 months) was completed in all patients; all these patients were alive and disease-free.

Conclusions: Prophylactic central neck dissection in patients without definitive evidence of improved recurrence rates or survival and the possibility of higher complication rates compared to total thyroidectomy alone. However, our data supports the addition of routine central lymph node dissection to total thyroidectomy for the treatment of PTC, as it upstages nearly one third of patients thereby changing the dose of radioactive iodine ablative therapy and brings forth clinically closer follow-ups.

No conflict of interest.

909 POSTER
The rate of incidental papillary microcarcinomas in total thyroidectomy specimens of patients with presumably benign thyroid disease: experience of a university hospital clinic
E. Unal1, A. Ozpek1, A. Acar1, T. Canbak1, K.H. Tolan1. 1 Health Sciences University Umraniye Training and Research Hospital, Department of General Surgery, Istanbul, Turkey

Background: In recent years, as the use of thyroid ultrasound and other neck imaging modalities has increased, nodules too small to be palpated are more often discovered, and papillary thyroid microcarcinomas (ptmc), defined as less than 1.0 cm in size, are being identified with greater frequency. Papillary thyroid microcarcinomas (ptmc) are also frequently identified incidentally at surgery for benign thyroid disorders. In the present study, our aim was to present our experience with papillary thyroid microcarcinomas of the thyroid as an incidental finding in patients treated surgically for presumably benign thyroid disease.

Materials and Method: The files of 315 patients who underwent total thyroidectomy for presumably benign thyroid disease (toxic nodular goitre, nodules 4 cm or larger with benign cytology) in our hospital from 2013 to 2016 were reviewed. All of the patients had benign fine needle aspiration cytology reports before surgery, and all underwent total thyroidectomy in conformity with our clinics’ algorithm. Data regarding patient’s demographics, pathology findings, management and outcomes were retrieved. Patients with a preoperative diagnosis of thyroid cancer were excluded from this study.

Results: The mean age of these patients was 42 ± 1.48 years and 258 (81.9%) were female. Thirty-two patients with PTCM were diagnosed incidentally following thyroid surgery for presumably benign thyroid disease (32/315 or 10.1%) were presented. Mean diameter of PTCM was 4.4 ± 2.7 mm. In 14 patients (43.7%) the tumor was multifocal and in about half of them tumor foci were found in both thyroid lobes. In two patients the tumor infiltrated the thyroid capsule. Interestingly, in 5 patients (5/315 or 1.5%), macrotumor/papillary thyroid carcinoma (mean 1.2 ± 0.4 cm) were detected as well, reflecting a total number of 37 patients (11.7%). There was no need for completion thyroidectomy in our series. All patients received suppression therapy and all of them were destined to radioactive iodine ablative therapy and brings forth clinically closer follow-ups. Follow-up (mean 2 years, range 4–46 months) was completed in 25 patients; all these patients were alive and disease-free.

Conclusion: PTMC is not an uncommon incidental finding after surgery for presumably benign thyroid disease (10.1% in our series). The possibility of an underlying PTMC should be taken into account in the management of patients with nodular thyroid disease; total thyroidectomy should be considered, at least in selected patients with presumably benign nodular thyroid disease.

No conflict of interest.

912 POSTER
Tongue flap reconstruction for defects after resection of oral cancer: a versatile flap
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Background: Defects following resection of oral cancer needs tissue replacement which provides coverage. Distant tissue transfer is not necessary for small intra-oral defects. Tongue flap can be versatile and dependable option. It can be a feasible alternative to technically demanding gold standard of free flap.

Material and Methods: This was a retrospective database review carried out at Department of Surgical Oncology, King George’s Medical University Lucknow, UP from May 2014 to May 2016.

Results: A total of 21 patients of oral cancer underwent tongue flap reconstruction. Median age was 45 years (35 to 80 years) with male:female ratio 4:3. Sixteen patients were of carcinoma buccal mucosa, four patients had carcinoma of lower alveolus and one patient had carcinoma of retromolar trigone. 18 patients underwent mandibulectomy (marginal mandibulectomy = 9 and segmental mandibulectomy = 9) 2 patients underwent upper alveolectomy and 2 patients had no bony resection. Median size of the defect was 5.0 cm (largest dimension). Average time to elevate the flap was 25 minute. Post surgery complications were bleeding 1/21 (4.8%); total flap loss 0/21; tip necrosis 2/21 (9.5%); fistula 2/21 (9.5%). All the complications were managed conservatively. Patients had satisfactory mouth opening, good mobility of tongue, swallowing & speech following surgery.

Conclusion: Tongue flap reconstruction is simple and a reliable local flap. It is associated with very few morbidities and functional outcomes are satisfactory. It also obviates need of distant tissue transfer.

No conflict of interest.

913 POSTER
Baseline characteristics of responders and nonresponders from the phase 3 study of (E7080) lenvatinib in differentiated cancer of the thyroid (SELECT)
C. Reuter1, X. Yu2, M. Baig2, C.E. Dutouss2. 1Hannover Medical School, Oncology- Hematology, Hannover, Germany; 2 Esiat Inc., Woodcliff Lake, NJ, USA

Background: In SELECT, lenvatinib (LEN) improved progression-free survival in patients (pts) with differentiated thyroid cancer compared with placebo (18.3 vs 3.6 months; hazard ratio 0.21; 99% CI 0.14–0.31; P < 0.0001). We report baseline characteristics and change in the sum of target lesion diameter for pts from SELECT who did and did not respond to LEN.

Materials and Methods: Pts were randomized 2:1 to receive LEN 24 mg/day or placebo. Tumor assessments were performed by independent radiologic review every 8 weeks during the randomization phase and by investigator review every 12 weeks during the extension phase. Responders were defined as pts who demonstrated either a partial or complete response. All other pts were categorized as nonresponders. The data cutoff was 15 November 2013.

Results: Of 261 LEN-treated pts, 169 were responders and 92 were nonresponders. Among responders, 66% were aged ≤65 years and 46% were male; 48% of nonresponders were aged ≤65 years and 51% were male. Responders showed lower tumor burden than nonresponders. For responders, 33% had baseline tumor burden <35 mm and 67% had
Eastern Cooperative Oncology Group performance status (ECOG PS) of 0. For nonresponders, 10% had baseline tumor burden <35 mm and 34% had ECOG PS of 0. The median duration of treatment was higher for responders than for nonresponders (14.8 months [range: 1.1–26.8] vs 5.5 months [range: 0.2–21.5]). Median baseline sum of target lesion diameters was 51.6 mm (range: 15.1–181.2) for responders and median maximum percent change from baseline was -52% (range: -100% to -30%). For nonresponders, median baseline sum of target lesion diameters was 71.5 mm (range: 15.9–331.2) and median maximum percent change from baseline was ~20% (range: ~38% to 66%). Results are shown in the table.

Conclusions: LEN was effective across tumor burdens in SELECT. In this analysis, the percentage of responders with lower tumor burden is higher compared with nonresponders. These data suggest that earlier use of LEN could be beneficial.

Conflict of interest: Ownership: C Reuter – None to disclose; X Yu – Eisai Employee; M Baig – Eisai Employee; CE Dutcus – Eisai Employee. Advisory Board: C Reuter – Advisory board member for Bayer, Eisai, Sanofi. Associations showed poor results with no improvement of overall survival (mOS). There are few data on second-line efficacy in patients treated in first line by EXTREME protocol, yet cetuximab is used to a large extent in our cancer center after in this indication. Hence, the question of cetuximab maintenance in second line arises. Here we present the outcome of HNSCC patients after EXTREME chemotherapy. All the patients treated with EXTREME protocol between 2010 and 2014 at the Paul STRAUSS Cancer Center were retrospectively collected and included in this analysis. PFS and OS were estimated with the Kaplan-Meier method and compared using log-rank test or Gehan test if curves cross dated. 122 patients were treated by the EXTREME protocol as a first line chemotherapy. Median age was 61 years (range 29 to 78), sex ratio HF was 4.1 and 38 patients (35%) had an OMS score ≥2; 59% of patients (n = 51) had a metastatic disease and 41% (n = 35) recurrent. Among them, 86 (70%) reached second-line chemotherapy and were included for analysis. Primary tumor sites were located in the oropharynx (40%), the hypopharynx (22%), the oral cavity (20%) and the larynx (19%). HPV status was available in 12 oropharynx tumors with all samples HPV+. In first-line treatment, 80 patients (93%) received carboplatin/5FU/cetuximab, others (7%) cisplatin/5FU/cetuximab. Second-line therapies were mainly combination chemotherapies (78%) including cetuximab for 55 patients (64%); paclitaxel/cetuximab (26%), carboplatin/paclitaxel/cetuximab (PCC) (21%), paclitaxel (19%), EXTREME (17%), carboplatin/ paclitaxel (12%), others (5%). Median progression-free survival (mPFS) was 3.6 months (95% CI: 2.8 to 4.4) and mOS was 8.2 months (95% CI: 6.9–9.6). Patients who received a combination therapy had a higher mOS than patients treated with monotherapies (p = 0.0003). Patients who received chemotherapy including cetuximab had a better survival (Gehan test p = 0.014); they displayed a mOS of 8.9 months (95% CI: 7.7–10.1) with cetuximab vs 3.5 months (95% CI: 2.2–5.0) in patients who did not receive cetuximab. Compared to other chemotherapy, patients who received a protocol combining cetuximab and platinum-based doublet had a higher mOS (p = 0.0008) and mPFS (p = 0.016).

In our monocentric study, around two-thirds of patients received a second line chemotherapy, which often included cetuximab. Despite substantial toxicity which may be a drawback to the delivery of cetuximab, further investigations are required to identify population subgroups who may benefit from cetuximab maintenance combined to platinum-doublet chemotherapy as second-line treatment.

No conflict of interest.

915 POSTER Circulating levels of cell free DNA in serum of head and neck cancer patients with special relation to clinicopathological status and stage of the disease – a pilot study from a developing country with a high incidence of tobacco related cancers
A. Anand1, A.A. Sonkar1, S. N1, N. Husain2, 1King George’s Medical University UP India, Surgery, Lucknow, India; 2RMIL Institute of Medical Sciences, Pathology, Lucknow, India

Background: Head and neck cancer (HNC) is a major problem that occurs in Asia, especially in Indian subcontinent. In comparison with the U.S. population, where HNC represents only about 3% of malignancies, it accounts for over 30% of all cancers in India. Younger individuals are the susceptible sector of the society, with an undue exposure of risk factors such as tobacco especially in developing countries. Besides smoking, use of smokeless tobacco is also widely prevalent. Increasing number of HNC patients belong to weaker socioeconomic section, lack awareness, hinder misconceptions. The additional fact of inadequate access to trained providers and limited health services lead to delayed detection of oral cancer. Other major burden in India is regarding the scarce diagnostic infrastructure, crucial investigative centers and services to the needy, is at paucity.

Recently in the past biomarkers have been detected in the patient’s body fluids capable of detecting the cancer at very early stages and its thereby potential application in management of the disease. One such biomarker is serum circulating cell free deoxyribonucleic acid (sCCFDA) and its potential role in oral cancer has been studied in this research work.

Methods: Between September 2014 and August 2015, n = 61 (M:F = 42:19) new patients with isolated HNC were enrolled after informed consent and ethical approval. Healthy Volunteers more than 35 years of both sexes were taken as controls. A 4-ml sample of peripheral blood was collected in silica gel vials for CC FDA extraction and estimated using PCR technique.

Results: The mean sCCFDA levels were 848.38 ng/ml in male patients and 1081.18 ng/ml in female patients. The mean sCC FDA levels in controls (109.02 ng/ml) were lower compared to cases (920.90 ng/ml) though not statistically significant.

The mean sCCFDA levels was seen higher in UICC Stage IV cancer, in tobacco abusers, in tumor size >4 cm and in metastatic disease though not statistically significant. In contrast the mean sCCFDA levels were higher in well-differentiated SCC and lowest in poorly differentiated SCC. Lymph node positive cases showed statistically higher sCCFDA levels compared to lymph node negative disease.

Conclusion: The CC FDA levels in oral cancer are found to be increased compared to that of healthy controls. There is lack of statistical significant association with stage and other significant histopathological parameters except the positive lymph node status. A large sample size study is needed to establish CC FDA as a biomarker for early detection, role in response to various modes of treatment and monitoring recurrence.

No conflict of interest.
joined their efforts into an intergroup called DIALOG. DIALOG launched a task force in order to develop a consensual geriatric minimum data set (MDS) for research purposes. To reach a consensus on a minimum set of geriatric data to be incorporated in clinical trials covering the elderly cancer population and allowing stratification according to geriatric risk profile.

Material and Methods: Following an adapted Delphi method, a panel of 7 pairs of geriatricians experts (GE) from 11 geriatric oncology clinics has been constituted. Seven domains of GA were selected. Based on the SIOG, EORTC and NCCN recommendations on GA, the GE had to: (1) list the tools available by domain; (2) determine the most commonly used tools; (3) search studies assessing sensitivity and specificity of these tools; (4) compare the tools available from the practical standpoint; (5) select the literature supporting the tools selection. After debate, the geriatrician’s panel proposed a first version of the MDS. In a second time, this MDS was presented and debated with the multidisciplinary and national DIALOG group leading to a second version, with a feedback to the geriatrician’s panel. Two other iterations (second and third rounds) were needed to reach a consensus statement. This MDS geriatric version was then diffused to evaluate appropriation in a large international panel of oncologists and geriatricians. Then a final version was obtained.

Results: After 3-round, tools chosen for each domain were: (1) Social assessment: Using two questions “Are you living alone” and “Would you have a person or caregiver able to help you”. (2) Functional autonomy: Activities of Daily Living (ADL) and short-IADL. (3) Mobility: walking speed (<0.8 m/s) or timed get up and go test (TGUG >20 s). (4) Nutrition: Mini Nutritional Assessment - short form (MNA-SF) <12/14, more than 10% of unintentional weight loss in last 6 months and Body Mass Index (BMI <21 kg/m²). (5) Cognitive assessment: Dubois’s 5 words and clock drawing test or Mini-Cog. (6) Thymic status: mini-Geriatric Depression Scale (m-GDS) <14. (7) Comorbidity: updated Charlson.

Conclusion: DIALOG intergroup reached an agreement for a short geriatric MDS to be incorporated in future clinical trials for the elderly. This initiative still needs to be evaluated for appropriation by a large international panel of oncologists and geriatricians.

No conflict of interest.

968

Understanding unwarranted variations of use of high-cost cancer drugs: a Comprehensive Cancer Care Network approach

U. De Giorgi1, D. Gallegati2, N. Gentili3, C. Masini1, I. Massa1, D. Amadori1, M. Attini1, 1Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST IRCCS, Health Economics and Outcomes Research Team, Meldola, Italy

Background: Unwarranted variation in health care service delivery, refers to geographic differences that cannot be explained by illness prevalence, resource need or evidence-based care. The purpose of our study is to examine the variability in per capita cancer drug costs and the relationship between the use of high-cost cancer drugs and the different clinical approach and management across three adjacent nodes (A, B, C) with similar population and independent clinical organization in the healthcare network of Romagna.

Material and Methods: In a prospective due diligence investigation, finalized to a unified and standardized clinical management in the Romagna Comprehensive Cancer Care Network (CCCN), we have explored the 2015 costs distribution (using administrative data, FED) for cancer drugs in Romagna focusing on the seven with higher health care costs (trastuzumab, bevacizumab, rituximab, imatinib, abiraterone, bortezomib and pemetrexed), which cover for nearly 50% of costs of all cancer drugs per head of population in Italy according to the 2015 report of the National Observatory on the Use of Medicines (OsMed) realized by the Italian Medicine Agency (AIFA). We analyzed per capita cost variability in the three nodes, and compared results of our analysis in Romagna with the use of the seven most expensive cancer drugs (7MECD) in Italy.

Table: 7MECD costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Per capita costs (€)</th>
<th>Vari - Italy</th>
<th>Total cost</th>
<th>Patients</th>
<th>Per patient costs</th>
<th>Incidence €/100,000</th>
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<td></td>
<td></td>
<td>Italy</td>
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<td></td>
<td></td>
<td>Node A</td>
<td>Node B</td>
<td>Node C</td>
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</tr>
</tbody>
</table>

Results: Costs of all cancer drugs per head of population were +3% in Romagna compared to Italy (+11% A, +6% B, -12% C), with a range of 8.96 € per capita which could increase by 3.7 million € or decrease by 6.4 million € the total costs. Costs of the 7MECD was +7% (+15% A,
Adherence to cancer treatment guidelines: influence of general and cancer-specific guideline characteristics

M. Heins1, J. De Jong2, I. Spronk1, V. Ho³, M. Brink3, J. Korevaar1.

Background: Guideline adherence remains a challenge in clinical practice, despite guidelines' ascribed potential to improve patient outcomes. We studied the level of adherence to recommendations from Dutch national cancer treatment guidelines, and the influence of general and cancer-specific characteristics on adherence.

Methods: Based on data from a national cancer registry, adherence was evaluated for fifteen treatment recommendations for breast, colorectal, prostate and lung cancer, and melanoma. Recommendations were selected by representatives of the medical specialist associations responsible for developing and implementing the guidelines. We used multivariable multilevel analysis to calculate mean adherence and variation between individual hospitals.

Results: Mean adherence to the different treatment recommendations ranged from 40% to 99%. Adherence differed only slightly between older and newer guidelines and between recommendations with low, moderate or high levels of evidence (range 79–84% and 77–91%, respectively), while adherence differed more between recommendations for different cancer types (range 54–99%), different treatment modalities (adherence ranged from 40% to 99%) or recommendations that advised against or recommended in favour of particular treatment (adherence ranged from 75% to 98%).

Conclusion: We found significant variation in adherence between different cancer treatment guidelines. While some guideline characteristics that seem to explain this variation may be considered difficult to modify, the potential for variance across cancer types and treatment modalities suggests that adherence could be further improved. At the same time, these results warrant tailored strategies for improvement of adherence to clinical practice guidelines.

No conflict of interest.

971 ORAL

A comparative analysis of orphan designations for rare neoplastic disorders versus other rare indications

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Background: Orphan designated medicinal products benefit from regulatory and economic incentives for orphan drug development. Orphan designations (OD) represent an attractive track for oncology drug development, with 36% of all OD involving rare neoplastic disorders. This study investigates if there are differences in characteristics of the products and the applicants between OD obtained for rare neoplastic disorders and OD obtained for other rare indications.

Methods: The study sample includes OD granted between January 1st 2002 and December 31st 2012 which are active on June 13th 2014 and for which no marketing authorization was granted over the study period. In November 2014, the OD application files and annual reports submitted by the applicant were consulted at the premises of the European medicines Agency to collect following information: prevalence of the disease, use of scientific benefit criterion at time of OD, applicant categorization based on Amadeus database, most advanced study at time of OD application and at time of latest annual report. Indications were categorized to OD for rare neoplastic disorders and OD for other rare indications based on Orphan linearization data. Chi² test was performed in IBM SPSS Statistics 23 to compare OD for rare neoplastic disorders versus other rare indications.

Table 1. Comparison of applicant categorization, prevalence segmentation and consideration of scientific benefit criterion for orphan designations for rare neoplastic disorders and other rare indications

<table>
<thead>
<tr>
<th>Applicant categorization</th>
<th>Rare neoplastic disorders (N=352)</th>
<th>Other rare indications (N=465)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic/Public body*</td>
<td>3% (0)</td>
<td>4% (20)</td>
</tr>
<tr>
<td>Consulting*</td>
<td>9% (35)</td>
<td>11% (32)</td>
</tr>
<tr>
<td>Physical person*</td>
<td>2% (6)</td>
<td>6% (27)</td>
</tr>
<tr>
<td>SME*</td>
<td>56% (150)</td>
<td>47% (258)</td>
</tr>
<tr>
<td>Small Pharma</td>
<td>13% (35)</td>
<td>16% (73)</td>
</tr>
<tr>
<td>Medium Pharma*</td>
<td>7% (35)</td>
<td>7% (31)</td>
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<tr>
<td>Large Pharma*</td>
<td>5% (24)</td>
<td>9% (40)</td>
</tr>
<tr>
<td>Prevalence segmentation</td>
<td>100 (N=465)</td>
<td>47.7% (220)</td>
</tr>
<tr>
<td>1–10/10,000</td>
<td>69.1% (186)</td>
<td>41.4% (91)</td>
</tr>
<tr>
<td>&gt;10/10,000</td>
<td>11.9% (34)</td>
<td>10.4% (29)</td>
</tr>
<tr>
<td>Consideration of scientific benefit criterion*</td>
<td>75.1% (202)</td>
<td>44.3% (204)</td>
</tr>
</tbody>
</table>

*Chi² test performed at 0.05 level based on category analysis.

Results: Significant differences between OD for rare neoplastic disorders and OD for other rare indications are observed for prevalence of the...
Clinician-guided versus USS-guided lymph node fine needle aspiration: Should we be performing more biopsies in clinic?

A. Strong, T. Banks, C. Lewis, S. Rannan-Eliya. Royal Victoria Infnitary, Department of Plastic Surgery, Newcastle upon Tyne, United Kingdom

Background: Regional metastases of skin malignancies to lymph node basins must be cytologically confirmed prior to lymph node dissection using fine needle aspiration (FNA) biopsy. FNA can be performed manually in clinic as an outpatient procedure or under ultrasound (USS) guidance. Anecdotally, clinician-guided FNA is time-consuming and samples may be insufficient requiring repeat sampling. However, waiting for ultrasound-guided FNA may lead to significant delay in treatment, heightened patient anxiety and increased health care costs. Thus, we aimed to evaluate waiting times, costs and the proportion of insufficient samples/inconclusive results for patients undergoing clinician or USS-guided FNA biopsies.

Materials and Methods: A retrospective analysis of all patients in a supra-regional service, undergoing clinician or USS-guided FNA biopsy for skin malignancy over a 5-year period. Lymph node sites identified as being suitable for clinic-based biopsy were those clinically palpable and which could be manually stabilised and away from high risk sites. To improve the diagnostic accuracy of clinician-guided FNA biopsy, cytology technicians were available in clinic to immediately evaluate sample quality.

Results: 180 patients were identified (102 male, 78 female; mean age 68 years, range 25–99 years) with a range of skin malignancies (133 melanoma; 10 Merkel cell carcinoma; 37 squamous cell carcinoma). 48 FNA biopsies were performed by surgeons in clinic, while 132 were USS-guided, with similar numbers performed in the neck, axilla and groin between both groups. Clinician-guided FNAs were performed in a mean time of 0 days (range 0–54 days) from decision to biopsy. Comparatively, mean time for USS-guided FNAs was 14 days (range 0–54 days). Insufficient/inconclusive samples were identified in 4/10% of clinician-guided biopsies and 5/7% of USS-guided biopsies. Overall, 85% of clinician-guided and 88% USS-guided biopsies provided a definitive result at first biopsy. Cost analysis identified a potential saving of £4800 per annum if suitable lymph nodes were biopsied in clinic versus under USS-guidance.

Conclusions: Thus, clinician-guided FNA biopsy should be offered over USS if expertise is available and lymph node site and stability are suitable. We feel this provides immediate validation of sample ‘adequacy’, less patient anxiety and earlier block dissection if required. Furthermore, clinician-guided FNAs are significantly cheaper than USS guided with comparable accuracy and results.

No conflict of interest.

Poster Session (Sunday 29 January 2017)

Health Economics of Cancer

Can biosimilar products enhance resources utilization and quality of services for cancer treatment?

A. Abotaleb, WHO consultant & MOH technical adviser, health economics & policies national fund, Cairo, Egypt

Background: One of the major products in treatment expenditures at oncology field is biological products, which increase economic burden on payers and may lead to treatment restrictions due to high cost of biologics. Introducing biosimilars products may offer safe, effective, sometimes cost saving alternative to innovator biological therapies.

Biosimilars definition: According to WHO, “Similar to an already licensed reference biotechnological product in terms of quality, safety & efficacy”.

The main objective is to measure the impact of introducing biosimilars to the oncology treatment through evaluating (guidelines modification, numbers of treated patients, price discounts for innovator products and quality of service introduced to the patients).

Methods: Data analyzed for 113,429 cancer patient for the last 3 years from national data base including (treatment guidelines – quality of service surveys – reimbursement lists – price offers for innovator). Local biosimilars guidelines was the reference for estimating local biosimilars.

Results: Introducing biosimilars products to Egyptian market in the last 3 years led to changing the following:

- Neutropenia guidelines were modified for including GCSF as a routine treatment for both prophylaxis and after chemotherapy.
- Breast cancer treatment guidelines were modified for HER2+ to include monoclonal second brand therapy as standard of care for both adjuvant and metastatic cases.
- Lymphoma treatment guidelines for NHL type were modified to include monoclonal antibodies second brand therapy as a standard of care.
- Price discounts for innovator products were found to be in the range of 35% to 66%. Surveys illustrated that reducing time of treatment for neutropenia patients, hospitalization time decreased due to modification of neutropenia guidelines. Was major findings at quality of service surveys.

Conclusion: Introducing biosimilars to the oncology field may lead to offer safe, effective efficient solution for controlling budget and enhancing health service. Biosimilars may have a major role for achieving perfect computation at oncology field. But there is a need for conducting more studies and tools to guarantee safety and efficacy of biosimilar products.

No conflict of interest.

Poster Session, Sunday 29 January 2017

POSTER

Prioritization of lines of hormonal treatment and its impact on patient outcomes and resources for metastatic breast cancer

A. Abotaleb, WHO consultant & MOH technical adviser, National Fund, Cairo, Egypt

Background: As a result of developing new lines of hormonal treatment for metastatic breast cancer patients the need was raised for prioritization strategy for enhancing patient outcomes including (quality of life – economic value – clinical effectiveness) and efficient resource management to treat more patients and reduce economic burden on payer.

The objective of this study is to determine impact of using Fluvestrant 500 mg prior to (Everolimus 10 mg + Exemestane) as line of treatment to enhance patient outcomes (quality of life – economic value – clinical effectiveness) & resource utilization for metastatic breast cancer of estrogen-receptor-positive, locally advanced or metastatic breast cancer in postmenopausal women whose cancer has relapsed on or after adjuvant anti-estrogen therapy, or who have disease progression on anti-estrogen therapy.

Methods: A cost-utility analysis from the payer perspective the Ministry of Health and Population was conducted to maximize health gain for the patients while ensuring the most efficient use of the finite resources available.

Markov chain simulation model: The model used a hypothetical cohort of 100 subjects with three health states: first, metastatic until disease progression; second, best supportive care; and third, death. Quality of life were incorporated in the model to make adjusted results. Quality of life was calculated using utility score derived from DA Cameron (2008). Clinical and safety data for Fluvestrant 500 were taken from the CONFIRM study and those for Everolimus plus Exemestane were taken from BELRO 2.

Study costs used were the local ones according to the national fund list. Discounting was applied at 3.5% annually. The results obtained were in terms of ICER and number of QALY’s.

Uncertainty analyses: To test the stability of our results to variation in the estimates of the input model parameters, we performed various one-dimensional sensitivity analyses.

Time horizon was estimated as 3 years.

Results: Total costs, QALY and ICER after three years, according to the model, are shown in the table.

<table>
<thead>
<tr>
<th>Treatment strategy</th>
<th>Cumulative cost</th>
<th>Cumulative QALY’s</th>
<th>ICER</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everolimus plus Exemestane</td>
<td>107,663 EGP</td>
<td>1.02</td>
<td>−8,775 EGP/QALY</td>
<td>Fluvestrant is dominating (cost saving)</td>
</tr>
<tr>
<td>Fluvestrant 500 mg</td>
<td>102,888 EGP</td>
<td>1.58</td>
<td>−6,953 EGP/QALY</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>−4,775 EGP</td>
<td>0.56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: The result of the study suggests that the impact of Fluvestrant 500 for enhancing patient outcomes is dominating. Using line of Fluvestrant 500 prior to (Everolimus 0mg + Exemestane) for treating metastatic breast cancer may have dominant effect on patient outcomes as a treatment strategy. No conflict of interest.

1025 POSTER SPOTLIGHT
Should the Republic of Ireland introduce a national prostate-specific antigen testing programme for the secondary detection of prostate cancer? Results from a population-based cost-effectiveness analysis
B. Burns1, F. Drummond2, F. Sullivan3, C. O’Neill4, L. Sharp5, 1University of Oxford, Health Economics Research Centre HERC- NDPH, Oxford, United Kingdom; 2University College Cork, Department of Epidemiology and Public Health, Cork, Ireland; 3National University of Ireland- Galway, Prostate Cancer Institute, Galway, Ireland; 4National University of Ireland- Galway, J.E. Cairnes School of Business and Economics, Galway, Ireland; 5Newcastle University, Institute of Health and Science, Newcastle upon Tyne, United Kingdom

Background: Prostate Cancer (PCa) incidence in the Republic of Ireland (RoI) has steadily increased over the last two decades and is among the highest across Europe. From 1994 the use of prostate specific antigen (PSA) testing for secondary detection has also increased dramatically and is in rising incidence rates in the RoI. The impact of increased PSA detection both on resource utilisation and quality of life (QoL) are not fully understood. Therefore, an economic evaluation of the introduction of several PSA-based screening strategies was undertaken.

Results: Results from a cost-effectiveness analysis adopting a lower PSA cut-off (>3ng/ml) suggested that at the upper bound WTP threshold of €45,000 per QALY gained, a once-off screen at 50 years and 55 years was cost-effective (incremental cost-effectiveness ratios (ICER) were €29,000 and €31,222, respectively). When using the higher PSA cut-off (>4ng/ml) consistent with current practice, the once-off screen at 50 years was cost-effective (ICER: €43,832).

Conclusions: Introducing a population-based, once-off PSA testing at ages 50 or 55 in the RoI could be deemed cost-effective. There is no doubt that PSA testing detects PCs; however, it cannot distinguish between cancer that leads to premature mortality and cancer that would have remained latent during a man’s life and so result in high levels of over diagnosis and overtreatment which have consequences both in terms of costs and quality-of-life. This analysis contributes to the ongoing accumulation of evidence on the costs and benefits of PSA testing internationally and may inform decision making within the Irish healthcare system. No conflict of interest.

1026 POSTER
Financial burden of cancer drug treatment in Lebanon
F. Elias1, 1Levant Hospital, Hematology – Oncology, Beirut, Lebanon

Background: The Ministry of Public Health (MOPH) in Lebanon provides cancer drugs free of charge for uninsured patients who account for more than half the total caseload. Other categories of cancer care are subsidized under more stringent eligibility criteria. MOPH’s large database offers an excellent opportunity to analyze the cost of cancer treatment in Lebanon.

Materials and Methods: Using utilization and spending data accumulated at MOPH during 20082013, the cost to the public budget of cancer drugs was assessed per case and per drug type.

Results: The average annual cost of cancer drugs was $6,475 per patient. Total cancer drug costs were highest for breast cancer, followed by chronic myeloid leukemia (CML), colorectal cancer, lung cancer, and NonHodgkin’s lymphoma (NHL), which together represented 74% of total MOPH cancer drug expenditure. The average annual cancer drug cost was highest for CML ($31,037), followed by NHL ($11,566). Trastuzumab represented 26% and Imatinib 15% of total MOPH cancer drug expenditure over six years.

Conclusions: Sustained increase in cancer drug cost threatens the sustainability of MOPH coverage, so crucial for socially vulnerable citizens. To enhance the bargaining position with pharmaceutical firms for drug cost containment in a small market like Lebanon, drug price comparisons with neighboring countries which have already obtained lower prices may succeed in lowering drug costs. PMID: 27509947 No conflict of interest.

1027 POSTER
Cost-effectiveness of Ipegfilgrastim from the Mexican payer perspective
A. Szende1, 2, B. Bussey2, E. Szabo3, J. Klastersky4, O. Tomé5, 1Covance, Global Health Economic and Outcomes Research, Leids, United Kingdom; 2Covance, Global Health Economics and Outcomes Research, Sydney- NSW, Australia, 3Teva Pharmaceuticals, Global Health Economics and Outcomes Research, Frazer- Pennsylvania, USA; 4Institut Jules Bordet- Centre des Tumeurs de l’Université Libre de Bruxelles, Department of Medicine, Brussels, Belgium; 5Teva Pharmaceuticals, Medical Affairs, Naucalpan de Juárez, Mexico; 6Teva Pharmaceuticals, Global Medical Affairs, Ulm, Germany

Background: Recombinant granulocyte-colony stimulating factors (G-CSFs) reduce the risk of chemotherapy-induced neutropenia. Ipegfilgrastim is a long-acting, once-per-cycle G-CSF not currently reimbursed in Mexico, while the short-acting G-CSF filgrastim is the reimbursed standard of care. This analysis evaluated the cost-effectiveness of ipegfilgrastim compared with filgrastim and pegfilgrastim in managing adult patients at risk of neutropenia from the perspective of the healthcare system in Mexico.

Material and Methods: A decision analytic model used inputs based on national data, clinical trial evidence including meta-analysis, and expert opinion to calculate the expected health outcomes and costs associated with each G-CSF regimen over a 30-year time horizon. Costs included direct drug and medical costs, outpatient and inpatient treatments of neutropenia, and adverse events. Health outcomes included life years (LYs) and quality-adjusted life years (QALYs) gained. Model outputs were used to estimate incremental cost-effectiveness ratios (ICE Rs) in terms of the incremental cost per L Y saved and incremental cost per QALY gained. Costs and outcomes were discounted annually at a rate of 5%; all costs expressed are in 2015 Mexican pesos (P$). One-way and multi-way probabilistic sensitivity analyses (SA) were conducted.

Results: Base-case results indicated the total cost per patient over a course of four chemotherapy cycles was estimated to be P$60,460 for ipegfilgrastim, P$62,496 for filgrastim, and P$68,193 for pegfilgrastim. The incidence of neutropenia (severe and febrile) and risk of mortality was lower with pegfilgrastim than in filgrastim and pegfilgrastim. Over a 30-year time horizon, including duration of chemotherapy, total life-time cost per patient was P$193,610 for ipegfilgrastim compared with P$196,672 for filgrastim. Health outcomes per patient were calculated as 12.93 LYs saved and 6.92 QALYs gained for ipegfilgrastim and 12.79 LYs saved and 6.76 QALYs gained for filgrastim. Ipegfilgrastim treatment had an incremental cost savings of P$3,062 and incremental LYs and QALYs of 0.14 and 0.16, respectively. The model was most sensitive to the per-administration cost of filgrastim or ipegfilgrastim; however, in the probabilistic SA, ipegfilgrastim treatment was cost-effective 60% of the time at a willingness-to-pay threshold of P$184,000 per QALY.

Conclusions: Due to reduced incidence of neutropenia, increased LYs/QALYs, and lower overall cost, ipegfilgrastim was the dominant treatment strategy over short-acting filgrastim and long-acting pegfilgrastim from the perspective of the Mexican healthcare system. Conflict of interest: Corporate-sponsored Research: Agota Szende and Brendon Bussey declare corporate-sponsored research funding from Teva Pharmaceuticals. Other Substantive Relationships: Erika Szabo, Omar Tomé, Udo W. Mueller, Susan Gabriel, and Boxtiong Tang, declare employment by Teva Pharmaceuticals; Udo W. Mueller declares stock options from Teva Pharmaceuticals.
1028 POSTER  
Budgetary impact of lipegfilgrastim to the Mexican healthcare system  
1 Covance, Global Health Economic and Outcomes Research, Leids, United Kingdom; 2 Covance, Global Health Economic and Outcomes Research, Sydney - NSW, Australia; 3 Teva Pharmaceuticals, Global Health Economics and Outcomes Research, Frazer - Pennsylvania, USA; 4 Institut Jules Bordet - Centre des Tumeurs de l’Université Libre de Bruxelles, Department of Medicine, Brussels, Belgium; 5 Teva Pharmaceuticals, Medical Affairs, Naucalpan de Juarez, Mexico; 6 Teva Pharmaceuticals, Global Medical Affairs, ULM, Germany.
Results: 819 patients were operated for different types of oncologic reasons in our clinic. The average period of hospital stay was 5 days (1–184), including longer hospitalization due to surgical complications or existing comorbidities. The postoperative stay in intensive care unit (ICU) was also included in this period. In our data, the main health insurance coverage was seen to be supplied by the state (n = 804, 96.1%). Of these patients, 8 were covered by a government financed green card programme which is applicable for only lowest income people. 11 of our patients (1.3%) were seen to prefer a state hospital clinic for their treatment even though they could apply any public hospital with their private insurance coverage. Only 4 patients (0.4%) used their own financial resources for their oncologic treatment.

Conclusions: The vast majority of oncology patients operated in our clinic is financed by general state health insurance plan. Taking the great amount of bill that a cancer patient should encounter, the importance of state insurance is obvious for the comfort of patient and the ease of financial portion of oncologic treatment.

No conflict of interest.

1032

POSTER SPOTLIGHT

Potential price reductions for cancer medicines on the WHO Essential Medicines List

M. Barber1, D. Gotham2, A. Hill3

1Centre of Development Studies, Cambridge University, Cambridge, United Kingdom; 2Imperial College London, Faculty of Medicine, London, United Kingdom; 3Chelsea & Westminster Hospital, St Stephen's AIDS Centre, London, United Kingdom

Background: Over 17 million people with HIV/AIDS are on treatment with low-cost generic antiretrovirals. We investigated the feasibility of similar reductions in medicines for cancer. The World Health Organization (WHO) lists 39 cancer medicines that are a high priority for treatment worldwide. The cost of active pharmaceutical ingredient (API) is a central component of drug cost of production.

Methods: Current unit prices in the US, UK, Spain, and India were collected for cancer drugs in the WHO EML using public databases. Data on per-kilogram cost of exported API were retrieved from an online database of Indian export logs, and used in an established cost algorithm to derive estimates for generic prices (target prices) assuming robust competition; percentage costs were calculated, to which a 40% margin was added to account for formulation costs, 0.35USD per month/cycle for packaging, and a 50% markup to incentivise generic market entry. Differences between current prices and target price were calculated. Generic status in the US was assessed through the Drugs@FDA website. Drugs used only to control side-effects were excluded.

Table: Potential price reductions represented by target price compared to current prices, by country

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target price per 28 days</th>
<th>US</th>
<th>UK</th>
<th>Spain</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>$0.92</td>
<td>77%</td>
<td>14%</td>
<td>53%</td>
<td>12%</td>
</tr>
<tr>
<td>All-trans retinol acid (ATRA)</td>
<td>$15.79</td>
<td>98%</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bendamustine</td>
<td>$44.33</td>
<td>99%</td>
<td>94%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capetitabine</td>
<td>$40.48</td>
<td>97%</td>
<td>73%</td>
<td>73%</td>
<td>84%</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>$42.27</td>
<td>9%</td>
<td>88%</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td>$12.53</td>
<td>56%</td>
<td>87%</td>
<td>78%</td>
<td>8%</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>$7.34</td>
<td>98%</td>
<td>88%</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Cytarabine</td>
<td>$4.00</td>
<td>62%</td>
<td>94%</td>
<td>89%</td>
<td>88%</td>
</tr>
<tr>
<td>Daesarbazine</td>
<td>$5.15</td>
<td>79%</td>
<td>93%</td>
<td>85%</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>$17.27</td>
<td>96%</td>
<td>98%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>$37.46</td>
<td>89%</td>
<td>96%</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>$3.18</td>
<td>62%</td>
<td>96%</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>$14.05</td>
<td>85%</td>
<td>86%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>$48.15</td>
<td>69%</td>
<td>95%</td>
<td>88%</td>
<td>89%</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>$48.19</td>
<td>90%</td>
<td>98%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imatinib</td>
<td>$54.24</td>
<td>98%</td>
<td>97%</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>Irotronetan</td>
<td>$3.31</td>
<td>94%</td>
<td>99%</td>
<td>97%</td>
<td>100%</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>$2.38</td>
<td>98%</td>
<td>99%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>$17.35</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>$23.44</td>
<td>78%</td>
<td>96%</td>
<td>92%</td>
<td>74%</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>$27.71</td>
<td>45%</td>
<td>97%</td>
<td>95%</td>
<td>83%</td>
</tr>
<tr>
<td>Rituximab</td>
<td>$918.46</td>
<td>81%</td>
<td>39%</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Vinblastine</td>
<td>$5.54</td>
<td>84%</td>
<td>76%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>Vinoreline</td>
<td>$10.21</td>
<td>74%</td>
<td>94%</td>
<td>79%</td>
<td></td>
</tr>
</tbody>
</table>

Blind: no data; NR: no reduction.

Results: Of the 39 cancer drugs in the EML, 36 were generic in the US. Calculated target prices were median 79% below US prices (21 drugs compared), 94% below UK prices (24 drugs compared), 85% below prices in Spain (21 drugs compared) and 56% below prices in India (18 drugs compared).

Conclusions: Robust, competitive generic production could substantially reduce the prices of cancer drugs on the EML. Mass production of generic cancer medicines is currently possible at prices that would allow substantial expansion of cancer treatment coverage.

No conflict of interest.

1033

Laparoscopic and open surgery for gastric cancer from a business intelligence viewpoint

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1Zuyderland Medisch Centrum, Surgery, Sittard, Netherlands; 2Hogeschool Zuyd, Division of Industrial Engineering & Management, Heerlen, Netherlands

Background: Laparoscopic surgical for gastric cancer has been worldwide been gaining popularity. It is been shown to be a safe technique for early gastric cancer. Cost aspects of this new technique have not been evaluated so far. The aim of this study was to analyze time efficiency in operative time and costs for hospitalization form business intelligence viewpoint for both laparoscopic and open gastrectomy for cancer.

Material and Methods: All data from patients who underwent gastrectomy for cancer January 2010 and January 2015 were included in this study. Primary outcome was costs of operating room usage and total cost admission (including re-admission and complication management) Secondary outcomes were efficiency in operating room processes, complications, length of stay, ICU stay and complications (including costs of these parameters). All these data were prospectively and consecutively collected in the hospital fully digitized patient information system.

Results: A total of 228 patients were included in this study. The laparoscopic gastrectomy was performed in 71 patients (mean age 67 years) and open gastrectomy in 157 patients (mean age 70 years). Mean length of hospital stay was significantly shorter for laparoscopic procedure: mean 7.04 (±4.09) days for laparoscopic procedure vs. 14.30 (±12.54) days for open procedure (p < 0.001). There were significantly fewer complications in patients who underwent laparoscopic gastrectomy (21.1% vs. 36.9% in open gastrectomy, p = 0.021). Total costs of hospitalization (i.e. total costs of surgery, ward stay/ICU and medical imaging) were significantly higher for open procedure €7857 (±6097) vs. €6366 (±2123) for laparoscopic procedure (p = 0.007).

Time of surgery was significantly longer for laparoscopic surgery 247±85 min vs. 183±68 min, p < 0.001. Difference in mean preparation time (i.e., time from arrival in theatre to incision) was 27±7 min and 36±59 min for open and laparoscopic gastrectomy respectively (p = 0.181). Also, difference in emergence from anesthesia was 30±102 min for open surgery and 13±42 min for laparoscopic surgery (p = 0.043).

Conclusions: The analysis from a business intelligence viewpoint shows that laparoscopic gastric surgery is overall more efficient in terms of operative time and hospital stay compared to open surgery. In this study the laparoscopic approach appears to be safer without expanding hospital costs.

No conflict of interest.
obtained from the original questionnaire used to describe nurses’ self-efficacy of their sensitive outcomes in five domains (i.e., health promotions; daily activities interferences; ancillary outcomes; avoid dangers; learning outcomes) where only items related to cancer patients cardiotoxicity effects were used (n = 15). The items rated on a five-point response scale (1 = completely no confidence; 5 = completely confidence).

Results: Nurses showed an overall low self-efficacy related to their sensitive outcomes in managing cancer patients cardiotoxicity effects (mean = 3.1 ± 0.47). There was a slight positive correlation between age and self-efficacy (r = +0.271; p-value = 0.021), therefore experienced nurses with a post-graduate education (n = 38) had higher self-efficacy scoring (r = 0.314; p-value = 0.003). Scores were not significantly different among hospitals (p-value >0.05). The items with the higher scoring were related to the patients’ education while the items with the lower scoring were related to the monitoring and understanding of cardiotoxicity effects. Besides, the analyzed items showed a good internal consistency (Cronbach’s α = 0.88).

Conclusions: Although this study has several limitations mainly related to the data collection (self-report measurement), the findings could be very useful to plan a tailored education for cancer nurses, considering how the nurses self-efficacy responses show a general low confidence to face with cardiotoxicity effects. Moreover, some important relations need to be further explored, especially regarding the age, the gender, and the education differences. Indeed, tailored educational path for cancer nurses have to be developed.

No conflict of interest.

1084 POSTER
Use of Cochrane evidence in supporting medical policies of oncology drugs in the United States
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Background: Cancer is the second leading cause of mortality in the US. Treatment of cancer imposes an enormous economic burden on US private payers. Private payer medical policies are developed using published clinical evidence. The systematic reviews (SR) is considered as the highest quality evidence and are used to inform the clinical guideline and medical policies. Cochrane collaboration develops SR to inform healthcare decisions making. This study assesses the influence of Cochrane SR on the private payers medical policies of the drugs used for the treatment of cancer.

Method: The publically available medical policy documents of the drugs used for the treatment of cancer were scanned for the top four private insurers from the US, which together cover half of the US market, namely: UnitedHealthcare (UHG), Anthem, Aetna, and Cigna. The Cochrane SR used to inform these policy documents were identified by hand-searching. The relevant information such as the use of Cochrane SR, number of SR used, context of use of SR, Impact of SR on policy, Cochrane review group and center to which SR belongs, and other data were extracted from each of the policy document.

Results: A total of 39 SR were used to inform 54 policy documents of the oncology therapies. Less than a quarter (22%) of policy documents of oncology drugs of US private payers has used SR. Overall, for policies where SR was used, 21% of SR supported the clinical usage of the drug and imparted high impact on 33% of policies. A maximum 39% of Aetna and minimum 13% of the Anthem oncology drug medical policies used SR as evidence while Cigna and UHG have not used SR as supporting evidence for oncology drugs.

Conclusions: Cochrane SR used to inform oncology therapy was quite a low. Scope persists to improve the usage of Cochrane SR to inform the payer policies of oncology drugs.

No conflict of interest.

1085 POSTER
Patients’ guardians, Practitioners and Population (3Ps) opinions in pediatric oncology clinical trials in developing country: a cross-sectional survey
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Background: Clinical Trials is the heart of clinical research. Pediatric cancer patients need this type of research to improve their survival and treatment especially in developing countries. The aims of this study are (1) Evaluate the public attitude toward the concept of clinical trials in general and in pediatric settings particularly, (2) Determine the most common barriers or challenges that face pediatric oncologists to participate in clinical trials in Egypt taking oncologists of Children’s Cancer Hospital Egypt-57357 [CCHE] as an example, (3) Determine the most common rationale/reasons of patients’ guardian to agree or not agree to participate in clinical trials.

Materials and Methods: A cross-sectional survey was carried out in three patients categories: Patients’ guardians, Practitioners and Population. Well-structured survey was used for each category. Twenty oncology physicians were contacted, One sixty five of patients’ guardian were contacted and five hundred and two from public were contacted.

Results: Nurses reported higher self-efficacy level. Furthermore, the cancer nurses with a postgraduate education (n = 38) had higher self-efficacy scoring (r = 0.314; p-value = 0.003). Scores were not significantly different among hospitals (p-value >0.05). The items with the higher scoring were related to the patients’ education while the items with the lower scoring were related to the monitoring and understanding of cardiotoxicity effects. Besides, the analyzed items showed a good internal consistency (Cronbach’s α = 0.88).

Conclusions: Although this study has several limitations mainly related to the data collection (self-report measurement), the findings could be very useful to plan a tailored education for cancer nurses, considering how the nurses self-efficacy responses show a general low confidence to face with cardiotoxicity effects. Moreover, some important relations need to be further explored, especially regarding the age, the gender, and the education differences. Indeed, tailored educational path for cancer nurses have to be developed.

No conflict of interest.

1086 POSTER
Identification and critical analysis of metastatic breast cancer policies to advance access to care and treatment in Europe: Research methodology and approaches used to survey the current policy environment
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Background: The European oncology policy landscape is rapidly evolving, evidenced by the increased awareness and prioritization of National Cancer Control Plans (NCCPs), which emphasize prevention, early detection, and treatment of common cancers, such as breast cancer. While multi-payer efforts have helped to address the needs of cancer patients, there is currently limited policy engagement by governments, healthcare professionals, and patient advocacy groups to address mBC patient care and treatment challenges. The growing burden of breast cancer, many of which are detected at later stages in low- and middle-income European countries, necessitates that these countries prioritize and implement effective policies that address this urgent public health issue.

Aim: To increase the understanding of the European metastatic breast cancer (mBC) policy landscape and identify opportunities to improve patient access to care and treatment.

Methods: To evaluate the current policy environment across the mBC care continuum, a comprehensive analysis of existing NCCPs and public health policies and programs was conducted in 7 European countries: Sweden, Poland, France, England, Netherlands, Italy & Germany. To identify key needs and best practices in mBC treatment and care policy, specific criteria were evaluated at each stage of the mBC patient care continuum agnostic to geography.

Criteria were rated as low, medium, or high based on the level of policy development in each country. These findings were further informed by regional stakeholder insights and measured against current government policies and non-governmental organizations (NGOs; eg, advocacy engagements). The compiled data provide country-specific evaluations of each mBC criteria along the care continuum.

Countries were then segmented based on government engagement, policy development, and NGO activity across the care continuum. Importantly, this characterization of countries strives to improve the implementation of mBC policy through the functional application of the findings to countries not included in the original analysis, as well as through the sharing of best practices.
Results and Conclusions: Initial findings reveal striking country discrepancies in mBC policy, healthcare access, as well as select best practices already in place. This study provides an opportunity to advance the European mBC policy conversation and present impactful recommendations for mBC-specific program development in an effort to improve patient care, treatment, and quality of life. Final results will be available in mid-2017.

Conflict of interest: Authors are employees of Pfizer Inc.

1087 POSTER
“Health: A Blessing to Defend, a Right to Uphold” - a manifesto for the rights of oncology patients

A. Mancuso1, 2Salute Donna Onlus, Presidente, Milan, Italy

In Italy in 2014 there were 3 million cancer patients. Cancer is the second cause of death after heart illnesses. There are approximately 366,000 new cases of cancer every year of which 196,000 among men and 269,000 among women. The most frequent cancer is rectum (4%), followed by breast (3%), prostate (11%) and lung (11%).

Cancer has a heavy impact on the quality of life, patients and their families as well as on national health finances.

AION (Italian Association of Medical Oncologists) 2016 Report indicated the survival for cancer patients has increased up to 68%

However there is still great diversity in the accessibility to early diagnosis and treatment from one Region to another despite the objectives of the National Cancer Plan 2013–2016.

In order to better defend the rights of oncology patients Salute Donna Onlus in collaboration with 13 sustaining patients associations, 13 Italian opinion leader active in Oncological field and 12 Scientific Society have promoted at Italian Parliament level, following the example of the European Union, the formation of an intergroup composed of 61 members of Italian Parliament of all the allians who are involved in promoting the fight against cancer as a priority in national health policies and orienting legislation in the right direction.

The result of the work of the team is a policy document requesting that:

– the State guarantees uniformity of health treatment over the whole national territory to avoid “journeys of hope”;
– an Authority is beforised for quality control and assurance of equal treatment and that Patient Advocacy Associations participate;
– in every Region at least one Oncology Center be instituted with the responsibility of defining treatment protocols for oncology illnesses as well as giving indication of the specific medicines, their equivalents or bio-similars, that they have a Genetics service networking with the other Regional specialized centers as well as keeping a Cancer Register;
– according to the European Directive 2011/24/EU regarding cross-border health care on the part of the Italian state be not in contrast with the safeguard of the principle of equality of all the citizens and the uniformity of care on all the national territory and include clear and uniform ways of assuring this right on a national level; the State in addition should cover the expenses of cross border travel of oncology patients in the cases where the in absentia trial to guarantee the same quality of treatment in Italy;
– the provisions, introduced in the Decree Law 69/2013 of the Minister of Health Beatrice Lorenzin, contemplate the introduction in the Handbook on the part of AIFA (Italian Association of Pharmacies) of orphan medicines or those of exceptional therapeutic value within 100 days after the approval on the part of EMA (European Medical Association).

No conflict of interest.

1089 POSTER DISCUSSION
Beyond aspirin and metformin: The untapped potential of drug repurposing in oncology

G. Bouche1, M. Pantziarka1, 2, L. Meheus3, 4Anticancer Fund, Brussels, Belgium; 5The George Pantziarka, London, United Kingdom

Drug repurposing can speed up access to new therapeutic options for cancer patients. It is also an efficient way to adapt to new knowledge about cancer. For instance, tadalfil inhibits myeloid-derived suppressor cells (MDSC) in cancer patients at doses approved for erectile dysfunction (Weed, 2015). New molecular entities against MDSC are being developed but this takes longer, costs more and requires risky first-in-human trials. With more than 2,000 drugs approved worldwide (DrugBank), and an average of 6 relevant targets per drug (Mestres, 2008), multiple opportunities exist. Even the repurposing of monoclonal antibodies has started to emerge (Fornoni 2011, Bogdanovitch 2015). Commercial repurposing is growing but drugs that are off-patent and indicated in non-cancer conditions are being neglected. These financial orphan drugs (FOD) offer no return on investment and less scientific reward, (e.g. high-impact publications), compared with new molecules. We have attempted to quantify the number of cancer repurposing opportunities of FOD, supported by preclinical or clinical data, to see how many potential opportunities have been missed.

Method and Methods: A literature search (PubMed) was performed to identify FOD which could be repurposed in one or more cancer types. Eligible drugs needed at least one peer-reviewed article showing an antitumor effect in vitro, in vivo or in humans. All eligible drugs were investigated to identify which drugs with human data, if any, were recommended in clinical guidelines (NCCN, ESMO).

Results: A total of 200 eligible FOD were identified. One hundred (50%) had human data in cancer patient(s). Four FOD repurposed for cancer were listed in clinical guidelines, namely thalidomide, all-trans retinoic acid, zoledronic acid and non-steroidal anti-inflammatory drugs (NSAID). In the first 3 cases, pharmaceutical companies took the lead and re-branded or re-formulated the drugs. This was not the case for NSAIDs, listed in desmoid tumours guidelines and used off-label. Aspirin for colorectal cancer is the only FOD with positive phase III data. Despite this, it is not being recommended in clinical guidelines. Other FOD with randomized trial data supporting a survival benefit include cimetidine (colorectal cancer), progesterone (breast cancer) or tramebolide (lung cancer). Of note, several other drugs showed high response rate in rare tumours (e.g. clarithromycin, timolol, propranolol).

Conclusions: The number of generic off-patent repurposing opportunities is high and keeps on increasing with reports of new findings or identification of previously missed publications. Until now, practice-changing examples have been limited and have often involved pharmaceutical companies. Joint non-commercial clinical development by academic, governmental and philanthropic organizations may bring new therapeutic options to patients
at low cost, especially in indications for which the industry has no incentive to invest in. Such an effort would be truly innovative and may relieve healthcare systems currently under high financial stress.

No conflict of interest.

Differential survival from colorectal cancer and health expenditure in 3 European countries

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Background: Cancer is a disease that causes a vast diversity in presentation and evolution and therefore poses challenges best met with a multidisciplinary team. The management should be in concordance with the most recent evidence as recommended in international guidelines. These practices have contributed to better homogeneity in the treatment of all types of cancers. Despite these efforts, survival remains different across Europe. It is known that health care expenditure is an important factor affecting health care policies and this is decided on a national level, therefore with significant differences between countries. From this follows that health care expenditure may affect survival from cancer and be the cause of the differential survival between countries.

Material and Methods: Data was collected on the 5-year age standardised survival from colon and rectal cancer in Portugal, United Kingdom and Iceland between the period of 1995 and 2009 from the published literature (CONCORD 2 study, 2015). Health care expenditure (HE) was defined in percentage of gross domestic product (GDP) and collected from the World Bank website database (http://databank.worldbank.org/), accessed 1st December 2016. 3 periods were defined for analysis (1995–1999; 2000–2004; 2005–2009) and HE averaged accordingly. To assess the strength of the association between HE and 5-year age standardised survival the Spearman’s rank correlation coefficient (rho) was used. Subgroup analysis for each country were run with linear regression. Association was statistically significant when the P-value was <0.05.

Results: HE has risen globally from the first period to the last (Table 1). Of note, the only decline was seen in Iceland in the last period. Survival has risen in every study period across every country albeit at different paces. The greatest increase has been rectal cancer survival in Iceland.

Table 1.

<table>
<thead>
<tr>
<th>Country</th>
<th>Period</th>
<th>HE (%GDP)</th>
<th>5-year survival Colon</th>
<th>5-year survival Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portugal</td>
<td>1995–1999</td>
<td>7.66</td>
<td>48.1</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>2000–2004</td>
<td>9.34</td>
<td>51.4</td>
<td>54.2</td>
</tr>
<tr>
<td></td>
<td>2005–2009</td>
<td>9.92</td>
<td>53.8</td>
<td>58.2</td>
</tr>
<tr>
<td>Iceland</td>
<td>1995–1999</td>
<td>8.48</td>
<td>54.1</td>
<td>51.7</td>
</tr>
<tr>
<td></td>
<td>2000–2004</td>
<td>9.43</td>
<td>60.6</td>
<td>68.2</td>
</tr>
<tr>
<td></td>
<td>2005–2009</td>
<td>8.98</td>
<td>65.1</td>
<td>76.5</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1995–1999</td>
<td>6.86</td>
<td>48.8</td>
<td>49.1</td>
</tr>
<tr>
<td></td>
<td>2000–2004</td>
<td>7.52</td>
<td>56.3</td>
<td>53.9</td>
</tr>
<tr>
<td></td>
<td>2005–2009</td>
<td>8.74</td>
<td>60.3</td>
<td>56.6</td>
</tr>
</tbody>
</table>

The correlation between HE and 5-year survival from colon cancer was 0.37 (p-value 0.332). The correlation between HE and 5-year survival from rectal cancer was 0.59 (p-value 0.094). In the linear models a positive association was found between rectal cancer 5-year survival and HE. The remaining models showed a non-significant trend towards positive correlation. Limitations of this work can be considered the use of health care expenditure as a function of GDP and the limited number of countries evaluated.

Conclusions: Increases in HE in terms of percentage of GDP are not correlated with increased survival. Even though a positive trend exists, this does not seem to be a major factor influencing survival. This conclusion should lead to increased efforts to clarify the reasons behind the observed differences in survival between different European countries.

No conflict of interest.

One size fits no-one: A response to national strategy for cancer care

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National cancer strategies are developed to improve the survival and experiences of those living with cancer. Achieving World-Class Cancer Outcomes, published July 2015, is the strategy for cancer care over the next 5 years in England. It provides a solid foundation on which to build, but focuses largely on the more common cancers. In the UK common cancers account for 53% of all cancers diagnosed each year and 47% of all cancer deaths. However, for rare and less common cancer patients the current and future situation appears less optimistic. The complexity of these cancers and their numerous sub-types, presentations, diagnoses and prognoses means that they do not fit the standard cancer model of care. Cancerous Neuroendocrine Tumour (NET) patients, alongside others with less common cancers, experience deficits in care related to limited awareness, lack of knowledge, delayed accurate and timely diagnosis and therefore more difficulty in accessing appropriate care. Part of the problem in providing appropriate care resources has been in accurately identifying the patient cohort, primarily due to limitations of the coding system for registering tumour types, and ensuring that their voices are heard. This year (2016) the National Cancer Registration and Analysis Service (NCRAS) at Public Health England (PHE) undertook a review, with funding support from the NET Patient Foundation, of coding for cancerous NETs. The charity, in response to the lack of NET representation in the NCPES 2014, commissioned its own Patient Experience Survey – identifying patients through collaboration with seven NHS Trusts in England providing specialist NET treatment.

The evidence from PHE suggests that cancerous NETs affects far more patients in England (8,100,000) than originally believed and generally reported. The NET Patient Survey Report highlighted some stark differences between the experiences of NET patients compared to all cancer patients, who completed the NCPES 2014 – most notably around diagnosis, information and treatment.

A national strategy that recommends a plan for most that will be appropriate and impactful, also needs to incorporate other pathways of care, specialist areas for those cancers that do not fit standard plans, to truly achieve world class outcomes. Recommendations, specifically for NETs (but that could be adapted for all other rare/less common cancer patient cohorts), include collaboration with the third sector and other tumour specific experts to ensure accurate data gathering regarding incidence and patient experience, collaboration and genuine inclusion of disease specific experts and patient organisations in national strategy and policy making, utilising and learning from exemplars of care (such as accredited NET Centres of Excellence), and commissioning of service specifications for complex cancers (and timely implementation).

No conflict of interest.

Melanoma

Impact of baseline serum lactate dehydrogenase concentration on the efficacy of pembrolizumab and ipilimumab in patients with advanced melanoma: data from KEYNOTE-006

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Background: An elevated serum lactate dehydrogenase concentration (LDH) concentration at baseline is known to be a poor prognostic
factor for advanced melanoma and to be associated with poor treatment outcomes. We assessed outcomes by baseline LDH level in the phase 3 KEYNOTE-006 study of pembrolizumab versus ipilimumab for advanced melanoma (NCT01866319).

Methods: 834 patients were randomized 1:1:1 to 2 years of pembrolizumab 10mg/kg Q2W or 10mg/kg Q3W or 4 doses of ipilimumab 3mg/kg Q3W. Treatment was continued until disease progression, intolerable toxicity, or patient or physician decision. Response was assessed per RECIST v1.1 by independent central review. Elevated LDH was defined as >1×ULN. The pembrolizumab arms were pooled for this analysis.

Results: Serum LDH was elevated at baseline in 179 of 556 (32%) patients in the pembrolizumab arms and 91 of 278 (33%) patients in the ipilimumab arm. ORR was higher with pembrolizumab compared with ipilimumab in patients with normal (44% vs 17%) and elevated LDH (26% vs 7%). Median duration of response was not reached for pembrolizumab or ipilimumab, regardless of baseline LDH (pembrolizumab: range 8 to 99+ weeks for normal, 11 to 99+ weeks for elevated; ipilimumab: range 5+ to 97+ weeks for normal, 5+ to 50+ weeks for elevated). PFS was improved with pembrolizumab in patients with normal LDH (HR 0.64 [95% CI 0.52–0.80], median 7.0 months vs 2.9 months) and in patients with elevated LDH (HR 0.55 [95% CI 0.40–0.74], median 2.8 months vs 2.5 months). Similar results were seen for OS (normal LDH: HR 0.64 [95% CI 0.52–0.80], median 14.7 months vs 6.2 months).

Conclusions: Although patients with advanced melanoma who have elevated LDH at baseline have shorter PFS and OS than those with normal serum LDH at baseline, patients with elevated LDH can achieve durable responses. Pembrolizumab was associated with improved efficacy over ipilimumab in patients with advanced melanoma regardless of serum LDH concentration at baseline.

Conflict of interest: Advisory Board: G. Long: Bristol-Myers Squibb, Merck, Novartis, Proventus, Roche; C. Blank: MSD, Bristol-Myers Squibb, Novartis, Roche, Pfizer, GlaxoSmithKline; A. Ribases: Merck; L. Mortier: Roche, Bristol-Myers Squibb, Amgen; M. Carlinio: MSD, Bristol-Myers Squibb, Novartis, Amgen, M. Lotem: Merck, CompuGen, P. Lorigan: Bristol-Myers Squibb, Merck, Amgen, Novartis, Roche, GlaxoSmithKline; T.M. Petrella: Merck, Bristol-Myers Squibb, Roche, Novartis; E. Richtig: Amgen, Bristol-Myers Squibb, Merck, GlaxoSmithKline, MSD, Novartis, Pfizer; S.J. O’Day: Merck; C. Lebbe: Roche, Bristol-Myers Squibb, Novartis, MSD, Amgen; J. Lutzky: Novartis; C. McNeil: MSD, Bristol-Myers Squibb, Roche, N. Steven: advisory board member. Corporate-sponsored Research: C. Blank: Novartis, A. Ribases: Merck, Bristol-Myers Squibb, Amgen; Novartis, Roche, Pfizer, GlaxoSmithKline; A. Arance: Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen; C. Hoeller: Novartis, Amgen, M. Lotem: NTBio Pharma; T.M. Petrella: Merck, Roche, Novartis; S.J. O’Day: Merck; C. Lebbe: Roche, Bristol-Myers Squibb; C. McNeil: MSD. Other Substantive Relationships: C. Blank: Travel expenses (Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen); Travel support (Bristol-Myers Squibb, Merck); C. Lebbe: Travel accommodations (Roche, Bristol-Myers Squibb, Novartis); J. Lutzky: Speakers’ bureau (Novartis, Merck, Bristol-Myers Squibb, D. Hille: Employee and stock options (Merck, GlaxoSmithKline); N. Ibrahim: Employee (Merck), Stock options (Merck, GlaxoSmithKline).

Efficacy of pembrolizumab in patients with advanced mucosal melanoma enrolled in the KEYNOTE-001, 002, and 006 studies

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Background: Pembrolizumab has demonstrated efficacy and a manageable safety profile in patients with advanced melanoma. We assessed outcomes of patients with advanced mucosal melanoma enrolled in the KEYNOTE-001 (NCT01295827), KEYNOTE-002 (NCT01704287), and KEYNOTE-006 (NCT01866319) studies of pembrolizumab.

Methods: Patients received pembrolizumab 2mg/kg Q3W, 10mg/kg Q3W, or 10mg/kg Q2W. Response was assessed per RECIST v1.1 by independent central review.

Results: Of the 1567 patients who received ≥1 dose of pembrolizumab, 84 (5%) had mucosal melanoma. Of these 84 patients, 57% were women, 49% were aged >65 years, 32% had ECOG performance status 1, 45% had elevated serum LDH, 8% had BRAFV600 mutant tumors, 81% had prior therapy including >1 prior therapy. 95% had baseline time to response ≥77.7 mm (ie, median in total population), and 70% with known PD-L1 status had PD-L1-positive tumors. 90% of patients received ≥1 prior therapy, including 37% who received 1, 45% who received 2, and 8% who received ≥3. 39% of patients received prior ipilimumab. In patients with mucosal melanoma, ORR was 19% (95% CI 12–29%), DCR was 31% (95% CI 22–42%), median PFS was 2.8 months (95% CI 2.7–2.8), and median OS was 11.3 months (95% CI 7.7–16.6). Among the 16 patients who experienced response, median duration of response was 12.4 weeks (range, 11.1–84.1), 12 (75%) were alive without subsequent progression, and median duration of response was 27.6 months (range, 1.1+ to 27.6). In the patients with ipilimumab-pretreated mucosal melanoma, ORR was 15% (95% CI 7–31%), DCR was 39% (95% CI 26–52%). Similar results were seen for OS (normal LDH: HR 0.77 [95% CI 0.58–1.02], median 14.7 months vs 6.2 months). Similar results were seen for OS (normal LDH: HR 0.77 [95% CI 0.58–1.02], median 14.7 months vs 6.2 months).

Conclusions: Pembrolizumab is active in advanced mucosal melanoma and provides durable activity regardless of whether the patients previously received ipilimumab.


Prediction of numbers of melanoma deaths by 2050

P. Autier1, A. Koechlin2, M. Boni2

1 International Prevention Research Institute, Population Research, Lyon, France; 2 International Prevention Research Institute, Statistics, Lyon, France

Background: It has been shown that subjects at highest risk to die from melanoma are those born between 1920 and 1960 and that the risk steadily decreases in successive generations (Autier et al, EJC, 2015). Taking Australia, the USA and Sweden as examples, the number of melanoma deaths until 2050 were predicted.

Methods: Age period cohort (APC) models were fitted to the melanoma mortality data reported by the WHO mortality database. Log-linear models taking into account projected increases in population and aging estimated the numbers of melanoma deaths for the period 2014–2050 according to 2 scenarios: 1) the APC model with no available efficient therapy; 2) the same model with addition of a treatment causing a 25% reduction in melanoma mortality from 2015 onwards. It is assumed that patients have immediate access to therapies.

Results: The peak age-adjusted melanoma mortality have occurred around 2015 and 1990 in Australian men and women, respectively. These peaks occurred around 2005 and 1995 in US men and women, and around 2010 in both Swedish men and women. In 2050, rates in Australia would be about 2.5 times lower than in peak years, back to rates prevailing in 1970 in men and before 1960 in women. In the USA, rates in 2050 would be about 2.5 to 3 times lower than in peak years, back to mortality rates that prevailed before 1960. In Sweden, rates in 2050 would be 1.5 times lower
than in peak years, back to mortality rates prevailing around 1985. But because of population growth and aging, the numbers of melanoma deaths will keep increasing until 2030–35 above levels suggested by changes in age-adjusted rates. In absence of effective therapy, in 2050 the number of melanoma deaths in Australian men and women will still be above numbers in 2010. In the USA, numbers of deaths will be equal to those around 2000 in men and 1985 in women. In Sweden, numbers of deaths in men and women will be equal to those of 10. With an effective therapy, decreases in the number of melanoma death will be observed before 2030. In 2050, the numbers of melanoma deaths in Australia will be equal to those around 2005; in the USA, equal to those of around 1990 for men and 1980 for women; and in Sweden, equal to those of around 2000. As time passes, melanoma deaths will become steadily rarer in subjects less than 50 years. After 2050, practically all melanoma deaths will occur in subjects aged over 70 years.

**Conclusions:** The quickest falls in the risk of melanoma death in all age subjects will be observed in the USA, mainly in women, then in Australia, and in Sweden, the age at melanoma death will steadily increase, the numbers melanoma deaths will start decreasing only after 2030. Efficient therapies may contribute to advance the year when numbers of melanoma deaths would start noticeably decrease.

**No conflict of interest.**

**1146 ORAL**

**Downsizing of locally advanced stage III (bulky) BRAF V600E/K melanoma with combination targeted therapy to achieve R0 resection**

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Patients with locally advanced/irresectable stage IIIc (bulky) melanoma have a poor prognosis and receive the same treatment as stage IV disease patients. For BRAF V600E/K mutated melanoma combination targeted therapy with BRAFi + MEKi has become standard of care with ORR of above 65% and PFS of around 11 months for stage IV disease. We initiated a phase II study for patients with locally advanced stage III (bulky) BRAF V600E/K mutated melanoma in order to try downsize the tumor to such an extent that tumors would become fully resectable (RO).

**Design:** 25 patients with stage IIIC, BRAF V600E/K mutated, bulky and according to the opinion of surgeons in a multidisciplinary team irresectable or locally advanced (high chance of an R+) disease are eligible for this study. Prior to treatment biopsies are taken and a PET and/or CT or MRI scan are made. Treatment consists of dabrafenib 150 mg twice a day plus trametinib 2 mg once a day. At t = 2 weeks a biopsy and PET-scan are made to measure the metabolic response to treatment. After 8 weeks of treatment patients are scheduled for surgery. Prior to surgery another PET and/or CT or MRI scan are made. The primary endpoint is the % of RO resection. Post-surgery patients undergo regular follow-up including lab test and radiological exams, but do not continue BRAFi/MEKi treatment.

**Statistics:** We hypothesize that if downsizing by dabrafenib + trametinib treatment results in an R0 resection in 45% or more of the patients, this treatment modality is highly interesting and should be tested further in a larger randomized trial. We consider an R0 resection in 20% or less of patients futile. To test this hypothesis we will make use of Simon Optim al two-phase design.

**Results:** Up to date 13 patients have been enrolled in this study. After 8 weeks of treatment 11 patients underwent surgery. 2 progressed on treatment. Of these 11 one patient still had irresectable disease at surgery. In 9 patients RO resection was achieved. Of these 9 patients (median mean follow-up of 9/11 months (range 3–22 months), 6 patients have recurred, 3 remain disease-free. The pattern of recurrence was distant in 2 patients, who were either re-treated with BRAFi/MEKi or immunotherapy. 4 recurrences were managed with new surgery.

**Conclusion:** Early results of a neoadjuvant targeted therapy approach for locally advanced/irresectable stage IV melanoma to achieve R0 resection seem promising. This trial will continue until 25 patients have been enrolled.

**Conflict of interest:** Advisory Board: Novartis. Corporate-sponsored Research: Novartis.
had stage 3 disease. By July 2016, 117 (59.3%) had died; mean survival from primary to death was 54 months (range 5–225). All mortalities were from eventual stage 4 disease. Survival rates decreased with increasing AJCC primary stage (p < 0.005) and both mean time to recurrence and death decreased with increasing AJCC stage.

Conclusions: Early detection of systemic disease enables therapy with increased survival and potential cure. First presentation of metastases with stage 4 disease occurred in 18.6% of our cohort. Screening CT scans therefore seem sensible to detect those with occult metastatic disease. New UK guidelines advise screening CT scans only for the higher risk 20% patients, but we believe that our own findings and published data support extending CT scanning to those with stage 2b disease (mean of 16 new cases per year at our unit), whose risk profile is similar. Furthermore, extending follow up to eight years would capture 95% of our cohort, further expediting access to life-lengthening oncological treatments.

No conflict of interest.

1199 POSTER DISCUSSION
Primary mucosal malignant melanoma of ano-rectal and vulvo-vagina: Epidemiology, clinic-pathological and survival characteristics with proposal for reconciliation of the tumor staging
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Background: Primary malignant mucosal melanoma (PMMM) arises from melanocytes located in mucosal membranes lining respiratory, gastrointestinal and urinary tract. The common sites of PMMM are nasal cavity, oral cavity, ano-rectum, vulva, and vagina. Most mucosal melanomas tend to occur in occult sites, which together with the lack of early and specific signs contributes to late diagnosis and thus poor prognosis. PMMM accounts for only 1.4% of all melanoma cases, and its incidence is reported in literature to have remained consistently stable over last many years. PMMMs arising in ano-rectum and vulvo-vagina carry poor prognosis in comparison to the conventional common histological types of cancers.

Material and Methods: We analysed patients who presented at our institute with PMMMs over the last decade, with the primary sites of ano-rectum and vulvo-vagina tract mucosa. We compared the PMMM of rectum and anal canal with aspect to epidemiology, clinical staging and treatment (surgical and non-surgical, including new targeted agents) and stage specific disease free and overall survival with adenocarcinoma of rectum and squamous cell carcinoma anal canal, respectively. PMMMs of ano-vagina compared with squamous cell carcinoma of vulva and vagina, respectively. Median follow up was 23 months (range 3–41 months) in all groups.

Results: At our institute, a tertiary cancer care centre, the proportion of PMMMs in comparison to cutaneous melanoma has increased over the last decade. We identified a total of 96 cases of PMMM, which include ano-rectal primary in 51, vulva primary in 31 and vaginal mucosal primary in 16 cases. PMMMs of ano-rectum and vulva-vagina presented with advance stage either with local infiltration or lymph node metastasis. Three-year overall survival (OS) of anal canal PMMM versus SCC in stage I to IV was 67% vs 89%, 41% vs 69%, 13% vs 52% and 9% vs 29%, respectively. Rectal PMMMs versus adenocarcinoma 3-year OS was 49% vs 92%, 42% vs 87%, 16% vs 47% and 4% vs 15% in stage I to IV, respectively. In PMMMs of vulva versus SCC vulva 3-year OS, 41% vs 88%, 36% vs 67%, 20% vs 37% and 7% vs 23%, and in vagina PMMMs, 39% vs 87%, 32% vs 59%, 17% vs 43% and 3% vs 19% in stage I, II, III and IV, respectively.

Conclusion: PMMMs are rare and aggressive tumours with poor prognosis. Each anatomic site has a peculiar approach to its treatment, in spite of the same tumour morphology and origin. PMMMs of ano-rectum and vulva-vagina have a poor prognosis in comparison to common types of cancer with respect to each pathological AJCC staging. Thus, we recommend further discussion regarding the reconciliation of the AJCC staging of ano-rectal and ano-vaginal PMMMs.

No conflict of interest.

1200A POSTER
Squamous cell carcinoma patients with malignant melanoma
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Background: Malignant melanoma is a tumor that arises from melanocytes and develops in a pre-existing lesion or in healthy-appearing skin. It is characterized by aggressive invasion, early metastasis and resistance to chemotheraphy or radiotherapy, which results in increased incidence and mortality.

Caveolin-1 (CAV1) is one of three members of the caveolin family and (Caveolin-2, 3) of proteins expressed by mammalian cells. CAV-1 plays an important role in the pathogenesis of oncogenic cell transformation, tumorgenesis, and metastasis and acts as a tumor promoter or suppressor depending on tumor type and stage.

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Fibronectin is one of the major structural components of the basement membrane which controls many fundamental biological processes such as adhesion, invasion, differentiation, and proliferation. Abnormal expression of the fibronectin has also been linked to metastatic melanoma progression.

There is strong evidence that the expression of fibronectin is strongly correlated with the acquisition of invasive and metastatic behavior of melanoma cells.

We aimed to research the serum levels of caveolin-1 and fibronectin in patients with malignant melanoma, who were not received any treatment. These results were compared with the healthy controls to investigate of serum caveolin-1 and fibronectin levels as useful markers for malignant melanoma patients.

Material and Methods: We measured serum caveolin-1 and fibronectin levels by enzyme-linked immunosorbent assay (ELISA) method in Oncology Institute, Istanbul, Turkey. We enrolled 60 malignant melanoma patients with a pathologically confirmed diagnosis and 30 healthy controls matched in age and sex. Area Under Curve (AUC) was calculated by using ROC (Receiver Operating Characteristic) curve analysis.

Results: The results were evaluated by the Mann–Whitney U-test using SPSS 21 (Chicago, IL, USA). There were significant difference in the serum caveolin-1 and fibronectin levels (p = 0.05 and p < 0.001, respectively)
between the patients with malignant melanoma and healthy control group. The baseline serum caveolin-1 (0.47 ng/ml) and fibronectin (0.51 ng/ml) levels of the patients with melanoma were significantly higher than in those in the control group (0.37 ng/ml and 0.192 ng/ml, respectively).

**Conclusions:** Higher serum levels of caveolin-1 and fibronectin indicate that these molecules may be useful as tumor markers in the diagnosis of malignant melanoma.

**No conflict of interest.**

**POSTER Ultraviolet irradiation for medical reasons and deadly melanoma**

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**Background:** Light-skinned subjects at highest risk to die from cutaneous melanoma were those born between 1900 and 1960. Generations with gradually lower risk of melanoma death are currently replacing generations at higher risk with the consequence that melanoma death rates will become increasingly uncommon after 2030 and will have nearly disappeared by the end of the 21st century. We explored possible reasons underlying the steep rise and fall in melanoma mortality with special attention to three factors: (a) Cancer screening influences cancer mortality through reducing the incidence rates of advanced cancers. (b) The carcinogenic effects of the ultraviolet radiation (UVR) are particularly marked in the period immediately following melanoma diagnosis. The risk of melanoma death is highest for subjects who were born in sunny areas than for subjects who migrated to sunny areas.

**Methods:** We performed systematic literature searches on time trends in thickness-specific melanoma incidence and on circumstances associated with the basal level of light-skinned children to UVR.

**Results:** Stable or steady increases in the incidence of thick melanomas are observed in virtually all fair-skinned populations, even in areas like Queensland (Australia) where skin screening is widespread since decades. Few data suggest declines in incidence of thick melanomas in younger age groups. Forty to 50% of melanoma deaths are due to tumours less than 2 mm thickness, that are hardly be screen-detected when thinner.

Beliefs in the healthiness virtues of the sun and UVR expanded among health professionals from 1880 to 1960. These beliefs were boosted by observations that exposure to UVR and sunlight could heal some cutaneous infections as well as rickets, and by the discovery of vitamin D. In 1920–50, a considerable variety of UVR-emitting devices were commercially available whose spectrum included substantial amounts of highly carcinogenic UVB and UVC. Infants and schoolchildren were the population categories most exposed to UVR-emitting devices. UVR-prophylaxis or therapy was also done through direct exposure of unclothed children to the midday sun. At the time, there was complete ignorance about the carcinogenic properties of UVR. This fashion faded away in the 1960s with the advent of effective medical methods (e.g., vaccines, antibiotics), improved lifestyle and increased recognition that sun exposure and sunburn experience during childhood are strong risk factors for skin cancer in adult life.

**Conclusions:** The considerable time variations in melanoma mortality are probably due to the exposures of numerous light-skinned children to intense natural and artificial sources of UVR from 1900 to 1960. UV protection of children is the main cause of declining melanoma mortality. The evidence that skin screening has influenced the risk of melanoma death remains scanty.

**No conflict of interest.**

**POSTER DISCUSSION Isolated limb perfusion for melanoma is safe and effective in elderly patients**

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**Background:** Data on isolated limb perfusion (ILP) in elderly melanoma patients with in-transit metastases is scarce. We aimed to evaluate the efficacy and safety of ILP in our institutional cohort of melanoma patients.

**Material and Methods:** We performed retrospective analysis of stage IIIB and IIIC melanoma patients who underwent ILP for melanoma in-transit metastases in our institution between 2000 and 2016. Non-melanoma deaths, liver metastasis, or melanoma death were considered as complications. Univariate and multivariate analysis were performed with SPSS.

**Results:** Eighty-six patients were included (44 patients >70 years). The overall response rate was 81%, with a complete response (CR) rate of 47%. The overall median locoregional PFS was 6 months, while patients with a CR had a median PFS of 16 months. Median MFS was 38 months. Three and five-year MFS were 52% and 38%. Toxicity, response rate or locoregional PFS did not differ significantly between younger and elderly patients. Multivariable analysis showed that CR was prognostic for improved locoregional PFS. Patients >70 compared to patients <70 and patients with stage IIIC versus IIIB had a higher risk of melanoma-specific death, while patients with a CR had a lower risk of melanoma-specific death.

**Conclusions:** Because of its safety profile and high CR rates, ILP is a viable option for (elderly) patients with bulky or multiple melanoma in-transit metastases.

**No conflict of interest.**

**POSTER Discussion**

**Isolated limb perfusion for melanoma is safe and effective in elderly patients**

**M. Madu 1, D. Marion 1, J. Van der Hage 1, K. Jözwiak 2, M. Wouters 1, A. Van Akkooi 1.** 1 The Netherlands Cancer Institute, Surgical Oncology, Amsterdam, Netherlands; 2 The Netherlands Cancer Institute, Epidemiology and Biostatistics, Amsterdam, Netherlands

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**Conclusions:** Because of its safety profile and high CR rates, ILP is a viable option for (elderly) patients with bulky or multiple melanoma in-transit metastases.

**No conflict of interest.**

**POSTER DISCUSSION**

**Clinical prognostic markers in stage IIIB melanoma**

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**Background:** Locoregional treatment is often insufficient to guarantee long-term disease free survival in AJCC stage IIIB melanoma. To improve survival, effective neo-adjuvant and adjuvant strategies are needed. Selecting patients for these strategies requires risk stratification, for which clinical and molecular biomarkers can be used. We aimed to find clinical biomarkers to identify high-risk stage IIIB melanoma patients.

**Patients and Methods:** We performed retrospective analysis of stage IIIB melanoma patients who underwent lymph node dissection (LND) in our institution between 2000 and 2015. SN-positive patients with ulcerated primary tumors and patients with clinically detectable nodal metastasis with non-ulcerated tumors were included. Baseline characteristics, melanoma specific survival (MSS), disease free survival (DFS) were assessed and prognostic factors for recurrence and survival were analyzed using univariate and multivariate analysis.

**Results:** Two hundred fifty patients were included. Median follow-up was 52 months (IQR 29–108 months). Median MSS was 141 months, median DFS was 36 months. Five- and 10-year MSS were 59% and 52%, 5-year and 10-year DFS were 47% and 41%. Age >50, Breslow thickness >2 mm versus ≤2 mm and N2 versus N1 all carried an increased risk of death by melanoma. Age >50 and extracapsular extension carried increased risk of disease recurrence after LND.
Conclusions: Age >50, Breslow thickness >2mm and N2 versus N1 are prognostic for poor survival in stage IIIB melanoma. These characteristics can be used to further stratify risk of death by melanoma in this already high-risk patient population and help select the appropriate population for adjuvant therapy (trials).

No conflict of interest.

1204A POSTER Implementation of the 7th edition AJCC staging system: effects on staging and survival for pT1 melanoma. A Dutch population based study

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Background: In the 7th edition of the AJCC staging system the mitotic rate criterion replaced Clark level to increase correct classification of high risk thin melanoma patients (pT1B). Additionally, sentinel node biopsy (SNB) was recommended for nodal staging for pT1B melanomas.

Aim: To evaluate the effects on pT1 substaging and clinical implications in the national pT1 melanoma population.

Material and Methods: All pT1 melanomas diagnosed in the Netherlands between 2003 and 2014 were selected from the Netherlands Cancer Registry (iKNL). Patients were stratified by cohort, according to AJCC edition: (1) 2003−2009 (6th) and (2) 2010−2014 (7th). Relative survival was calculated to estimate melanoma specific survival.

Results: A total of 29,546 pT1 melanoma patients were included. The pT1b proportion increased from 10.1% in cohort 1, to 21.5% in cohort 2. The proportion of performed SNBs per cohort increased: for pT1b melanomas alone from 4.5% to 13.0%. SNB positivity rate decreased from 10.5% to 8.8% for the entire pT1 population, and for pT1b melanomas from 11.3% to 8.6%.

Conclusions: At 5 years, the relative survival rate was similar for pT1a and pT1b in both cohorts, namely pT1a 100% vs pT1b 97% (cohort 1) and pT1a 100% vs pT1b 98% (cohort 2). The 7th edition of the AJCC staging system has caused an increased number of patients to undergo SNB, without an increase in SNB positivity rate. Survival between pT1 subgroups remains similar. The mitotic rate criterion for pT1b classification and the recommendation to perform SNB for pT1b melanomas should be reconsidered.

No conflict of interest.

1205 POSTER SPOTLIGHT PET/CT surveillance detects asymptomatic recurrences in stage IIIB and IIIC melanoma patients: a prospective cohort study

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Background: AJCC stage IIIB and IIIC melanoma patients are at risk for disease relapse or progression. The advent of effective systemic therapies has made curative treatment of progressive disease a possibility. Since resection of oligometastatic disease can confer a survival benefit and immunotherapy is possibly most effective in a low tumor load setting, there is a likely benefit to early detection of progression. The aim of this pilot study was to evaluate a PET/CT surveillance schedule for resected stage IIIB and IIIC melanoma.

Study design: From 1-2015, stage IIIB and IIIC melanoma patients at our institution underwent 6-monthly surveillance with PET/CT, together with 3-monthly S100B assessment. When symptoms or elevated S100B were detected, an additional PET/CT was performed. Descriptive statistics were used to evaluate outcomes for this surveillance schedule.

Results: Twenty-five patients were included. Fourteen patients (56%) were suspected of relapse on PET/CT. Relapses were confirmed in 11 patients. Recurrences were mostly regional in stage IIIB patients (2 out of 3) and mostly distant in stage IIIC cases (5 out of 5). Three cases were false positive. There were no false negatives. All recurrences detected by PET/CT were asymptomatic at that time, with a normal range S100B. Nine patients received curative treatment after diagnosis of relapse.

Conclusions: Surveillance imaging with S100B in combination with PET/CT seems an effective strategy to detect asymptomatic recurrence in stage IIIB and IIIC melanoma patients in the first months after complete surgical resection.

No conflict of interest.

1205A POSTER Positive sentinel node in the groin area: Extent of completion lymphadenectomy and prognosis for melanoma patients

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Background: The therapeutic effect of completion lymphadenectomy (CLND) after a positive sentinel node biopsy (SNB) is still being investigated. The optimal surgical extent of 5-year CLND, i.e. superficial groin dissection (SGD) or combined superficial and deep groin dissection (CGD) including additional removal of pelvic nodes, is a highly controversial topic. The aim of the present study is to investigate whether the extent of CLND after a positive inguinal SNB is associated with better survival outcome.

Methods: Data of all sentinel node (SN) positive patients who underwent a groin CLND at four tertiary melanoma referral centers were retrieved retrospectively. Inclusion was based on complete CLND details and absence of positive SNs outside the groin area. Baseline, patient, tumor characteristics were collected for descriptive statistics, survival analyses and Cox proportional hazards regression analyses. Recurrence pattern, disease free survival (DFS), distant metastasis free survival (DMFS), and melanoma specific survival (MSS) were analyzed across both treatment groups.

Results: A total of 255 patients were included, of which 125 (49%) were men. Median age was 51 years [interquartile range (IQR) 39–62 years], median follow-up was 51 months [IQR 26–59 months]. Median Breslow thickness was 2.90 mm [IQR 1.80–4.55 mm], and 106 (42%) patients had ulcerated primaries. One-hundred-thirty-seven (54%) patients underwent SGD, and 118 (46%) CGD. The overall non-SN metastasis rate was 19%, the inguinal non-SN metastasis rate was 16% and the pelvic non-SN metastasis rate was 10%. The inguinal non-SN metastasis rate after CGD was significantly higher than after SGD (21% vs. 11%, P = 0.025), but the median number of excised inguinal nodes was similar (8 [IQR 5−11], P = 0.417). Recurrence pattern was similar between SGD and CGD. In a MSS Cox-proportional hazards model CLND type was not significant univariate nor after adjustment for known risk factors.

Conclusions: CGD compared to SGD was not associated with better outcome in patients with a positive SN. The risk of pelvic nodal involvement in these patients was low (10%). These results illustrate that SGD may be a safe first approach as CLND in most patients with micrometastatic disease.

No conflict of interest.

1206 POSTER A possibility for therapy of metastatic cutaneous melanoma with cationic peptides

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Introduction: Cutaneous melanoma (CM) is the most aggressive form of skin cancer in human. Metastatic dissemination is responsible for the majority of melanoma-related mortalities. Nucleophosmin/NPM1 and nucleolin/NCL are multifunctional nuclear phosphoproteins, which play a key role in cell cycle regulation, ribosome biogenesis, transcription and translation, molecular transport and signaling. As a rule, high levels of NPM1/NCL expression in tumors is correlated with poor clinical outcome. Highly expressed NPM1/NCL in tumor cells are considered as a possible targets for anticancer treatment. Cationic peptides (CP) are promising as a low-toxic and resistant to intercellular degradation molecule, which can penetrate cells and induce tumor cell death.

Material and Methods: A group of CP with different molecular structure, including linear and dendritic ones, has been tested in vitro. The dynamics of cell proliferation and toxicity of CP was studied on CM cell lines mH745 and mIS223 and human fibroblast line H1036 as a control. Structure and expression of NPM1/NCL genes were analyzed by PCR, subsequent PAGE, RT PCR and western-blotting, using p53 and NCL-specific antibodies. The BRAF/FRAS1 oncogene and TP53 gene mutations were analyzed by PCR followed by direct sequencing. Peptide toxicity was determined by standard MTT assay.

No conflict of interest.
Results: PCR analysis has revealed BRAF V600E mutation (codon 600, exon 15 of BRAF gene) in combination with several basic polymorphic variants of NCL/NPM genes in the both CM cell lines, while TP53 gene mutations were not detected. Before the incubation of CM cells and normal cells with CP solution in concentration from 0.25 μg/ml to 4.0 μg/ml, the level of NCL mRNA in CM cells was significantly (5.0–11.0 times) higher than in normal cells. After 3 days of incubation with dendrimeric CPs, the level of NCL mRNA in CM cells was only 1.1 time higher than in normal cells, while TP53 mRNA level was increased in 1.5 times. MTT assay has revealed toxic effect for tumor and no toxicity for normal cells. MTT cell apoptosis was confirmed by fluorescent annexin and Hechst 33342 staining and with “Live-DEad molecular probes” assay. The interaction between p53 and NCL molecule was confirmed by blotting. A possible mechanism of selective toxicity for CP under study is interaction between CP molecule and cytoplasmic fraction of NCL subsequent activation of p53 and apoptosis after reduction of free nucleolin level in cytoplasm due to its binding with CP molecule which are transported by cell surface NCL.

Conclusions: Selective toxicity of CPs, mainly with dendrimeric molecular structure, for CM cell lines, carrying BRAF V600E mutation, has been revealed. Tumor cell surface nucleolin is considered as a possible target for molecular therapy of CM with dendrimeric CPs.

No conflict of interest.

1207 POSTER DISCUSSION
EURO-VOYAGE: Effectiveness and safety of ipilimumab (IPI) administration in a European Expanded Access Programme (EAP) in patients with advanced melanoma (MEL)

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Background: IPI blocks cytotoxic T-lymphocyte-associated antigen 4 to potentiate antitumor T-cell responses, and is approved worldwide as monotherapy for the treatment of MEL in the USA as an adjuvant treatment for resected stage III melanoma. IPI is also approved in combination with nivolumab (anti-programmed death-1 antibody) in patients (pts) with MEL. IPI has shown improved overall survival (OS) in pts with MEL, but also adverse events (AEs) that can be severe and/or long-lasting. Limited data exist to distinguish pts with an increased risk of toxicity or decreased survival. We report interim data on the treatment outcomes from an EAP of IPI monotherapy.

Material and Methods: EURO-VOYAGE is an observational, retrospective study of previously treated pts with MEL who received IPI in an EAP from 15 European countries. Eligible pts had an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2, asymptomatic brain metastases, and were not enrolled in a registration trial with a survival endpoint. The primary objectives were OS and the occurrence/ discontinuation of AEs. Any grade of treatment-related AEs led to discontinuation in 9% of pts and 17 pts (~2%) experienced treatment-related AEs that resulted in death.

Conclusions: These initial data from EURO-VOYAGE show a consistent safety profile for IPI, with no unexpected AEs compared with previous clinical trial experience. Future analyses will investigate the contribution of treatment and patient/disease characteristics on the observed OS.


1208 POSTER SPOTLIGHT
Antitumor activity of ipilimumab after pembrolizumab in patients with advanced melanoma in KEYNOTE-006

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Background: The efficacy and safety of PD-1 inhibition in patients with advanced melanoma previously treated with the CTLA-4 inhibitor ipilimumab has been established in several studies, including the KEYNOTE-001 and 002 trials of pembrolizumab. Conversely, the efficacy of CTLA-4 inhibition with ipilimumab following anti-PD-1 therapy is not clearly established. We assessed outcomes in patients enrolled in KEYNOTE-006 (NCT01866319) who received ipilimumab monotherapy after pembrolizumab.

Methods: Patients in KEYNOTE-006 were randomized 1:1:1 to 2 years of pembrolizumab 10 mg/kg Q2W (n = 279) 10 mg/kg Q3W (n = 277) or 4 doses of ipilimumab 3 mg/kg Q3W (n = 278). Treatment was continued until disease progression, intolerable toxicity, or patient or physician decision. After study treatment discontinuation, subsequent antiPD therapy and outcomes were reported.

Results: As of December 3, 2015, ipilimumab was recorded as a subsequent therapy for 129 pembrolizumab-treated patients, including 97
for whom ipilimumab was the first post-study therapy. Of these 97 patients, 64% had M1c disease, 33% had elevated serum LDH at baseline, and 16% had BRAF V600-mutant tumors at baseline. Best response to pembrolizumab (RECIST v1.1, central review) was PR in 16%, SD in 12%, nonCR/nonPD in 52%, and nonevaluable/not assessed in 4%. Median duration of pembrolizumab before the start of ipilimumab was 18 weeks (range 0–90), and the median time between the last pembrolizumab dose and first ipilimumab dose was 5 weeks (range 1–42). Median duration of ipilimumab was 8 weeks (range 0–17). The reported ORR for ipilimumab was 14%, with a best overall response of CR, PR in 11%, SD in 33%, PD in 33%, and unknown in 23%; subsequent progression occurred in 40% of patients with PR and 48% with SD. Best response to pembrolizumab (central RECIST v1.1) in the 13 patients who responded to ipilimumab was SD in 1, nonCR/nonPD in 2, PD in 8, and not assessed in 2. Best response to ipilimumab in the 16 responders to pembrolizumab who received ≥1 ipilimumab dose was SD in 8, PD in 3, and unknown in 5. Fifty-seven of 97 patients had died, and median OS from randomization was 19.6 months (95% CI 16.4–23.5).

Conclusions: Ipilimumab has antitumor activity following pembrolizumab in patients with advanced melanoma, including those whose best response to pembrolizumab was PD, with an ORR consistent with historical data.

Conflict of Interest: Advisory Board: G. Long; Bristol-Myers Squibb, Merck, Novartis, Proventus, Roche; C. Robert: Amgen, Bristol-Myers Squibb, Merck, Roche, Novartis; A. Arance: Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen; C. Blank: MSD, Bristol-Myers Squibb, Novartis, Pfizer; G. Lorigan: Bristol-Myers Squibb, Merck, Amgen, Novartis, Roche, GlaxoSmithKline; L. Mortier: Roche, Bristol-Myers Squibb, GlaxoSmithKline, Novartis, Amgen, J. Schachter: MSD, M. Szolay: Symphogen, Lion Biotechnology, Amgen; M. Sznol: Paid consultant; B. Schwartz-Bloom: Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen; L. Ornoss; N. Steven: advisory board member. Corporate-sponsored Research: C. Blank: Novartis; A. Ribas: Merck; L. Mortier: Roche, Bristol-Myers Squibb, GlaxoSmithKline, Novartis, Amgen; A. Arance: Roche; M. Sznol: Pfizer, Novartis, Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen; J. Schachter: MSD, M. Szolay: Symphogen, Lion Biotechnology, Amgen; A. Ribas: Travel expenses (Roche, MSD, Bristol-Myers Squibb, Novartis, Amgen); Travel expenses (Roche, MSD, Bristol-Myers Squibb); C. Blank: Travel expenses (Roche, MSD). Expert testimony (Bristol-Myers Squibb); P. Lorigan: Travel support (Bristol-Myers Squibb, Merck); M. Sznol: Media consultant (Genentech-Roche, Bristol-Myers Squibb, AstraZeneca/MedImmune, Pfizer, Novartis, Kyowa-Kirin, Amgen, neras, Seattle Genetics, Immune Design, Prometheus, Aneraohemaph, Astellas, Agensys, Nektar, NeoStem, Pierre-Fabre, Lilly, Merck, Alexion, Theravance, Biodex, Vaccinex, Janssen-Johnson and Johnson, Lycera, Modulate Therapy, Inc., Bavaria, Ch. Zhou: Employee and stock options (Merck & Co., Inc.); S. Ebbinghaus: Employee and stock options (Merck & Co., Inc.); N. Ibrahim: Employee (Merck & Co., Inc.). Stock options (Merck & Co., Inc., GlaxoSmithKline).

Organisation of Cancer Care Delivery

8LBa POSTER SPOTLIGHT

LATE-BREAKING ABSTRACT: Two year overall survival rate of all advanced melanoma patients treated with ipilimumab in Australia 2013–2014

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Background: Australia has one of the world’s highest melanoma incidence rates (e.g. 2012: 34 per 100,000 in Australia vs 13.2 per 100,000 in the European Union). Until recently treatment of advanced melanoma was largely ineffective. Ipilimumab (IPI), the first registered immunotherapy for the use as an anti-cancer medicine, was approved for listing on the Australian Pharmaceutical Benefits Schedule (PBS) for treatment of advanced melanoma (any line of therapy) in Aug-13. Pooled 10 year outcome data across 12 clinical trials has been published by Schadendorf et al. (2015). However there is still some uncertainty for clinicians and patients as to how trial results would translate into real world clinical practice.

As a condition the 2 year overall survival (OS) had to be reported in the first year’s cohort of patients. The rationale was to ensure pay for performance as demonstrated in the cost effectiveness analysis presented in the reimbursement submission to the Pharmaceutical Benefits Advisory Committee (PBAC). A 2-year survival rate of 21.6% to 23.5% was cited in the PBAC submission.

This cohort study reports the 2-year OS in all patients receiving PBS subsidised IPI between 01-Aug-13 to 31-Jul-14 in Australia.

Material and Methods: The main data gathering tool was a web portal integrated into the supply chain. Physicians were required to do mandatory training on treatment of CR in 3%, PR in 11%, SD in 33%, PD in 33%, and unknown in 23%; subsequent progression occurred in 40% of patients with PR and 48% with SD. Best response to pembrolizumab in the 13 patients who responded to ipilimumab was SD in 1, nonCR/nonPD in 2, PD in 8, and not assessed in 2. Best response to ipilimumab in the 16 responders to pembrolizumab who received ≥1 ipilimumab dose was SD in 8, PD in 3, and unknown in 5. Fifty-seven of 97 patients had died, and median OS from randomization was 19.6 months (95% CI 16.4–23.5).

Conclusions: Ipilimumab has antitumor activity following pembrolizumab in patients with advanced melanoma, including those whose best response to pembrolizumab was PD, with an ORR consistent with historical data.

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Poster Session (Sunday 29 January 2017)
Patients see doctors of introduced department after radiotherapy was finished. We investigated that how many patients wish to take the re-examinations of Radiation Oncologist.

**Materials and Methods:** The subjects were 109 consecutive patients who underwent radiotherapy. All patients undergo post-radiotherapy follow-up examinations at the referral departments. We see 400 patients per year at our hospital.

Patients were asked to complete the questionnaire, whether you desire to undergo a follow-up examination of Radiation Oncologist after the completion of treatment. The dependent variable was whether or not the patients desired a follow-up examination. The exploratory variables were gender, age, irradiation objective, dose, and anatomical location.

**Results:** A significantly greater number of women desired follow-up examinations (p = 0.04), whereas a significantly greater number of brain tumor patients did not desire follow-up examinations (p = 0.04).

**Conclusion:** Forty-three percentage of patients wishes to take re-examinations. Radiation oncologists should ask to the patient whether they want to see doctors or not.

**No conflict of interest.**

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1261  **POSTER**

Factors influencing communication skills and abilities for empathy of oncology nurses.

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**Background:** This study was conducted descriptively in order to determine factors influencing communication skills and abilities for empathy of oncology nurses.

**Material and Methods:** This research was conducted with participation of 107 radiology nurses who were working in oncology departments between 15/10/2014 and 20/12/2015. In the research, data was obtained using a 15-question questionnaire, Empathic Tendency Scale and Communication Skill Assessment Scale. Empathic Tendency Scale is a 20-item likert scale which was developed by Dökmen and tests empathizing tendencies of individuals in their daily lives. Higher scores obtained from this scale indicate higher empathizing tendencies and lower scores indicate indicates lower empathizing tendencies. Communication Skill Assessment Scale is a 25-expression likert scale which was developed by Korkut and determines how individuals evaluate their communication skills. The maximum score that can be obtained from this scale is 100, the lowest one is 0. Higher score indicates that individuals evaluate their communication skills positively. In evaluation of data, percentage estimation, Mann–Whitney U, Kruskal–Wallis and Spearman correlation tests were used.

**Results:** It was determined that, of the nurses who participated in the research; 62% were married, 42.3% graduated from vocational school of health, 56.2% had been working as a nurse for 1–6 years, 82.5% loved their occupation and 13% declared their satisfaction from the department they work in. The median Empathic Tendency Scale point of nurses was determined to be 55 (38–69), median Communication Skill Assessment Scale point was determined to be 83 (34–100). It was determined that there was a relationship between Communication Skill Assessment Scale score and Empathic Tendency Scale score (r = 0.066, p = 0.440).

**Conclusion:** In this study, it has been concluded that some characteristics of nurses such as educational level, status of loving occupation, status of being satisfied from the department that they work in, status of being satisfied from occupational life of nurses influence their communication skills and empathic tendencies.

**No conflict of interest.**

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1262  **POSTER**

Innovation in cancer care delivery

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**Background:** There is continuous need for innovation in the healthcare industry. Alongside dramatic advances in cancer medicine, there have been many recent innovations in healthcare delivery, such as telemedicine, cancer type, units, and links to community health workers. Such innovations offer the potential for dramatic improvements in quality of life for patients. What remains a great paradox is that despite these many innovations, only a small fraction of the patients who could potentially benefit from them actually are doing so. Why so?

**Material and Methods:** I would like to address fundamental flaws in healthcare. There are remarkable innovations are happening all over the world, but these value-adding innovations are not spreading. The speed and extent to which even remarkable breakthroughs have been adopted is highly variable. Habits and beliefs need to be changed first.

**Results:** Specialist care is expensive and various initiatives exist to improve efficiency and efficacy. However, little information is shared among different centers, countries and research groups. Important topics are: • Innovations in IT, communication, organizational dynamics are adapted only slowly in clinical practice and research. • Breaking down traditional specialty-based units and replace them with cross-disciplinary groups and multidisciplinary consultations and tumor boards that the dependent patient’s outcomes and satisfaction. • Communication between primary and specialist care need to be improved, to obtain benefit of screening, prevention and correct cancer follow-up. • Fluidity of medical information, digitalization and new IT tools avoid errors, toxicities and multiple consultations • Encouraging people to adopt new delivery methods sounds straightforward, but it often takes time, and a few failures along the way.

**Conclusions:** But getting people to ‘adapt with pride’ takes a shift in mindset. Adapting ideas from elsewhere requires a culture of openness, creativity and experimentation. ECO can help in creating space for (co)effectiveness compared to ipilimumab. TIL is highly personalized, however complex and requests substantial upfront investments. Therefore we aimed to provide an early and comprehensive overview of the impact of implementation of this complex adoptive cell therapy.

**Results:** cTIL and cPDC in the early stage constructive technology assessment (CTA) was conducted to identify relevant elements, regarding the dynamic nature of the new technology focusing on six aspects: (I) clinical, (II) patient-related, (III) organizational, (IV) technological, (V) economic and (VI) future perspectives. These aspects were evaluated by means of tailored semi-structured interviews with nine relevant stakeholders i.e. medical and management staff (n = 6), researchers (n = 3), staff of the production facility (n = 3) and patients (n = 4) during the pilot and start of CED phase. On an economical level an activity based costing analysis was conducted. To identify future implementation and diffusion scenario’s, issues regarding developments in research and technology, and clinical improvements were discussed with all relevant stakeholders.

**Results:** Fourteen interviews were held. We revealed on a clinical level, the TIL process, and the work routines that already changed in the pilot series: (1) lowering the dose of and (2) less interferlein-2 (IL-2) cycles, and (3) more stringent inclusion criteria. Patients’ impact of TIL therapy was described as substantial especially regarding anxiety and stress during screening, TIL-infusion and IL-2 therapy. Key organizational aspects were: training of medical and nursing staff, extremely tight logistics and communication. The key technical issues were: time-consuming quality and safety regulations according to Good Manufacturing Practices and the Dutch Medicines Act (ZGw), expensive lab-equipment and intensive training of technicians. On the economic level total costs for TIL were €67,000,− per patient, with the hospital days (€25,000,−) and production costs (€35,500,−) as important drivers. Examples of future scenarios are identification of a biomarker for TIL success and other immunotherapies, availability of competing immunotherapies and application of TIL in other tumors, especially in ovarian and renal cell carcinomas.
Conclusion: Implementing TIL therapy in advanced melanoma is feasible, but complex, especially with regard to the issues: quality and safety regulation of TIL production, implementation and intervention costs, logistics and intensive training.

No conflict of interest.

1264 POSTER
Transmural care for glioma patients and their family caregivers: utility and feasibility as perceived by professional caregivers

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Background: Patients with glioma, a type of brain tumor, face not only a poor prognosis but also debilitating symptoms and a progressive loss of capabilities. This also affects family caregivers (FC), who are grieving and addressing patients’ care needs at the same time. In the ambulatory treatment setting of glioma, needs of patients and FC easily remain under-detected. We implemented a transmural care pathway (TCP) delivered by a nurse coordinator at the hospital and a home nurse, who offer counseling to patients and FC, actively screen their problems, and offer timely and targeted support. The multidisciplinary team to plan appropriate action. Funding for this project was provided by Kom Op Tegen Kanker. The aim of this study was to evaluate utility and feasibility of the TCP as perceived by professional caregivers.

Material and Methods: Perceived clinical utility and feasibility were explored using self-constructed questionnaires, combining closed and open questions. All healthcare professionals involved in the TCP (general practitioners (GPs), hospital doctors, home and hospital nurses and the psychosocial team) were invited to participate. Closed questions were analyzed descriptively and qualitative data were screened on relevant themes.

Results: Representing 34 patients and FC included in the TCP 64 health-care professionals were invited to participate. Forty-six questionnaires were completed (response 71.90%). The large majority reported a positive impact for patients (93.48%), family caregivers (91.11%) and for their own caregiving role (79.07%). Goals and content of the TCP were clear to the majority of the respondents (91.30%). Access to and use of patient records reporting the observations and recommendations of the hospital and home nurse coordinators was adequate, except by some GPs (14.29%) and most clinical nurses (77.33%). Professionals reported the significant role of the nurse coordinators, who build trust with the care team, enabling better problem detection and care. Also, they find that they benefit from the coordinators’ assessment and referral themselves. Most professionals feel reassured that the coordinators provide highly needed care, while some GPs regret the introduction of new nursing roles. The majority believes that this type of care would be useful to other patients with cancer too. At the same time, some express concerns about the cost of the TCP.

Conclusion: Professional caregivers for glioma patients and FC perceived the TCP as a valuable care program, both for care receivers as for themselves. Further actions should focus on adequate exchange of information and on active involvement of the entire multidisciplinary team.

No conflict of interest.

1265 POSTER DISCUSSION
Communication between clinicians and patients with advanced cancer: assessing the ‘face validity’ and acceptability of a serious illness care guide to improve clinical communication

T. McClintechy1, S. Mason1, A. Roberts1, A. Coalkey2, M. Maguire2, F. Maloney2, J. Sanders2, J. Paladino2, S. Block2, J. Ellershaw2, P. Kirkbridge2, 1Marie Curie Palliative Care Institute Liverpool, University of Liverpool, Liverpool, United Kingdom; 2Clatterbridge Cancer Centre NHS Foundation Trust, Cancer Centre, Wirral, United Kingdom; 2Brigham and Women’s Hospital and Harvard T.H. Chan School of Public Health, Ariadne Labs, Boston, USA

Background: The Serious Illness Care Programme UK is being undertaken in one cancer centre in the North West. A National pilot is underway at three NHS, funded by NHS England. Re-designing the COP was necessary to assess the appropriateness of the SICG for use within the UK, and make recommendations for amendment if required.

Methods: Two groups of stakeholders reviewed the SICG: 1. Nominal Group Technique with 3 ‘expert’ groups (5 Oncologists, 5 Communication Skills experts, 4 Palliative Care specialists) to: review SICG; reach consensus; comment on applicability within the UK. 2. Cognitive Interview Technique with 6 patient and public representatives to: understand how respondents perceive and interpret prompts in the SICG; assess format, context and language.

Results: Nominal Group Technique: Consensus that the SICG provides support for clinicians to initiate difficult conversations. Minimal amendments to wording were suggested.

Cognitive Interviews:
- Overall concept valued; promoting a ‘partnership’ approach to care planning;
- Some wording/phrases too ‘formal’: e.g. ‘goals’, ‘priorities and wishes’, ‘abilities’, ‘critical’;
- Education and training key; SICG should enable flexibility;
- Phrase ‘we’re in this together’ to be removed.

No conflict of interest.

1266 POSTER
Acute oncology education: developing a pedagogy with stakeholders using online learning to enhance learning, clinical practice and patient care

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Background: The Independent Cancer Task force (2015) estimate that every two minutes someone in England will be informed they have cancer and that half the population born since 1960 will have a cancer diagnosis in their lifetime. With this increasing incidence of cancer and the wider availability of treatment options, a significant proportion of acute admissions to hospitals are accounted for by cancer patients. The aim of Acute Oncology (AO) is to provide specialist advice to improve the care and length of stay for acutely unwell cancer patients in alignment with national standards. Consequently, the management of these acutely unwell patients requires both a multidisciplinary and evidence based approach. In turn effective delivery of healthcare learning for clinicians needs to be up to date and flexible in order to meet the needs of the individual, their patients and the constantly evolving National Health Service (NHS).

Materials and Methods: A multidisciplinary specialist group consisting of clinical stakeholders from the North West of England and educationalists from The University of Liverpool (UoL) developed an online 15 credit, Masters level acute clinical oncology module. The focus was designed towards the development of AO clinical practitioners through the use of a social constructivist (Morris 2003) and student-centred (Cotton 2005) paradigm. The delivery method of the module allowed for asynchronous access to learning materials to align with the demands of clinical job roles and personal commitments. Emphasis was placed upon the development of learning materials which were inter-professional, evidence based, patient centred and ‘fit for purpose’. The module consisted of online lectures, discussion boards, quizzes, supporting articles and key documents. Salmon’s “5-Stage Model” was used to introduce the acute oncology E-learning materials to avoid overwhelming learners. Additionally learners were encouraged to reflect critically on their professional development throughout the duration of the module utilising Schön’s ‘Reflective Practitioner Model’ (1991).

Results: The module is currently commencing its 5th iteration. Thematic analysis of the discussion fora and module evaluations indicate that the resources meet the learning needs of clinicians. Comments from learners identify that they feel better informed in regards to their daily clinical practice and that knowledge gained from the module has helped develop their local AO service.

- “The module encouraged me to reflect on different aspects of my role and potential areas of development for me personally as well as for the service.” Anonymous Online Acute Oncology Student UoL 2015.

Conclusion: To date, module evaluations and thematic analysis of data indicates a positive impact on the individual learner, their local AO service and ultimately patient care.

No conflict of interest.
1267 POSTER Piloting a transmural care pathway for glioma patients and their family caregivers: an explorative study of their perceptions
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Background: Patients with a glioma, a type of brain tumor, face a poor prognosis and a progressive functional and cognitive decline. These affect not only the patient, but place high demands on family caregivers. In the context of a pilot project (2014–2016), a transmural care pathway (TCP) was offered to newly diagnosed glioma patients starting chemotherapy at the University Hospitals Leuven and their FC. The TCP includes patient and FC follow-up by a hospital and home care coordinator, aimed at early detection of their needs and planning adapted multidisciplinary care.

Material and Methods: Eligible patients and FC were at six months after the start of the TCP (coinciding with the end of treatment). Satisfaction with the main components of the TCP was explored using a self-constructed questionnaire combining closed and open-ended questions. Closed questions were analyzed descriptively and a summed score (0–36) was calculated to overall satisfaction with the TCP. Qualitative data were screened on relevant themes.

Results: Nineteen of 18 FC participated. Patients had a mean age of 54.5 years (±15.93) and the majority were male (73.7%). FC were mostly women (83.3%) and almost all were the patient’s spouse (88.9%). Composite scores of 31.2 (±5.9) for the patients and 30.4 (±5.2) for the FC indicated the high level of overall satisfaction with the TCP. Almost all patients (94.7%) find the contacts with the hospital care coordinator valuable and 89.5%, 84.2% and 77.8% feel they can share their feelings, practical concerns and professional concerns with the nurse coordinator. The scores of the FC are similar. While 84.2% of the patients rate the contacts with the home coordinator as valuable, only 66.7% of the FC do. Most patients (73.7%) and FC (72.2%) find that they can express their questions to the home nurse coordinator and respectively 57.9% of the patients and 66.6% of the FC can share their practical concerns. The majority of the patients (78.9%) and FC (88.9%) found the collaboration between their home and hospital coordinator adequate. The qualitative data indicate that, with the nurse coordinators being willing to listen and offering the time for a conversation, the TCP is a great source of support to both patients and FC. They value the coordinators’ personal attention and feedback. FC found it easy to get support without having to ask for it. Generally, the noncommittal offer of a home visit by the home coordinator was appreciated. Follow-up at home was experienced to facilitate communication by some respondents, while one FC perceived this as a barrier to communication.

Conclusion: Patients and FC experienced the contacts with the hospital and home care coordinator in the TCP highly valuable. Further research should explore preferences of patients and FC regarding home care follow-up and possible methods for FC support.

No conflict of interest.

1268 POSTER SPOTLIGHT How do cancer centres communicate clinical trials opportunities to patients on their websites?

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Background: Communicating ongoing clinical trials (OCTs) is central for cancer centres, which aim at promoting their research and informing patients about experimental treatments that are potentially accessible. Because the presentation of clinical trial opportunities may influence patients when choosing a treatment center, we analyzed how a group of institutions, recognized as uppermost the highest quality care integrated into research, communicate their OCTs.

Material and Methods: We performed a systematic exploration of the websites of 15 Comprehensive Cancer Centres (CCC) certified by the Organisation of European Cancer Institutes (April 2016). The first step was to identify on their website sections, where OCTs are presented, taking into account both national languages and English versions of the websites. Then, six parameters were evaluated to assess the online presentation of OCTs: accessibility, website localization, level of details, date of update, form of presentation, identifiability of the trial.

Results: We found that the 15 CCC (100%) mention that they are running clinical trials. Three out of 15 centres (20%) do not give any information of current trials, three (20%) give examples of OCTs, and 9 (60%) try to exhaustively list OCTs, we found that 5 of them (55%) lack instructions of research and care. However, some of these results bring substantial concern; especially the finding that many institutions present outdated or incomplete information about OCTs on their websites. Indeed, in the digital age, where cancer patients should be able to access and gather information about clinical trials to make individual health choices, failing to efficiently communicate OCTs might be detrimental to the relationship between cancer centres and their patients.

No conflict of interest.

1270 POSTER Awareness campaign about the irrational use of medicinal plants during cancer treatment

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Some plants have medicinal value when used under strictly controlled conditions, but the irrational use of medicinal plants poses serious public health problems, particularly for patients undergoing cancer treatment; they can be source of various disorders that can even cause death. The aim of the study is first to analyze the use of medicinal plants, to understand the possible consequences of the trivialization of the irrational use of these plants in patients of the National Institute of Oncology, Secondly the reduction in overall consumption of medicinal plants with the spread of information about side effects of these plants and public education. This information was transmitted in the form of awareness sessions whose design was based on a triptych information—education—communication.
This set has been created taking into account the uncontrolled use of medicinal plants and problems of the appearance of side effects of this plants. The awareness campaign included three parts: Collection of information about the use of medicinal plants by cancer patients, patient education about the consequences of irrational use of medicinal plants, and a communication part (part dedicated to answer questions of patients). This awareness was concerning patients who confirmed the use of plants (before treatment or after treatment or in conjunction with treatment). In addition, awareness materials (posters, brochures, awareness videos) are being developed with targeted messages about the irrational practice of medicinal plants and the consequences of such use and the need to respect health professionals’ advice.

Ignoring toxic risks of the use of certain plants, all over Morocco, can cause more or less serious poisoning. Our results showed the need for awareness against the irrational and excessive use of these plants.

No conflict of interest.

1271
POSTER
Incidents reported at the Cytotoxic Preparation Unit of the National Institute of Oncology, Rabat, Morocco
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Background: Over the years, the National Oncology Institute of Rabat is experiencing a considerable increase in patients staff greeted. Consequently a significant increase in cytotoxic preparation unit activity (UPC), this panel reflects a number of obstacles that hinder the fluidity of preparation circuit and thus driving a delay of patient’s hospitalization and an increase in management costs. The present work is intended to highlight the critical failures of the circuit of preparations anticancer to prioritize measures implemented to fluidity this circuit.

Material and Methods: This is a prospective, descriptive study, in a period of 10 months - from October 2014 to July 2015 - divided in 2 periods of 5 months each. According to method failure modes, effects and criticality analysis (FMEA), failure modes (incidents) detected during the first period were quantified by a criticality index (CI) calculated on the basis of the frequency, severity and the detection probability of incident. An reassessment of the incident’s CI is performed at the end of the second period, after the establishment of an improvement in quality measures.

Results and Discussion: For 70 identified incidents, we have established a criticality index to 3 parameters, whose criticality threshold is set at 12. 27.14% of the incidents are unacceptable (16 ≤ CI < 44), 15.72% of the incidents are undesirable (CI = 2) and 57.14% of the incidents are acceptable (CI < 1).

Among the critical incidents: Pocket transfer error, delay in sending preparation, preparation’s return, labeling error, prescribing error, double preparation of the same cure. The improvement measures: Training of pharmacy technicians on intrathecal preparation, automatic labeling of pockets, display in the clean room a stability referential for available specialties, a shuttle’s register between the pharmacy and nursing services. The establishment of improvement actions shows amelioration in the preparation circuit: only 5.71% of incidents remain unacceptable and 4.29% of incidents are undesirable.

Conclusion: To ensure continuity and the safety of care administered to patients with oncology, a continuous improvement of the preparation circuit, based mainly on multidisciplinary meetings and ongoing training of all UPC staff, must be required.

No conflict of interest.

1272
POSTER
Determination of level of job satisfaction and burnout of oncology nurses
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Background: This study was conducted descriptively in order to determine level of job satisfaction and burnout of oncology nurses.

Material and Methods: This research was conducted with participation of 129 nurses who were working in oncology department between 10/02/2016 and 18/05/2016. In the research, data was obtained using a 19-question questionnaire, Maslach Burnout Inventory and Minnesota Job Satisfaction Scale. Maslach Burnout Inventory is a scale which was developed by Maslach and Jackson and is comprised of three sub-dimensions: emotional exhaustion, depersonalization and personal success. Minnesota Job Satisfaction Scale is a scale which was developed by Weiss et al. and is comprised of three sub-dimensions: general satisfaction, intrinsic satisfaction and extrinsic satisfaction. In evaluation of data; percentage estimation, Mann-Whitney U, Kruskal-Wallis and Spearman correlation tests were used.

Results: It was determined that, of the nurses who participated in the research, 26.4% were married, 67.4% graduates from vocational school of health, 81.4% had been working as a nurse for 1-11 years, 85.3% loved their occupations and 68.2% declared their satisfaction from the department they work in. Median Maslach Burnout Inventory score of nurses was determined to be 41 (28-68); median scores for emotional exhaustion, depersonalization and personal success were determined to be 12 (2-30), 3 (0-13) and 25 (10-32), respectively. Median Minnesota Job Satisfaction Scale scores for general satisfaction, intrinsic satisfaction and extrinsic satisfaction of nurses were determined to be 7 (5-10), 3.4 (1.4-6) and 3.7 (1.8-4.6), respectively. It was also determined that there was a poor, negative correlation between Maslach Burnout Inventory score and Minnesota Job Satisfaction Scale score and as Maslach Burnout Inventory scores of nurses increased, their Minnesota Job Satisfaction Scale scores decreased (p<0.001).

Conclusion: In this study, it has been concluded that some socio-demographical and occupational characteristics of nurses such as age, gender, marital status, level of income, duration of working experience, working type, status of loving occupation and level of job satisfaction influence their levels of burnout and job satisfaction.

No conflict of interest.

1273
POSTER
We have managed to reduce the time patients spend in hospital by changing cancer nurse’s logistics and workflow routines
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Background: At the cancer clinic at Molde Hospital our daily tasks are to treat patients in the form of chemotherapy, manage side effects, provide counselling, palliative care, teaching and support for both patients and their relatives. Our major aim was to develop new routines that meant less time in hospital for the patient and to provide a better working environment for the cancer nurses. We also wanted to improve the workflow and communication between the laboratories, oncologists and pharmacy.

Methods: In 2014 we had to change our patient logistics and workflow routines because our patient number increased steadily, while we had the same number of resources. From 2015, all patients were offered pre-consultation with a cancer nurse, which includes consultation the day before chemotherapy treatments. During this consultation the patient’s side-effects were evaluated, blood test taken and blood results evaluated, we also update weight and nutritional status which we document in the patient’s medical file.

For this study, we registered treatment times from six different chemotherapy-agents and all patients seen during 4 weeks in 2014 and 4 weeks in 2016. To test the difference between the results from 2014 and 2016 we have used an unpaired t-test to compare the means of treatment times between the two years. Significance level was set to <0.05.

Results: During spring 2015 we had ~25 pre-consultation per month, during autumn 2015 we had 52 pre-consultation per month and in 2016 we have ~85 pre-consultation per month, which shows a steady increase in consultations. We have managed to show that the treatment time for six different chemotherapy treatments have decreased significantly by offering pre-consultation the day before chemotherapy treatment. By doing small changes to our routines we have managed to decrease the time patients have to spend in hospital by several hours.

Conclusion: Our work routines have freed up time for both the patients and nurses. We have received feedback from the patients, laboratory, pharmacy and oncologists that the new routines are brilliant and have also made their day more efficient and easier to plan.

No conflict of interest.
The GASTROS study: standardising outcome reporting in gastric cancer surgery research

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Aims: Partial or total gastrectomy is the mainstay of treatment with curative intent for gastric cancer. Surgery, however, is associated with complications and a significant impact on quality of life. Identifying the best surgical approaches for gastric cancer includes comparing and synthesizing data from surgical studies in systematic reviews and meta-analyses. This is presently difficult as there is great heterogeneity in the reporting of outcomes in surgical trials. Many trials do not report ‘quality of life’ or ‘patient-reported outcomes’.

GASTROS (Gastric Cancer Surgery Trials Reported Outcome Standardisation) is an international study which aims to develop a core outcome set (COS) – a minimum standardized group of outcomes – which should be reported by all future gastric cancer surgery trials to enable more accurate comparison of different surgical approaches. GASTROS is fully funded by the United Kingdom’s National Institute for Health Research and supported by the Medical Research Council’s Hubs for Trials Methodology Research. Here we present our study protocol.

Methods: The GASTROS study has 3 stages. Stage 1 involves undertaking a systematic review of randomized control trials to identify a ‘long-list’ of possible outcomes to include in the COS. Qualitative interviews with gastric cancer patients will be undertaken to identify any further outcomes which patients deem important. Stage 2 involves 3 rounds of a Delphi process with key stakeholders (surgeons, cancer nurse specialists and patients) to determine which outcomes to include in the COS. Stage 3 will focus on identifying the most appropriate methods of measuring these outcomes.

Anticipated Benefits: This study will enable more reliable and accurate comparison of surgical interventions for gastric cancer. It will inform the design of future gastric cancer surgical trials, clinical practice and surgical audits by developing a standardized, well-defined group of outcomes which are important and relevant to both patients and clinicians.

No conflict of interest.

Reporting of outcomes in gastric cancer surgery trials: a systematic review

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Background: Inconsistent reporting of outcomes in trials impacts negatively on the ability to produce robust evidence-based recommendations for clinical practice. This review examines the degree of variation in the reporting of outcomes described by gastric cancer surgery trials.

Methods: Systematic literature searches were undertaken to identify randomised control trials (RCTs) published between 1996 and 2016 investigating therapeutic surgical interventions for gastric cancer. Outcomes were listed verbatim, categorized into groups (outcome domains) and examined for definitions and measurement instructions.

Results: Of 2794 abstracts screened, 52 eligible publications from 32 trials (9,073 participants) were identified. A total of 756 outcomes were reported of which 660 (87 percent) were undefined. No single outcome was reported by all trials. ‘Short-term’ was the most frequently reported ‘outcome domain’ in which 252 unique terms were described. 12 trials (38 percent) classified complications according to severity, with 5 (16 percent) using a formal classification system (Clavien-Dindo or Accordion scale). A total of 33 unique terms were used to describe ‘mortality’ after surgery. Of 27 trials which described ‘short-term’ mortality, 17 (63 percent) provided one of 5 definitions. Seven trials (22 percent) described ‘patient-reported outcomes’ and 3 (9 percent) measured ‘quality of life’ after surgery.

Conclusions: Reporting of outcomes in gastric cancer surgery trials is inconsistent and lacks methodological rigour. A consensus approach to develop a minimum set of well-defined, standardised outcomes to be used by all future trials examining therapeutic surgical interventions for gastric cancer is needed. This should take into account the views of all key stakeholders including patients. The GASTROS (Gastric Cancer Surgery Trials Reported Outcome Standardisation) study aims to address this problem.

No conflict of interest.

Phase 1 study of lurbinectedin (PM01183) in combination with cisplatin (CDDP) with or without aprepitant in patients (pts) with advanced solid tumors


Background: PM01183 is a new chemical entity with promising antiproliferative activity. It inhibits transcription and blocks the nucleotide excision repair (NER) system, inducing DNA breaks and apoptosis. Cisplatin (CDDP) covalently binds to DNA interfering with transcription and replication. The mechanisms of DNA repair of PM01183 and CDDP are different; NER proficient tumor cells are sensitive to PM01183 and resistant to CDDP. This different drug sensitivity in cells with DNA repair abnormalities supports their combination. Synergy of PM01183 plus CDDP has been found in human tumor models in vitro and in vivo. Aprepitant is effective in preventing platinum induced nausea and vomiting, but inhibits cytochrome P450 (CYP) 3A4, of which PM01183 is a substrate.

Material and Methods: A phase I trial evaluated CDDP at a dose of 60 mg/m² followed by escalating doses of PM01183 every three weeks in pts with advanced solid tumors. Pts were sequentially enrolled into two arms, one with aprepitant (Arm A) as antiemetic prophylaxis and one without aprepitant (Arm B), to analyze any potential drug interaction between aprepitant and PM01183.

Results: 41 pts were treated: 17 in Arm A and 24 in Arm B. Twenty five (61%) were females; median age: 60 (range: 20–76); most frequent tumor types were ovarian (n=10, 24%), colorectal (n=5, 12%), and cervix carcinoma (n=4, 10%). Median number of prior lines was 2 (1–9). The median number of cycles given was 4 (1–18). The recommended dose (RD) of PM01183 for arms A and B was 1.1mg/m² and 1.4mg/m², respectively. Dose limiting toxicities were grade (G) 4 neutropenia and thrombocytopenia, G4 acute renal failure and G3 fatigue, at 1.7mg/m². Most common adverse events in both groups were G1–3: fatigue (76%), nausea (49%) and anorexia (44%). Hematological toxicities were short-lasting G3/4 in Arm A (n=7 in Arm A, n=12 in Arm B) and G3/4 thrombocytopenia (n=3 in Arm A, n=1 in Arm B). One pt had G4 neutropenia, thrombocytopenia and renal failure leading to death. Antitumor activity included 3 partial responses in mesothelioma, ovarian carcinoma and carcinoma of unknown primary site, and multiple disease stabilizations lasting more than 4 months (4–9.3) in ovarian carcinoma (n=5), colorectal, biliary tract, pancreas, parotid, cervix, esophageal carcinoma, mesothelioma, SCLC and melanoma. Progression free survival for the whole population was 3.6 months 95% CI (2.4–6.2). Patients treated with aprepitant had a PM01183 clearance decrease of about 50% with respect to those not treated with aprepitant.

Conclusions: The CDDP + PM01183 combination seems feasible and shows promising antitumor activity, despite the expected hematological toxicity. The RD is CDDP 60 mg/m² with PM01183 1.4 mg/m². Aprepitant interferes in the catabolism of PM01183, increasing patient exposure by 50% and its concomitant use with PM01183 is not recommended.

Conflict of interest: Corporate-sponsored Research: PharmaMar SA has sponsored this study.
A study of the factors predicting radiation exposure to contacts of Saudi patients treated with low dose radioactive iodine (I-131)

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To measure exposure levels to family members and caregivers of Saudi patients treated with 131I therapy, and household radiation exposure rate to predict different factors that can affect radiation exposure.

All patients with hyperthyroidism or cancer thyroid referred for 131I therapy on outpatient basis are included. Radiation protection procedures are given to the participant and family members in details. TLDs were dispensed to each participant of the family members living in the household. TLDs are collected at day 5 post-dispense from patients who agreed to have a home visit during which the household is inspected & level of radiation contamination of surfaces was measured.

32 patients were enrolled, with a mean age of 43.1±17.1 years. 25 patients are females. 131I therapy was given in 20 patients for cancer thyroid and for toxic goiter in the rest 12 patients, with an overall mean 131I dose of 24.1±7.5 mCi that is relatively higher in the former. The overall number of household family members of patients are 139, 77 are females & 62 males with a mean age of 29.8±17.6. The mean period of contact with the patient is 7.6±5.6 hours. The cumulative radiation exposure show that radiation exposure to all family members are below the exposure controlling level (1 mSv), with a range of 109 to 503 uSv, and a mean value of 220.9±91.9 uSv. Numerical data shows a little higher exposure rate for family members of those who receive higher dose 131I (patients with thyroid cancer) & household members who spent longer time with the patient, yet, the difference is statistically insignificant (P>0.05). Besides, no significant correlation was found between the degree of cumulative exposure of the family members to their gender, age, socioeconomic standard, educational level and residential factors. In the 21 home visits all data from bedrooms, reception areas and kitchens are below hazardous limits (0.5 uSv/h). The reported contamination of surfaces was measured. Family members of patients treated with 131I on outpatient basis have a good compliance to radiation protection instruction if given properly with a cumulative radiation exposure rate evidently beyond the radiation exposure constraints of 1 mSv. Given 131I dose, hours spent with the patient, age, gender, socioeconomic standard, educational level and residential factors have no significant correlation with the cumulative radiation exposure. The patient bathroom exhibits more radiation exposure rate, needing more strict instructions for patient bathroom use and health hygiene.

No conflict of interest.

POSTER 1328

Multiple primary cancers: an exploratory research

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Background: The majority of patients have one type of cancer. However, subsequent or coincidental occurrence of multiple cancer types may occur. We investigated the occurrence of known and unknown combinations of primary cancers in a population of patients with multiple primaries.

Methods: Patients at the Antoni van Leeuwenhoek Hospital with multiple malignancies were eligible for this study. Patients were registered at the tumor registration of The Netherlands Cancer Institute (NKI). Malignancies were categorized based on the WHO coding system (ICD-0-3 and ICD-9). The Fisher's exact test was used to test every combination of categories on correlation. A 5% significance level together with the Goeman-Solarli's method was used to evaluate outcomes.

Results: In total, 16,428 patients were identified. The average age at diagnosis of the first primary tumor was 58.6 years. Most patients had two malignancies (N=14,623), 1,622 patients had three malignancies and 183 patients had four or more malignancies. Positive correlations were found in 113 combinations of which 23 were significant. Most of these known combinations such as breast and ovarian cancer (OR = 2.40) or were expected based on location. Three known cancer syndromes are confirmed: hereditary breast and ovarian cancer syndrome, Cowden syndrome and FAP syndrome. Four combinations of tumor site categories were unexpected and cannot be explained by localization or previous (oncogenic) treatment. These categories are Breast, female with Corpus Uteri (OR = 2.0), Breast, female with ‘Cervix Uteri’ (OR = 1.29) and Hodgkin Lymphoma with ‘Liver’ (OR = 2.70).

Conclusions: This study confirms three known cancer syndromes and identifies four new combinations of cancer. These new combinations need confirmation in national registry studies.

No conflict of interest.

POSTER 1329

Long-term survivorship for patients with non-small cell lung cancer (NSCLC) treated with nivolumab (nivo): a response-based modeling approach

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Background: Long-term overall survival (OS) rates in patients with NSCLC after failure of first-line chemotherapy have historically been very low; however, recently approved immuno-oncology agents (e.g., nivo) have

of stored biosamples by Immunohistochemistry, nucleic acids isolation, quantification, electrophoresis and feedback from end users.

Results: At present we have 1475 tumor tissue (TT), 1500 normal tissue (NT), 451 buffy coat (bc), 565 plasma (pp) from 530 Breast patients; 204 TT, 192 NT, 60 BC, 82 PP from 68 kidney patients; and 6 TT, 6 NT, 1 BC, 2 PP from 2 gall bladder cancer patients with Clinic-epidemiological and follow up data.

Conclusions: Biorepository forms an integral part of translational cancer research. The aim of RGC&RC Biorepository is to accelerate cancer research. Biorepository collects, process and disseminate the highest quality biospecimens, based on the intended research use. It is a first and biggest tumor biorepository in north India. We have been involving in many research projects which results would be highly useful in biomarker discovery and translational research.

No conflict of interest.

POSTER 1327

RGCIR C Biorepository: accelerating cancer research to seek tomorrow’s cure

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Background: Cancer is a biggest challenge, humanity facing at present. It is set to become one of the most common causes of death despite the dramatic progress in detection and treatment options, due to the increased longevity and increasing control over various communicable and non-communicable diseases. Translational research in the field of cancer, is become necessary in which “bench to bedside” translational of knowledge from basic science to produce betterment of clinical practice and health decision making. For translational research, sustainable supplies of high quality human biosamples are necessary. A significant step towards to obtaining a highly annotated biosamples is to the establishment of tumor bio bank. Rajiv Gandhi Cancer Institute & research center established world class biorepository on 16 May 2013, to meet the needs of scientific community focused on cancer and allied research.

Methods: The Biorepository collects, process and store a wide array of biospecimens (tumor tissue, adjacent normal tissue, blood, plasma, serum, buffy coat, …) using validated SOPs. Clinic-epidemiological information are linked to the collected biosamples. We perform quality control
the potential to produce long-term OS gains over standard of care with docetaxel (doc). Robust estimates of mean OS are needed to understand long-term treatment benefit and to support health technology assessment. We developed a response-based modeling approach to extrapolate OS beyond observed clinical trial data for patients with NSCLC treated with nivo.

Materials and Methods: Data from three prospective clinical trials (CheckMate 003, 017, and 063) were used to estimate OS curves for patients with advanced NSCLC treated with second- or third-line nivo. Long-term OS beyond end-of-trial was projected via developed parametric curves and cancer registry data with longer follow-up, conditional on the RECIST response (complete/partial response [CR/PR], stable disease [SD], or progressive disease/non-evaluable response [PD/NE]) at two landmark points (6 or 12 months [mo]). For patients with CR/PR, three alternative nivo treatment effect durations (0, 5, or 10 years [y] beyond the trial period) were modeled. Mean OS (life expectancy) was calculated based on a weighted average of response-based curves. The goodness of fit and clinical validity of survival extrapolation were also assessed.

Table. Life expectancy estimates

<table>
<thead>
<tr>
<th>Duration of nivo effect beyond trial, yr</th>
<th>Stratification</th>
<th>All trial initiation</th>
<th>At 6 months</th>
<th>At 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>0.33−5.0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>0.18−5.0</td>
<td>1.00−3.5</td>
<td>0.50−2.5</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>0.10−2.0</td>
<td>0.50−1.0</td>
<td>1.00−2.0</td>
</tr>
</tbody>
</table>

Results: Results from the long-term OS extrapolation are summarized in the table. Life expectancy for patients treated with nivo ranged from 17 to 26 mo, compared with 9 mo for patients treated with doc (CheckMate 017 comparator). When stratified by response, life expectancy with nivo was 34–92 mo, 16–18 mo, and 8–11 mo, respectively, for patients with CR/PR, SD, and PD/NE. For comparison, a simple parametric extrapolation of trial data without stratifying by response suggested a life expectancy of 14 mo for patients treated with nivo.

Conclusions: In light of immature survival data from clinical trials, a response-based modeling approach incorporating response status at a landmark avoids potential immortal time bias and improves the estimation of life expectancy for previously treated patients with advanced NSCLC treated with nivo. These methods may improve our understanding of the clinical and economic benefits of immuno-oncology agents in metastatic cancer.

Conflict of interest: Ownership: J.R. Penrod and H. Dastani have stock ownership in Bristol-Myers Squibb. Other Substantive Relationships: J.R. Penrod, Y. Yuan, and H. Dastani are employees of Bristol-Myers Squibb; J. Thornton Snider, A. Sexton Ward, E. van Eijndhoven, and A. Chandra are employees of Precision Health Economics, which received consulting payments from Bristol-Myers Squibb for this work; A. Chandra is a professor at Harvard University, which was not involved in the research in any way, and serves on the Congressional Budget Office’s Panel of Health Advisors.

1330 POSTER
Comparative efficacy and safety of nivolumab (nivo) vs relevant treatments (txs) in pretreated non-small cell lung cancer (aNSCLC): Results from a systematic literature review (SLR) and indirect treatment comparisons (ITCs) of randomized controlled trials (RCTs)


Background: CheckMate (CM) 057, a global, randomized, open-label, phase 3 trial, evaluated the efficacy and safety of nivo vs docetaxel (doc) in second- and third-line (2L/3L) NSQ aNSCLC patients (pts). Nivo is approved in the US and the EU in pretreated aNSCLC. We present results from an ITC against relevant txs not included in CM 057. ITCs are a methodology used to provide exploratory relative efficacy and safety estimates across txs linked through common comparators.

Methods: An SLR of efficacy and safety data from RCTs (January 2000 to October 2015) assessing txs in the 2L/3L aNSCLC setting was conducted. When >1 RCT was available for a tx pair, data were summarized using a meta-analysis random effects approach. Separate ITCs were conducted (using the Bucher method) based on: (1) results from intent-to-treat (ITT) populations that included 2L/3L NSQ (and potentially SQ) pts; (2) RCTs reporting NSQ subgroup results. Overall survival (OS) data were summarized as hazard ratios (HRs) and binary data as risk ratios (RRs). Analyses were performed using both constant and time-varying HRs.

Results: RCT data were available for pemetrexed (pem), erlotinib (erl), gefitinib (ge), ramucirumab (ram) + doc, nintedanib (nin) + doc, and best supportive care (BSC). Data from CM 057 and ITC results based on ITT evidence are reported (table). Further analyses based on an updated SLR incorporating additional tx comparators are ongoing.

Table. Nivo vs comparators in 2L/3L NSQ aNSCLC based on ITT evidence from relevant RCTs

<table>
<thead>
<tr>
<th>Comparator</th>
<th>No. of RCTs</th>
<th>OS, HR (95% CI)</th>
<th>PFS, HR (95% CI)</th>
<th>ORR, RR (95% CI)</th>
<th>DTDTEs, RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doc</td>
<td>1</td>
<td>0.73 (0.59–0.89)</td>
<td>0.92 (0.77–1.11)</td>
<td>1.55 (1.00–2.37)</td>
<td>0.33 (0.18–0.59)</td>
</tr>
<tr>
<td>Pem</td>
<td>4</td>
<td>0.71 (0.56–0.91)</td>
<td>0.86 (0.66–1.11)</td>
<td>1.33 (0.80–2.22)</td>
<td>0.44 (0.10–1.87)</td>
</tr>
<tr>
<td>Erl</td>
<td>3</td>
<td>0.69 (0.53–0.91)</td>
<td>0.78 (0.60–1.02)</td>
<td>3.26 (0.67–16.00)</td>
<td>0.33 (0.08–1.34)</td>
</tr>
<tr>
<td>Ge</td>
<td>2</td>
<td>0.71 (0.57–0.89)</td>
<td>0.95 (0.76–1.19)</td>
<td>0.98 (0.54–1.77)</td>
<td>0.62 (0.23–1.80)</td>
</tr>
<tr>
<td>Ram+Doc</td>
<td>1</td>
<td>0.86 (0.66–1.09)</td>
<td>0.93 (0.59–1.49)</td>
<td>0.93 (0.59–1.49)</td>
<td>0.19 (0.05–0.78)</td>
</tr>
<tr>
<td>Nin+Doc</td>
<td>2</td>
<td>0.78 (0.61–0.98)</td>
<td>1.17 (0.92–1.48)</td>
<td>3.92 (0.25–64.32)</td>
<td>0.31 (0.17–0.58)</td>
</tr>
<tr>
<td>BSC</td>
<td>3</td>
<td>0.43 (0.30–0.62)</td>
<td>0.44 (0.32–0.60)</td>
<td>NA</td>
<td>1.07 (0.77–1.42)</td>
</tr>
</tbody>
</table>

Conclusion: ITC evidence suggests that nivo generally improved OS relative to relevant 2L/3L treatments for NSQ aNSCLC (except ram + doc; CI included no effect). CIs for ITC estimates for PFS and ORR generally included no effect. ITC estimates of DTDTEs vs active tx comparators often favored nivo and were statistically significant for chemo-containing regimens (except pem). Limitations include differences in study design and pt populations across RCTs.

Conflict of interest: Ownership: J.R. Penrod, D. Healey, and B. Korytowsky have stock ownership in Bristol-Myers Squibb. Advisory Board: M. Reck is an advisory board member for Hoffman-La Roche, Lilly, MSD, BMS, AstraZeneca, Boehringer-Ingelheim, Pfizer, and Novartis. Other Substantive Relationships: J.R. Penrod, C. Makris, D. Healey, and B. Korytowsky are employees of Bristol-Myers Squibb; A. Shrestha, K. Bognar, E. van Eijndhoven, S. Cope, and J. Vanderpuye-Orgle are employees of Precision Health Economics, which received consulting fees from BMS for this work.

1331 POSTER
Comparative efficacy and safety of nivolumab (nivo) vs relevant treatments (txs) in pretreated squamous (SQ) advanced non-small cell lung cancer (aNSCLC): Results from a systematic literature review (SLR) and indirect treatment comparisons (ITCs) of randomized controlled trials (RCTs)

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Abstract withdrawn.
FBXO39, ETS-1 and H3F3B genes as three candidates for prognosis of colorectal cancer metastasis

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Background: Colorectal cancer (CRC) is one of the prevalent cancers worldwide. Despite recent progression in diagnosis and treatment of cancer, it is still one of the health problems in the world and therefore requires further studies. Many studies have shown many biomarkers for colorectal cancer and according to the presented study we want to report three genes with capability of prognostic markers for metastatic colorectal cancer. The aim of the present study was to investigate the FBXO39, ETS-1, ETV-6, H3F3B and BMI-1 genes expression in CRC patients as potential prognostic biomarkers to evaluate the risk of metastasis in CRC patients.

Material and Methods: Thirty six patients with locally advanced colorectal cancer admitted to Hazrat-e-Rasoul Hospital, Tehran, were enrolled in this study. The expression pattern of FBXO39 and ETS-1 genes were investigated using RT-PCR and H3F3B, BMI-1 and ETV-6 genes were quantified by real-time RT-PCR in CRC tumoral and adjacent normal tissues.

Results: Our results indicated the expression pattern of FBXO39 gene was restricted to tumoral tissues and the gene expression was not observed in the adjacent normal tissues. The expression of this gene was detected in all stage-0 tumoral samples in our patients and there was a significant relation between FBXO39 gene expression and the lymph node involvement. Also there was a significant relation between ETS-1 gene expression with tumor size, lymph node involvement and metastasis. Our studies on H3F3B gene indicated that this gene significantly overexpressed in colorectal cancer tissue compare to adjacent normal tissue and there was a significant association between the expression level of H3F3B gene with the stage of colorectal cancer and lymph node involvement. Also according to our studies there is no association between BMI-1 and ETV-6 genes with colorectal cancer.

Conclusion: Since the involvement of lymph nodes is an introduction to the occurrence of metastasis in patients, it is more possible that the expression of FBXO39, ETS-1 and H3F3B genes are an alarm for the occurrence of metastasis and as three candidate genes for prognostic marker for metastasis of colorectal cancer patients.

No conflict of interest.

The reporting of confounding variables in gastric cancer surgery trials

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Background: Surgery is the primary treatment for gastric cancer, however it is associated with a risk of significant short and long-term complications. Trials examining therapeutic surgical interventions aim to reduce these risks and improve long-term survival for patients. Understanding the external validity of these trials is essential prior to implementing new interventions into clinical practice. This can only be achieved if there is a clear understanding of the impact confounding variables may have on the outcomes reported. The aim of this study was to examine the reporting of confounding variables described in gastric cancer surgery trials.

Material and Methods: Systematic literature searches of English-language RCTs examining therapeutic surgical interventions between 1996 and 2016 were undertaken. All variables not related to the interventions being examined (e.g. patient, treatment and tumour characteristics) were recorded independently by two researchers.

Results: 50 publications were identified from 32 RCTs which had recruited a total of 8673 patients. In total, 144 unique potentially confounding variables were reported.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of publications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient factors</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>50 (100%)</td>
</tr>
<tr>
<td>Sex</td>
<td>50 (100%)</td>
</tr>
<tr>
<td>BMI</td>
<td>16 (32%)</td>
</tr>
<tr>
<td>Weight</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Height</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>ASA</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>11 (22%)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td>6 (12%)</td>
</tr>
<tr>
<td><strong>Treatment factors</strong></td>
<td></td>
</tr>
<tr>
<td>Previous chemotherapy</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>Previous radiotherapy</td>
<td>16 (32%)</td>
</tr>
<tr>
<td><strong>Tumour factors</strong></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>20 (40%)</td>
</tr>
<tr>
<td>Depth</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Location (anatomical)</td>
<td>28 (56%)</td>
</tr>
<tr>
<td>Location (by classification)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Histological type</td>
<td>19 (38%)</td>
</tr>
<tr>
<td>Grade</td>
<td>27 (54%)</td>
</tr>
<tr>
<td>TMN</td>
<td>21 (42%)</td>
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</tbody>
</table>

ECOG PS, Eastern Cooperative Oncology Group Performance Status.

While patients’ age and gender were included in all publications, there were considerable variations in the reporting of other variables. Twenty-one publications (42%) stated the patients’ BMI or weight. Seventeen publications (34%) provided information on the patients’ general health (ASA 10%, co-morbidities 22%, and performance status 12%). Fourteen and sixteen publications (28% and 32%) stated if patients had chemotherapy or radiotherapy previously for any malignancy respectively.
Among the publications that provided this information, no patients were given neo-adjuvant chemotherapy. Twenty-one publications (42%) reported if adjuvant chemotherapy was given to patients. Tumour size and depth were reported in twenty (40%) and nine (18%) publications, respectively. Twenty-nine publications (58%) specified the location of the tumour. Tumour histological type was reported in eighteen publications (36%). Tumour grade or TNM stage were reported in twenty-seven publications (54%).

Conclusions: The reporting of baseline data in gastric cancer surgery trials is markedly inconsistent. A consensus-based approach is required.

Results: A total of 278 studies were included in the systematic review. Of these, 246 (89%) describe clinical benefit in cancer randomized controlled trials (RCTs). To respond to this problem, the Setting International Standards for the Analysis of HRQL data in Cancer RCTs (SISAQOL) initiative was established.

Methods: We present the steps undertaken to form the SISAQOL initiative: an open discussion among various stakeholders regarding current needs, and agreement on a standardization and improvement plan. The SISAQOL Consortium is composed of over 40 leading international experts including: HRQL researchers and statisticians, key individuals from various international oncology and medical societies, pharmaceutical industry, regulatory and advisory bodies (US Food and Drug Administration, European Medicines Agency, Health Canada, Institute for Quality and Efficiency in Health Care), and academic societies (International Society for Pharmacoeconomics and Outcomes Research, International Society for Quality of Life Research, Multinational Association of Supportive Care in Cancer), cancer institutes (National Cancer Institute, Mayo Clinic, EORTC) and patient organizations (International Brain Tumour Alliance). We met in 2006 to bring together the various stakeholders and discuss solutions. A workplan was developed to a) examine current statistical methods and challenges in interpreting HRQL in cancer RCTs, and b) consider general methodological guidelines proposed by different regulatory bodies and academic societies. These reports will be collated and a formal consensus will be set-up to deliberate on how to resolve these issues.

Conclusions: RCTs cost time, money and effort; and patients, in the interest of improving their situations and helping others, voluntarily give their time to complete HRQL questionnaires for these trials. Therefore, the data from these trials must be exploited to the full, with appropriate and standardized statistical analyses. The aim of SISAQOL is to develop clear, internationally standards for the analysis of HRQL data in cancer RCTs. We anticipate that the availability of guidelines will lead to more reliable findings, stemming from use of higher quality statistical methods.

Conflict of interest: Other Substantive Relationships: An unrestricted education grant was received from Boehringer Ingelheim GmbH to initiate this work.
coefficient 0.988), high sensitivity 9.28 μA.mL⁻¹ cm⁻² with acceptable lower detection limit of 0.21 μA.mL⁻¹. The obtained results show good correlation with gold standard technique for protein biomarker detection i.e. enzyme linked immunosorbent assay (ELISA).

Conclusions: Probes are considered to be attractive and cost-effective technique that can be used for detection of oral cancer. We have fabricated a label free, non-invasive and efficient biosensor, which can be used in the detection of oral cancer.

No conflict of interest.

1335 Systematic registration of outcome in a radiotherapy institute

L. Boersma¹, I. Nijsten ¹, M. Brouns ¹, A. Dekker ¹, K. Smits ¹. ¹MAASTRO clinic, Radiotherapy, Maastricht, Netherlands

Background: Over the last years there has been an increasing focus on registration and national audits of quality indicators, since it is assumed that insight in the quality of a certain treatment will increase quality. Two important indicators of quality of radiotherapy (RT) are (1) the incidence and severity of RT-related acute and late side-effects, and (2) the incidence of locoregional control. However, in many RT institutes, patients receive their follow-up after RT in the referring hospitals, thereby hampering the recording of outcome by radiation-oncologists (RTOs). Therefore, the aim of the current project was to set up a systematic tumor and toxicity outcome data collection, to be presented in dashboards. In the present part of the project we first focussed on obtaining data on radiation-induced toxicity.

Material and Methods: For RT-induced toxicity, we discriminate Patient Reported Outcome Measures (PROMs) and Doctor Reported Outcome Measures (DROMs), the latter referring to medical sources in its broadest sense. During intake, baseline patient variables, such as age, sex, and WHO-score, are recorded in the electronic medical record (EMR). Acute toxicity is scored in the EMR during and directly after RT according to CTC-AE4 (DROMs). The PROM-questionnaires consist of validated questionnaires (acc. to the guidelines of the Dutch Federation for University Hospitals and the ICHOM [1] datasets) in combination with some additional questions on specific RT toxicity, according to CTC-AE4 criteria. Baseline questionnaires are personally handed to the patient during intake, follow-up PROMs are sent to the patient by regular mail at 3 weeks, 3 and 6 months, and 1 year after RT, and thereafter annually for at least 5 years. Returned PROMs are digitalized and linked to the EMR and to our data warehouse. From the data warehouse, the toxicities are presented to the tumor workgroups using dashboards. DROMs with scores of Grade 3 are immediately sent to the treating RTO, to ensure adequate treatment of the patient.

Results: Acute DROMs are being recorded for all tumor groups; late DROMs are systematically being recorded for Gynaecology, Urology, and Head and Neck Cancer. PROM questionnaires for both acute and late toxicity are sent out for nine tumour groups: Gynaecology, Urology, Gastro-Intestinal (lower), Gastro-Intestinal (upper), Breast, Lung, Head and Neck, Urology, Palliation. Preliminary analyses of the response rates showed promising figures: for Head and Neck patients 84% of the baseline PROM questionnaires were returned.

Conclusions: We have been able to set up a robust system to acquire data on acute and late RT-induced toxicity, and to present this in interactive dashboards. Further effort will be put in adding data on case-mix and treatment-mix, to allow proper benchmarking.

References

No conflict of interest.

1336 Health-related quality of life in adolescent and young adult (AYA) cancer patients: a longitudinal study

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Background: The aim of this study was to examine changes in health-related quality of life (HRQoL) and its predictors over the first two years after initial cancer diagnosis in adolescent and young adult (AYA) cancer patients.

Material and Methods: A multicenter, longitudinal, prospective study was conducted among a diverse sample of AYA cancer patients aged 14–39 years. One hundred seventy-six patients completed a self-report measure of HRQoL (Short-Form-36 [SF-36]) within the first four months of diagnosis and again 12 and 24 months later. Linear mixed models with random intercept and slope estimated changes in QoL.

Results: Recently diagnosed AYA cancer patients had significantly worse physical component scores (PCS: 38.7 vs. 52.8; p <0.001) and mental component scores (MCS: 42.9 vs. 48.9; p=0.001) when compared to population norms. Significant improvements in PCS and MCS from baseline to 24-month follow-up were observed; however, these increases were largest during the first 12 months. At 24-month follow-up, AYAs still had significantly lower PCS (48.0 vs. 52.8; p <0.001) and MCS (45.8 vs. 48.9; p=0.002) when compared to population norms. Multivariate analyses revealed that improvements in PCS and MCS were primarily a function of being off-treatment and being involved in school or work. PCS but not MCS was worse for AYAs diagnosed with cancers with poorer prognoses, suggesting a substantial impact even in the context of malignancies with relatively good prognosis.

Conclusion: Although improved over time, HRQoL was still compromised 24 months after primary diagnosis. Given relatively little observed difference in HRQoL in AYAs compared to adults, AYAs may benefit from (psychosocial) support interventions administered during the second year following diagnosis.

No conflict of interest.

1337 Translation and validation of PREM-questionnaire

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Background: Several questionnaires to measure patient reported outcomes (PROMs) exist within the health care system and have become an increasingly popular source to gather information on various aspects of the patient condition. A number of these, mainly Patient Reported Outcome Measures (PROM) questionnaires, are used in clinical trials but as well as in routine care such as EORTC-QOL. While the health care system gains significant knowledge of e.g. patients’ symptoms and QOL from extracting information, little is known, however, on how patients perceive filling out these questionnaires. To get more knowledge on patient perception of PROMs, a standardized Danish Patient Reported Experience Measures (PREM) questionnaire was needed. Despite thorough research, it was not possible to find a Danish PREM. This study describes the translation into Danish and validation among Danish patients of an American PREM questionnaire form ‘Patient Feedback Form’. The form consists of 13 questions.

Material and Methods: Having gained permission from the original developer of the form, Claire Snyder Associate Professor of Medicine at Johns Hopkins School of Medicine, the first phase of the process began. The translation and cultural adaption process was carried out according to existing guidelines with forward and backward translation, consensus meetings and cognitive interviewing. Hereafter, cognitive interviewing with seven cancer patients (46–86 years old, 6 men and 2 women) and six elder care patients (19–51 years) was done to make sure that the questions were easy to understand and made sense in a Danish population. Phase 2 was the qualitative validation where 100–150 cancer patients were asked to fill out the questionnaire after having responded to a PROM questionnaire to make sure that none of the questions went against the general context.

Result: There were only minor disagreements in the translation process and the reconciliation went smoothly. In a few places, however, it was difficult to find just the right expression, despite qualified suggestions from the translators. Through the qualitative validation process, the right wording was found. The semantics of one of the questions was altered slightly as a result of the cognitive interviewing. The results from the quantitative validation will be analyzed in October 2016 using key psychometric parameters.

Conclusion: Originally, the form was intended to be used in a clinical trial where cancer patients evaluate how they experience filling out an electronic questionnaire on immune-related adverse events (A PREM-tool). However, it is expected that the feedback form, due to its generic nature, can be used in many other areas within the health care system as well.

No conflict of interest.
1338 POSTER Is there a role for antithrombotic prophylaxis in oncologic patients who undergo central venous access placement? M. Cefalì1, V. Fregoni2, G. Piacentini1, C. Sansi1, L. Gervaso1, L. Pavesi2, A. Riccardi2. 1Università degli Studi di Pavia – Fondazione S. Maugeri, Oncologia, Pavia, Italy; 2Fondazione S. Maugeri, Oncologia, Pavia, Italy

Background: Insertion of a PICC (Peripherally Inserted Central Catheter) is common practice in oncology; while it relevantly increases the patient's quality of life, it can also induce complications, mainly infection and thrombosis. However, the opportunity and potential modalities of antithrombotic prophylaxis remain controversial.

Materials and Methods: Data on 210 patients with a history of neoplasia who underwent positioning of a PICC or CVC (central venous catheter) between 2012 and 2014 were extracted from our institution's database. A statistical analysis was carried out; we investigated the association between LMWH (Low Molecula Weight Heparin) prophylaxis and thrombotic events, as well as between thrombotic events and supposed risk factors such as age, sex, smoking status, venous access site (i.e. basilic vein versus deeper veins). Time to thrombotic complication and the association between thrombosis and D-dimer levels were also studied.

Results: 48 out of 210 patients underwent LMWH prophylaxis for reasons unrelated to catheter placement. 23 upper limb thrombotic events were registered, 6 in LMWH treated patients and 17 in non-treated patients (i.e. 10.5% versus 12.5%, p-value 0.89, no statistical significance). Elevated levels of D-dimer were detected in 22% of patients who had thrombosis and 11% of patients who did not (p-value 0.12, no statistical significance). Mean time to thrombotic complication was 16 days in all patients; LMWH prophylaxis appeared to delay the inaccuracy of thrombosis (median of 16 days in non-treated patients versus 54 days in treated patients; p-value 0.83, non-significant). The association between our supposed risk factors and thrombosis did not emerge as statistically significant, although occurrence was higher in at-risk categories. It was also observed that almost all patients were receiving multi-agent chemotherapy at the time when thrombosis occurred.

Conclusions: While routine prophylaxis is not yet recommended, a further prospective randomized study is warranted to investigate the usefulness of LMWH prophylaxis during the highest-risk window (12 hours before to 15–20 days after insertion) versus repeated higher limb ultrasound in the same timeframe, aimed at early thrombus detection.

No conflict of interest.

1339 POSTER Asymptomatic versus symptomatic pulmonary embolism in oncologic patients: Does clinical presentation influence outcome? G. Piacentini1, V. Fregoni2, L. Gervaso1, C. Sansi1, M. Cefalì1, L. Pavesi2, A. Riccardi2. 1Università degli Studi di Pavia – Fondazione S. Maugeri, Oncologia, Pavia, Italy; 2Fondazione S. Maugeri, Oncologia, Pavia, Italy

BACKGROUND: Incidentally diagnosed pulmonary embolism (IPE) in cancer patients is a growing problem. Due to the improvements in the quality of computed tomography (CT) examinations, pulmonary embolism (PE) is increasingly detected incidentally during routine cancer staging. Although available data show a similar outcome for symptomatic and asymptomatic PE, the most appropriate treatment is still debated. Determining the clinical significance of these incidental findings on the prognosis of cancer patients could be of relevance.

Materials and Methods: We conducted a retrospective cohort study of cancer patients at Oncology Unit of IRCCS Fondazione Maugeri of Pavia (Italy) from 2008 to 2014. Cross-checking data from Hospital discharge register and radiologic medical reports, we collected 758 cases. Inclusion criteria were: age >18 years, personal history of cancer, objectively proven PE (CT scan or ventilation/perfusion scan). Multiple clinical and demographic variables and mortality outcomes were collected.

Results: Between January 2008 and December 2014, 124 cancer patients with established PE were identified; 32 (26%) were symptomatic at diagnosis, while 92 cases (74%) were incidentally diagnosed. In this second group, the embolism was found at baseline staging (18%) or during restaging after therapy (82%). The cumulative incidence was found to be 2.9% in the IPE group and 0.9% in the other one. PE occurred more frequently in advanced-stage disease (stage IV) than in all other stages (respectively 78% vs 22% in both groups), and in patients given active treatment (chemotherapy and/or hormone therapy) in the last 30 days (67% vs 33% in IPE group; 78% vs 22% in symptomatic group). Low molecular weight heparin (LMWH) was the treatment of choice and was administered to 94% of symptomatic patients but only to 72% of asymptomatic cases.

As regards the outcome, one month-mortality was approximately double in symptomatic PE vs IPE (18.7% vs 9.7%); the cause of death was the embolism in one third of IPE patients and in half of the symptomatic patients. On the other hand one year mortality was about 50% in both groups.

Conclusion: Our study confirmed the epidemiological and prognostic importance of incidental pulmonary embolism in cancer patients. Cumulative mortality in asymptomatic vs symptomatic event was similar, suggesting that the clinical manifestation does not modify prognosis. The only difference in terms of outcome concerns the short-term mortality (<1 month), which was almost double in the symptomatic group, maybe related to acute cardiac dysfunction.

At present, there is still no agreement on the most appropriate treatment of PE. Our findings suggest that treating IPE in the same way as symptomatic embolism is currently the most appropriate approach. Given the magnitude of the problem, further studies are encouraged.

No conflict of interest.

1340 POSTER Tolerability and efficacy of rolapitant for prevention of chemotherapy induced nausea and vomiting: a systematic review and meta-analysis of active-controlled trials H. Ahmed1, A. Hammad2, M. Zidan3, M. Saleh4, A. Negida2. 1Faculty of Medicine- Zagazig University- Zagazig- El-Sharky- Egypt, Faculty of Medicine, Zagazig, Egypt; 2Faculty of Medicine- Cairo University- Cairo- Egypt, Faculty of Medicine, Cairo, Egypt; 3Faculty of Medicine- Tanta University- Egypt, Faculty of Medicine, Tanta, Egypt; 4Faculty of Medicine- Al Azhar University- Cairo- Egypt, Faculty of Medicine, Cairo, Egypt; 5School of Medicine- Liverpool University- UK, School of Medicine, Liverpool, United Kingdom

Background: Chemotherapy-induced nausea and vomiting (CINV) is a common side-effect of many antineoplastic regimens. Many studies evaluated the safety and efficacy of neurokinin-1 receptor antagonist rolapitant, in combination with a serotonin (5-HT3) receptor antagonist and dexamethasone for the prevention of CINV. The aim of this study is to synthesize the evidence for safety and efficacy of rolapitant in combination with other antiemetic for prevention of chemotherapy-induced nausea and vomiting.

Material and Methods: A computer literature search of PubMed, SCOPUS, EMBASE, Web of science, and Cochrane CENTRAL has been conducted using relevant keywords. Studies were screened for eligibility and data were extracted. The efficacy endpoints (complete response) and the safety endpoints (all other endpoints) were pooled in the final analysis. Raloxifene 180mg in combination with a 5-HT3 receptor antagonist and dexamethasone was statistically superior to active control (RR 1.06, 95% CI [1.03,1.1]); RR 1.19, 95% CI [1.13,1.25]) in term of CR in the acute phase (RR 1.06, 95% CI [1.03,1.1]); CR in the delayed phase (RR 1.19, 95% CI [1.13,1.25]). Rates of no emesis were significantly higher with rolapitant 180 mg group versus active control group in the overall, acute, and delayed phases (RR 1.07, 95% CI [1.04,1.1], RR 1.17, 95% CI [1.12,1.25]), retrospectively. Moreover, rates of complete protection were significantly higher with rolapitant 180 mg group than active control group in the overall, acute, and delayed phases (RR 1.18, 95% CI [1.11,1.28], RR 1.05, 95% CI [1.01,1.07], RR 1.17, 95% CI [1.11,1.24]), retrospectively. The incidence of adverse events was similar in rolapitant and control groups, with the most frequently reported treatment-related emergent adverse events being fatigue, constipation, and headache.

Conclusion: Raloxifene combination with a 5-HT3 receptor antagonist and dexamethasone is well tolerated and shows superiority over active control for the prevention of CINV. No conflict of interest.

1341 POSTER Burkitt lymphoma in Northern Tunisia: Incidence, trend and projection H. Ben Khadrha1, M. Hsairi1. 1Tunisian Cancer Institute, Epidemiology department, Tunisia, Tunisia

Background: First discovered amongst children in Africa, Burkitt lymphoma (BL) is a rare aggressive B cell non-Hodgkin lymphoma more frequent in developing countries than in developed regions; its highest incidence was recorded in Eastern Africa. The clinical-epidemiological characteristics of Burkitt Lymphoma led to distinguish three forms of this malignancy; the endemic form, the sporadic form and the HIV associated
form. The risk factors for BL are still poorly understood, the worldwide difference of its incidence can provide a basis on which hypotheses about its etiopathogenic mechanism could be constructed. In Tunisia the latest data on BL are from the year 2006. The aim of this study was to give an updated trend of lymphoma epidemiology in Northern Tunisia.

**Materials and Methods:** This study used Northern-Tunisia Cancer Registry (NTCR) data. Cases of BL were coded according to the World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues. Cancer incidences were calculated from 1997 to 2009, as cases per 100,000 persons-year. Age standardization incidence rates (ASIR) were calculated on the basis of WHO population standard. Annual percentage change (APC) was estimated by using the Joinpoint Regression Analysis program. To perform incidence projection for 2024, Age-Period-Cohort model was used assuming a Poisson distribution for the counts.

**Results:** Between 1997 and 2009, 109 cases of BL were collected by the NTCR. The median age was 9 years (Interquartile range: 12 years). Most cases occurred among males (70.6%). At the time of the diagnosis, 22% of BL cases were localized in the lymph nodes. The age-standardized BL rate described a downward trend with a non significant APC; it went from 0.14 cases per 100,000 persons-year in 1997 to 0.12 cases per 100,000 persons-year in 2009. The male-to-female AR was 0.96 in 1997 to 12.9 in 1998 then fell to 2.1 in 2009. The BL age standardized rate among males decreased between 1997 and 2009, which was also the case among females. The APC for both genders was not significant. Under the age of fifteen, the AR of BL decreased significantly by 7.2% (95% 1.2%) it went from 0.14 cases per 100,000 persons-year in 1997 to 0.17 cases per 100,000 persons-year in 2009. The projection estimated that BL incidence would continue to decrease to reach 0.10 cases per 100,000 persons-year by the year 2024.

**Conclusions:** In our country the BL affects males more than females and occurs mainly amongst population under the age of fifteen. The downward trend of this lymphoma, observed during the study period, independently from gender or age, may be subsequent to an eventual change in the trend of the risk factors of BL, thus, further investigations should be conducted toward this hypothesis.

**No conflict of interest.**

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**1342 POSTER DISCUSSION**

**Treatment patterns and clinical outcomes in ER+ HER2− metastatic breast cancer in German real world settings**

D. Mitra1, S. Kusoryski2, J. Kaye3, N. Harbeck4, J. Pfister- Inc, Global Outcomes & Evidence, New York City, USA; 2Rti Health Solutions, Health Economics, Research Triangle Park, USA; 3Rti Health Solutions, Epidemiology, Waltham, USA; 4University of Munich LMU, Breast Center, Munich, Germany

**Background:** To examine treatment patterns and clinical outcomes among postmenopausal patients with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2−) metastatic breast cancer (MBC) in Germany real-world settings registries from all 16 federal states. Material and Methods: A retrospective review of medical records was conducted in Germany as part of a larger multi-country study. Records were abstracted for ER+/HER2− MBC patients who received at least two lines of metastatic disease between January 1, 2008 and March 1, 2014. Patient and clinical characteristics, treatment patterns, and time to progression (TTP) by treatment line were assessed.

**Results:** Medical records were reviewed for 251 patients by 58 physicians across Germany. Patients’ mean age was 63 years at metastatic diagnosis, and over 96% were white. Bone was the most common site of metastasis (69%), followed by liver (51%), and lung/pleura (47%); Majority had visceral disease (73%) and were ECOG performance status 0 or 1 (86%). In the 1st line MBC setting, 50% of patients received endocrine therapy (ET) alone; 27% received chemotherapy (CT) alone, and the remainder received both (in combination [18%] or CT followed by ET [6%]). Anastrozole (24%), letrozole (22%) and paclitaxel (19%) were the 3 most common 1st line (in combination [18%] or CT followed by ET [6%]). Anastrazole (24%), letrozole (22%) and paclitaxel (19%) were the 3 most common 1st line agents. Nearly 80% of patients progressed on 1st line with a median TTP of 8.2 months (9 months for those on ET alone; 5.4 months for those receiving CT alone). Among those on ET alone, 84% discontinued treatment due to disease progression, of which nearly 100% due to endocrine therapy resistance as reported by the physician. In the 2nd line, 51% received ET alone, 35% received CT alone, 10% received combination ET and CT, while 4% received CT followed by ET. The most common 2nd line agents were exemestane (20%), fulvestrant (18%), and paclitaxel (14%). Progression on 2nd line treatment was seen in 87% of patients with a median TTP of 6.0 months (7.3 months for ET alone, 4 months for CT alone). 73% of patients on ET alone discontinued due to disease progression, of which 96% were attributed to endocrine resistance by the physicians.

**Conclusions:** In ER+ HER2− MBC, more than 50% of patients received ET alone in both first and second line of therapy. Median TTP on ET is well below 1 year (9 months for first line, 7 months for second line), with TTP for those on CT alone under 6 months for both first and second line. Note that a comparison of outcomes between treatment groups (ET vs chemotherapy) may be confounded by severity in an observational study (i.e., “channeling” of patients with a worse prognosis to receive chemotherapy rather than ET). Endocrine treatment discontinuation was attributed to endocrine resistance by physicians in the majority of patients.

**Conflict of interest: Corporate-sponsored Research:** This study is sponsored by Pfizer Inc.

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**1343 POSTER**

**Prevalence of cancer in Colombia: What kind of methodologies has been used to obtain prevalence?**

O. Valencia1, P. Sanchez1, L. Acuña1, D. Uribe1. 1Cuenta de Alto Costo, Knowledge Management, Bogota, Colombia

**Background:** Prevalence is an important indicator of burden disease and influences decision making for health policies and the health system function. The aim of this study is to revise different methodologies to obtain prevalence of cancer in Colombia.

**Material and Methods:** In this cross-sectional study, the information comes from the integrated data base of Cancer, which the Colombian government was promoting entities provided to the High Cost Diseases Fund (Cuenta de Alto Costo CAC). A described analysis was conducted and the observed prevalence (OP) was determinate by the report of adult patients alive with cancer Diagnosis attended before January 1st 2014 from 32 departments of Colombia; the diagnosis could be obtained in this period or before. The estimated prevalence (EP) was extracted from GLOBOCAN population facts and sheets 2012; 5-year EP was calculated using incidence and survival rates. STATA V13 Software has been used for statistics analysis.

**Results:** A total of 172,879 records were analyzed, 97% of them were adults (169,166 records). The OP is 479 cases per 100,000 population in this lapse; while EP 5 years is 501.2 per 100,000 population. The number of estimates cases of cancer in 2012 by GLOBOCAN is higher than observed cases in 2014 by CAC. EP 5 years is an estimation based on Incidence and survival dates; the incidence information comes from four Colombian cities, this data has been high quality classified, in the lapse 2003–2007; and survival for South American countries was estimated from the average of Asian countries, alongside the registries in Uganda and Zimbabwe. OP comes of the CAC data base that contain registries from all insurance companies; they report the records interested in obtaining economic resources from the mechanism that distributes economic resources, it is regulated for the CAC and is supervised by the Colombian Ministry of health.

**Conclusions:** The OP is a remarkable difference in the prevalence because the methodologies to collect the information, dates treatment are not comparable. For making decisions in a national level to provide high quality services, is important to have recent and robust data of patients with cancer. The OP obtained from the CAC offers an opportunity to have more information with cancer registries observed in one year from the 32 departments of the country, and in a future; could provide better results with a following of more years to evaluate the management of insurance companies.

**No conflict of interest.**

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**1344 POSTER**

**Cancer incidence in Colombia acquired immunodeficiency syndrome**

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**Background:** To identify cancers that occur at higher rate in patients with acquired immunodeficiency syndrome(AIDS) in Colombia.

**Methods:** Given the registries compiled by the Colombian Fund of High Cost Diseases (CFHC), we compared the National Cancer Registry with the HIV Administrative Registry to identify the patients that had been diagnosed with both Cancer and HIV. From the 525 cases found, we considered only two registries that were diagnosed with Cancer during the years before or after being diagnosed with AIDS, remaining with a final sample of individuals of 291, aged from 17 to 84 years old, diagnosed with AIDS between 1998 and 2015. For those individuals, using Stata Software, we computed and analyzed the Standardized Incidence Ratios (SIRs) to determine the Cancer Risk.

**Results:** Results suggest, that patients with AIDS display an elevated SIRs of developing specific types of cancer such as Kaposi’s sarcoma (male and female, 143.1); No Hodgkin lymphoma (male and female, 12.05);
Hodgkin’s disease (male and female, 11.42); biliary tract, pancreas, and anus cancer (male and female, 2.35); Brain and eye neoplasm (male and female, 1.96); Cervical cancer (female 3.98).

Conclusions: The study concludes that there is an increased cancer odds ratio in AIDS population. This administrative registry assesses cancer risk in population with HIV, and hence provides evidence to argue that immunosuppression related to AIDS, increases furthermore the odds to develop specific types of cancers.

No conflict of interest.

1345 POSTER
Diffuse large B-cell lymphoma in the Northern Tunisian population: Incidence, trend and projection
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Background: Diffuse Large B-Cell Lymphoma (DLBCL) is the more common histological subtype of non Hodgkin lymphoma worldwide accounting approximately for 40% of all cases. Non Hodgkin lymphoma data showed an increase in the incidence more marked in developed countries than in developing ones in which data about DLBCL are limited. Further epidemiological studies about this malignancy are needed in order to point out the global burden. The aim of this study was to give the latest data about DLBCL incidence and its trend in Northern Tunisia.

Methods: This study used Northern-Tunisia Cancer Registry (NTCR) data. The registry collects the data from 11 out of 24 Tunisian governorates. Cases of DLBCL were coded according to the World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues. After eliminating the invalid data, cancer incidences were calculated, for 5-year age groups and for each year from 1997 to 2009, as cases per 100,000 persons-year. Age standardization incidence rates (ASR) were calculated on the basis of WHO population standard. To analyze the trend of DLBCL incidence over the total study period, annual percentage change (APC) was estimated by using the Joinpoint Regression Analysis program, version 4.2.2.1. To perform an incidence projection for 2024, we extrapolated the calculated incidences; Age-Period-Cohort model was used assuming a Poisson distribution for the counts.

Results: A total of 954 cases of DLBCL Lymphoma were registered in Northern Tunisia between 1997 and 2009. The mean age was 55±16.5. Most cases occurred in males (58.4%). The DLBCL primary site was the lymph nodes in 32% of the cases. The DLBCL ASR significantly increased between 1997 and 2009 with an APC of 6.6% (95% CI: [0.5%,13.1%]), it went from 1.6 cases per 100,000 persons year in 1997 to 3.2 cases per 100,000 persons year in 2009. Within this period two patterns could be described; between 1997 and 2004 the ASR decreased with a non significant APC, then, from 2004 to 2009, the ASR of the DLBCL increased with a significant APC of 29.5% (95% CI: [14.1%, 47.2%]). The estimated number of DLBCL cases is expected to reach 244 by the year 2024 with an ASR of 6.47 cases per 100,000 persons-year.

Conclusion: As observed in developed countries, the DLBCL burden is not negligible in developing regions especially in Tunisia. This study supplemented data needed to provide an estimable access to The DLBCL different treatments options which requires the association of the national health system efforts with those of the international organizations.

No conflict of interest.

1346 POSTER
Cancer in the elderly in Northern Tunisia: Incidence and trends
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Background: Due to the increasing of life expectancy in Tunisia and in other developing countries, the proportion of elderly people (aged 65 years and over) is also increasing. Thus, many diseases affecting elderly persons will become more prevalent, which is the case of malignancies. This study aimed to fill in the gap in the available data of cancers incidences and its trends amongst the elderly in the Northern-Tunisian population, with a highlight on two different sites in both gender.

Material and Methods: This study used Northern-Tunisia Cancer Registry (NTCR) data. Cancer incidences were calculated from 1994 to 2009, as cases per 100,000 persons-year. Age standardization incidence rates (ASR) were calculated on the basis of WHO population standard. To analyze the trend of the different cancers incidence over the total study period, annual percentage change (APC) was estimated by using the Jointpoint Regression Analysis program, version 4.2.2.1.

Results: Between 2007 and 2009, the number of cancer cases, all sites included, in Northern Tunisia amongst elderly people was equal to 6845 which represented 38.8% of all cancer cases, all ages included. The ASR for the age 65 years and over in both gender, was 631.22 cases per 100,000 persons-year all sites included. Incidence trend for both gender, amongst elderly people, all sites included, between 1994 and 2009, was in overall almost stable, with a non significant annual percentage change (APC) of -0.06%.

Conclusion: Between 2007 and 2009, the ASR of prostate cancer amongst elderly men was 121 cases per 100,000 persons-year. Prostate cancer incidence trend analysis between 1994 and 2004, among the same population, showed a minor but a non significant increase in the incidence with an APC of 1.14%. As for bladder cancer, the ASR amongst elderly men was 139.9 cases per 100,000 persons-year with a non significant increase of the incidence trend of this cancer between 1994 and 2009. Regarding female cancer, the ASR of breast cancer between 2007 and 2009 amongst elderly women, was 86.8 cases per 100,000 persons-year with an overall significant increase in the incidence between 1994 and 2009; the APC was 2.2% (95% CI: [0.8%, 3.6%]). The ASR of cervix cancer between 2007 and 2009 amongst elderly women was 17.3 cases per 100,000 persons-year. The analysis of cervix cancer trend between 2004 and 2009 showed an non significant change in the incidence.

Conclusion: The aging of our population is positively correlated with an increase in the number of cancer cases among elderly people which is expected to become more prevalent, which is the case of malignancies. This study highlighted the importance of implementing preventive health strategies, such as health education programs, to reduce the incidence of cancer among elderly Tunisians. Furthermore, the study also identified the major sites of cancer in the elderly population, which can serve as a foundation for future research and targeted interventions.

No conflict of interest.
1396  POSTER

Effectiveness of a relaxation intervention technique (progressive muscle relaxation and guided imagery techniques) to reduce anxiety of parents of hospitalized children

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Introduction: The diagnosis of Malignancy in a child is a source of intense stress in patient and their family. Anxiety, depression, anger and low self-esteem are some of the emotional reactions experienced by parents in response to the fear of loss and future relapse. To investigate the effect of Progressive Muscle Relaxation (PMR) and Guided Imagery (GI) interventions, in reducing anxiety levels among parents of children diagnosed with any type of malignancy receiving active treatment at the Paediatric Oncology unit.

Material and Method: A parallel group randomized non-blinded control trial, conducted between April 2012 to October 2013, at two public hospitals in Cyprus and Athens. Fifty four parents of children hospitalized with malignancy were randomly assigned to the intervention (PMR and GI) (n = 28) or control group (n = 25). Parents were randomized to receive in individual sessions, a script process of Progressive Muscle Relaxation and Guided Imagery techniques, once a week for 25 minutes in a private room at the Paediatric Oncology unit of the hospital, for three weeks. Parents randomized to the control group did not receive any additional intervention beyond the usual psychological support.

The outcome variables of the study were changes in anxiety levels (Hamilton’s Anxiety Scale), and mood (Questionnaire of Mood States Brief), at 3 weeks’ time.

Results and Discussion: Significant differences of mean were found in the Hamilton Anxiety Scale between T0 and T1 in the two groups. In the POMs Brief scale, there was a statistically significant difference in tension at the T1 measurement in the intervention group were significantly less sad (p = 0.001), and significantly less tense and anxious (p = 0.031).

The findings showed the beneficial nature of relaxation to reduce anxiety and improve mood in parents of children with malignancy. This research was supported by the acceptance, the effectiveness and the impact of these techniques to reduce the anxiety of the parents of children with malignancy. The study was registered in the ClinicalTrials.gov: NCT01590524.

No conflict of interest.

1397  POSTER

Integrative analysis of bone marrow disease in neuroblastoma patients by DNA, RNA and protein markers


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Background: Methotrexate (MTX), key drug in childhood B-Acute Lymphoblastic Leukemia (ALL) therapy, often causes toxicity. Association between genetic variants in MTX transport genes and toxicity has been reported. It is known that these transporters are regulated by microRNAs (miRNAs). Despite miRNA SNPs interfere with miRNA levels or function, studies of miRNA polymorphisms and drug toxicity has been almost absent. Regarding B-ALL, we have previously found rs56103835 in miR-323b and miR-6083 that might affect SLC46A1, SLC19A1 and SLCO1A2 MTX transport genes regulation and could affect MTX levels in patients with B-ALL.

Methods: Blood samples of 167 Spanish patients with pediatric B-ALL treated with LAL/SHOP protocol were analyzed. We selected all the SNPs described in pre-miRNAs with a MAF >1% (213 SNPs in 206 miRNAs) that could regulate MTX transporters. Genotyping was performed with VeraCode GoldenGate platform.

Results: Among the most significant results, we found rs59262801 in miR-5189, rs4909237 in miR-595 and rs78790512 in miR-6083 were associated with MTX plasma levels. Nowadays, a large amount of new miRNAs have been annotated. Therefore, the aim of this study was to determine if there are other variants in miRNAs associated with MTX levels.

Methods: Blood samples of 167 Spanish patients with pediatric B-ALL treated with LAL/SHOP protocol were analyzed. We selected all the SNPs described in pre-miRNAs with a MAF >1% (213 SNPs in 206 miRNAs) that could regulate MTX transporters. Genotyping was performed with VeraCode GoldenGate platform.

Results: Among the most significant results, we found rs59262801 in miR-5189, rs4909237 in miR-595 and rs78790512 in miR-6083 were associated with MTX plasma levels. These miRNAs were predicted, in silico, to regulate genes involved in MTX uptake: SLCA46A1, SLCA19A1 and SLCO1A2.

Conclusion: In this study we detected 3 SNPs in miR-5189, miR-595 and miR-6083 that might affect SLCA46A1, SLCA19A1 and SLCO1A2 MTX transport genes regulation and could affect MTX levels in patients with pediatric B-ALL.

This project was supported by RETICS (RD/12/0036/0060 and RD/12/0036/0036) and Basque Government (IT661−13).

No conflict of interest.
1399 POSTER
Involvement of SNPs in CDKN2A/B locus in childhood acute lymphoblastic leukemia susceptibility in the Spanish population
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Background: Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy in children. A genetic basis of ALL susceptibility is supported by genome-wide association studies (GWAS) findings. Two GWASs independently identified variants in ARID5B, IKZF1 and CEBPE genes associated with ALL risk, results that have been validated by several groups. A following work discovered an additional susceptibility variant in CDKN2A/B locus. In this case, subsequent studies have also validated this result, but others were unable to replicate the association. In CDKN2A/B locus, other studies have found different variants in this locus associated with ALL risk. Thus, it is possible that different variants in the region are related to ALL risk. Therefore, the aim of this study was to determine the effect of SNPs at the CDKN2A/B locus in a Spanish population.

Methods: Blood samples of 217 pediatric patients with B-cell ALL in complete remission and 330 healthy controls of Spanish origin were analyzed. A total of 6 SNPs in this locus were selected. VeraCode GoldenGate platform was used.

Results: We studied a total of 6 SNP which give information of a total of 46 SNPs at the locus. From them, in a preliminary study, we found 3 SNPs significantly associated with B-ALL risk, rs2811712 located in CDKN2B (p = 0.0001), rs2317992 in CDKN2B and CDKN2B-AS1 (p = 0.009) and rs2811709 in CDKN2A (p = 0.014). rs2811712 and rs2811709 have been previously reported in association with B-ALL susceptibility in 4 studies.

Conclusion: These results provide evidence for the influence of genetic variants at CDKN2A/B locus with the risk of developing B-ALL. This project was supported by RETICS (RD12/0036/0060, RD12/0036/0036), UPV/EHU (UFI 11/35) and Basque Government (IT661−13).

No conflict of interest.

1400 POSTER
Involvement of SNPs in mir3117 and mir3689 in pediatric acute lymphoblastic leukemia susceptibility
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Background: Recently, several Genome wide associations studies (GWAS) have found genetic variants in ARID5B, IKZF1, CEBPE, CDKN2A and BM1-P1P4K2A genes associated with pediatric acute lymphoblastic leukemia (ALL) risk. These studies were mainly focused in coding regions. However, nowadays it is known that more than 40% of significant variants associated with cancer risk are situated in non-coding regions, where non-coding RNA molecules are located. MicroRNAs (miRNAs) are non-coding RNA molecules dysregulated in ALL, suggesting that they may have a role in ALL risk. Despite miRNA SNPs interfere with miRNA levels or function, only 3 studies in ALL susceptibility have been done. In those studies, 5 SNPs in 5 miRNAs have shown association with B-ALL. These results suggest that variants in miRNAs could contribute to childhood B-ALL predisposition. Nowadays, a large number of new miRNAs have been annotated. Therefore, the aim of this study was to determine if any of these SNPs in these new miRNAs are involved in B-ALL susceptibility.

Material and Methods: Blood samples of 217 pediatric patients with B-cell ALL in complete remission and 330 healthy controls of Spanish origin were analyzed. We selected all the SNPs described in pre-miRNAs with a MAF >1% (213 SNPs in 236 miRNAs). VeraCode GoldenGate platform was used.

Results: The SNPs rs12402181 in mir3117 and rs6257144 in mir3689d2 were associated with B-ALL risk possibly through its effect on MAFK signaling pathway.

Conclusion: Therefore, in this study we found rs12402181 in mir3117 and rs6257144 in mir3689 associated with B-ALL risk. These SNPs could be novel markers for B-ALL susceptibility.
and supracalvarial retroperitoneal lymphadenopathy. The biopsy report of the lesion was compatible with CCCR. I was administered sunitinib and observed regression of the metastasis and disease stabilization. However, an irregular follow-up care of the patient permitted the development of a severe cardiac dysfunction and TSH above 100. He was admitted to the Pediatric ICU, but died of cardiacogenic shock.

Conclusions: CCCR is a rare condition in children and sunitinib as a target therapy has proved to be an efficient and safe treatment, once the survival rate of these patients has been increased by a close monitoring of adverse effects.

No conflict of interest.

1402A POSTER

Retinoblastoma – pattern, presentation and management – a quintessential experience of 5 years

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Background: Retinoblastoma is the most common primary intraocular malignancy of childhood. The diagnosis is mainly clinical, but histology determines the diagnosis and the extent of the tumour. Prompt referral and appropriate management by a multidisciplinary team are necessary to optimize visual outcome and survival.

Objective: To determine the pattern of presentation and management of retinoblastoma patients at a tertiary cancer care centre in South India during a period of 5 years (1st November 2009 to 1st December 2014).

Materials and Methods: The study is a retrospective case series. It was carried out primarily by identifying the hospital number of relevant records of retinoblastoma patients from attendance, admission and discharge/death at the cancer care centre. The hospital number was used to retrieve relevant files from the records department with the help of a records clerk. Relevant clinical information recorded was extracted and entered into a structured data excel sheet for analysis. Information sought is demographic characteristics, clinical presentation, investigations done, the methods of management of retinoblastoma patients and the discharge/death records. Data collected was analysed. Descriptive statistics were used to summarize the data and results were presented.

Results: Total number of cases studied was 31. Out of which, 18 (58%) were female and 13 (42%) were male. Of the 31 cases, 16 (52%) had bilateral involvement and 15 (48%) had unilateral involvement. Age of onset of 13 (42%) cases was less than or equal to 12 months. Age of onset of 11 (35%) was between more than 12 months to less than or equal to 36 months. Age of onset of 7 cases (22%) was more than 36 months. History of consanguinity in the parents was found in 2 cases (6.5%). Both of these cases had bilateral eye involvement. The commonest mode of presentation was a white reflex in the eye (17out of 31 cases 55%). Other presentations included defective vision and swelling of the eye. Out of 47 eyes studied, 1 (2%) was in Group A, 1 (2%) was in Group B, 4 (9%) were in Group C, 14 (30%) were in Group D and 27 (57%) were in Group E. Out of the 47 eyes, 20 (43%) eyes were enucleated by 47 eyes, 13 (28%) eyes were irradiated. 7 (23%) out of 31 cases were metastatic at presentation. Out of the 10 metastatic eyes, 5 eyes were Group D and 5 eyes were Group E. 6 (19%) out of 31 cases succumbed to death.

Conclusion: Retinoblastoma continues to be a challenge both diagnostically and therapeutically. Many factors enter into management decisions such as patient age, tumour laterality, size, location, and extent, and anticipated visual prognosis. Chemotherapy has changed the approach to retinoblastoma in recent years and have permitted many children to optimize visual outcome and survival.

No conflict of interest.

1403A POSTER

Outcome of children with medulloblastoma at a tertiary cancer hospital in Karachi, Pakistan

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Background: Medulloblastoma is one of the most common central nervous system (CNS) tumours with good prognosis in developed areas. In developing countries like Pakistan, multiple problems exist which compromise the survival. These include delay in presentation, high abandonment rate, lack of multidisciplinary team including expert surgical skills and good supportive care. There is also paucity of data on survival of children with medulloblastoma in Pakistan. To our knowledge, this is the first study on Medulloblastoma in children in Pakistan. The main objective of our study is to determine the overall survival of patients with Medulloblastoma and to identify various factors related to poor survival.

Materials and Methods: A retrospective chart review of patients treated at the Indus Children’s Cancer Hospital- ICH (CCCH) from June 1997 to November 2016. Ages ranged from 0 to 18 years. Risk stratification, chemotherapy and radiation techniques were according to the standard guidelines. Data was collected from the Health Management Information System (HMIS) and analysed using SPSS 21. The demography, clinical presentation and overall survival were determined and gaps were identified for decrease in survival.

Result: Total 63/341 (19%) CNS tumours were Medulloblastoma. Mean age of presentation was 8±4.4 years. 5/8 (6%) were less than age of 3 years. Male to female ratio 2:1. The most common symptom was headache (20%), followed by vomiting (19%). Mean delay of 4±3.7 months from first symptom till surgery. 38% presented with metastatic disease, leptomeningeal spread being the most common site (23%). Because of limitation of data and record availability only 47 out of 63 were risk stratified. 47% in which 19% were standard risk and 56% high risk. 42/63 patients (66%) received treatment at CCCH, remaining had advanced disease at presentation so left before treatment as family opted for supportive care at home. 23/42 (55%) completed treatment. 12/42 (29%) are alive, 8/42 (19%) are alive and on treatment at the time of analysis and remaining died due to relapse or progressive disease. Overall survival of entire cohort is 32% including abandonment and 48% without abandonment.

Conclusion: Delay in the diagnosis leading to advance disease at presentation, poor socioeconomic status, lack of infrastructure and
neurosurgical expertise, limited neuro-oncological centers and high rate of treatment abandonment are the major challenges leading to poor overall survival. Survival can be improved by addressing and improving above mentioned challenges. **No conflict of interest.**

1404 POSTER

The shift from delayed radiotherapy to localized radiotherapy strategy in treatment of infantile medulloblastoma – challenging experience from LMIC


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Background and Objectives: Medulloblastoma patients below 3 years had inferior survival rates due to several reasons. We aim to investigate the treatment end-results of medulloblastoma under 3 years old and determine the factors affecting its prognosis.

Design and Methods: Twenty-eight children below the age of 3 years were treated at Children’s Cancer Hospital Egypt during the period from July 2007 to October 2015. Gross total resection was performed in 19 children (67.8%), subtotal excision in 10 children (35.7%) and biopsy in one patient. Twenty (71.4%) were non-metastatic, while 8 (28.6%) metastatic M1–3. Twelve (42.8%) children received infantile medulloblastoma chemotherapy protocol and localized posterior fossa irradiation, while the other 16 (57.2%) delayed craniospinal radiotherapy protocol post chemotherapy. Eight metastatic children received craniospinal irradiation (CSI). Twelve of the M0 patients received posterior fossa (PF) irradiation, while the other 6 received CSI at age of 3 years.

Results: The 4 year OS for non-metastatic was 80±6.7% and 37.5±9.1% for M+ children. The EFS for nonmetastatic was 58.4±8.3% and 37.4±11.8% respectively. The infantile chemotherapy protocol with localized radiotherapy in M0 patients led to 4-year OS of 76.8±7.9% compared to 62.5±12.6% for delayed craniospinal radiotherapy for M0 patients. The OS for delayed CSI for M0 was 37.5±13%. OS of GTR and less than GTR is 78.6±8.2%, 62.5±6.8% respectively. EFS for localized PF radiotherapy protocol as 83.3±7.7, and 37.5±12.3. EFS for delayed CSI M+ was 25±11.8. Two patients of the CSI group developed CNS relapse and other two patients had spinal relapse. No relapse in patients who received PF irradiation. Non of the these detected differences were statistically significant.

Conclusion: Nonmetastatic status in infantile medulloblastoma carries better OAS and EFS than metastatic category irrespective of the treatment protocol. Shift from delayed CSI post chemotherapy to the localized PF protocol is unique experience that improved survival profile and to decrease toxicity profile. **No conflict of interest.**

1405 POSTER

Effect of delaying local control radiotherapy on outcome of localized pediatric bladder/prostate rhabdomyosarcoma


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Background and Objectives: Multidisciplinary treatment approach is used in treatment of bladder/prostate rhabdomyosarcoma (RMS), yet it is unclear, which treatment strategy is optimal for local control. Radiotherapy is the main local control method. The study evaluate the impact of timing of radiotherapy (RTH) and intensity modulated radiotherapy (IMRT) technique on cancer control outcomes for children with bladder/prostate RMS.

Design and Methods: Retrospective analysis of 29 patients treated as local control by RTH at Children’s Cancer Hospital Egypt in August 2007-December 2015. Seventeen patients (58.6%) were treated by conformal radiotherapy and 12 patients (41.3%) treated by IMRT technique.

Results: Seventeen (58.6%) patients started Local radiotherapy before/at week 12 and 12 (41.4%) patients started after. Four years failure-free survival (FFS) and Overall survival (OS) for those who had early and delayed local control are (94.1±7% vs. 33.3±15.1%, p = 0.007), (100% vs. 56.8±6.5%, p = 0.007), respectively. Failure free survival for patients who treated Over treatment time (OTT) <5 weeks and >5 weeks is (49.4±14%, 81.5±9.8%) respectively. Although they show difference, yet not statistically significant (0.6). Ten patients (83.3%) who had OTT <5 weeks were treated by IMRT.

Conclusion: Earlier local control was associated with better outcome in children with bladder/Prostate RMS. IMRT shows tendency to improve survival profile due to decrease toxicity yet decrease OTT. **No conflict of interest.**

1406 POSTER

Management and early complications of totally implantable venous access port systems in 81 children diagnosed with cancer

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Background: Port systems for permanent central venous are recommended in patients with cancer for long-term use of chemotherapy and other procedures. Placement and postoperative care of Totally Implantable Venous Access Port Systems (TIVAPS) require a collaborative and interdisciplinary effort, especially in childhood. The aim of the study is to investigate changes in the implantation surgical procedures, initial management, morbidity and infectious complications in the first month after TIVAPS implantation in children and adolescents diagnosed with cancer.

Material and Methods: Retrospective study of the epidemiological and clinical data of 145 paediatric patients with cancer and analysis of early TIVAPS related complications in 81 cases diagnosed with cancer from 2013 to 2015. SPSS software was used for statistical analysis.

Results: Clinical data of the 81 patients: 45 males and 36 females; median age at cancer diagnosis: 5.62 years-old (range: 0–16.41 years-old). Type of neoplasm: 27 leukemia, 17 sarcoma, 11 lymphoma, 10 brain tumour, 9 neuroblastoma, 1 Wilms tumour, and 6 other oncologic diseases. Before TIVAPS implantation, all patients received intravenous antibiotic prophylaxis. Also sterile technique was used for TIVAPS manipulation in all cases. Surgical placement was closed in 50 and open in 31 patients. The main vein for TIVAPS insertion was right internal jugular in 27 cases, from TIVAPS in 2 and 1 venipuncture. Seven microbiological studies were positive (5 Gram+, 1 fungi and 1 virus). One surgical wound infections with positive culture were found (Bacillus sp.).

Conclusions: Changes in the technical surgical procedures and initial management of Totally Implantable Venous Access Port Systems (TIVAPS) were implemented in children diagnosed with cancer in the last two years. Functionality was good in nearly all patients (80/81) and initial early complications were low (3.7%). The most infectious complications were documented: accidental subclavian artery dissection, bent catheter and suture dehiscence. Re-surgery was needed in four for catheter removal due to infection (3) and catheter migration (1). TIVAPS functionality was good (permeable and blood flowed out) in 80, only one did not flow out during the first month, 30 patients developed fever associated with multiple factors. Neutrophils median at the time of surgical procedure was 2,800 cell/mm3. Blood cultures were collected from TIVAPS and venipuncture approach in 27 cases, from TIVAPS in 2 and 1 venipuncture. Seven microbiological studies were positive (5 Gram+, 1 fungi and 1 virus). One surgical wound infections with positive culture were found (Bacillus sp.).

No conflict of interest.
Background: Tumor Lysis Syndrome (TLS) is a complication of malignancies with high tumor cell proliferation, tumor burden and chemosensitivity like leukemias and lymphomas. TLS can occur spontaneously or during aggressive chemotherapy and may lead to serious complications. An early recognition and proper management is crucial in pediatric patients. The aim is to review clinical and biochemical data in children diagnosed with acute leukemias, acute lymphoblastic leukemia (ALL), Acute Myeloid Leukemia (AML) and Non-Hodgkin Lymphomas (NHL) and to analyse the initial characterisation, prophylaxis, treatment and complications observed during induction therapy in patients.

Material and Methods: Retrospective review of clinical and analytical data of patients ≤18 years-old diagnosed with ALL, AML and NHL between 2005–2015 at Pediatric Oncology Unit in a tertiary hospital. All the patients were treated according to national (SEHOP, PETHEMA) or international (BIOCRUCES) protocols. Statistical analysis was performed by SPSS.

Results: A total of 115 pediatric patients with risk of developing TLS were enrolled in the study: 85 ALL, 13 AML, 17 stage III−IV NHL (12 Burkitt lymphomas and 5 Lymphoblastic Lymphoma). Twenty-one (18.2%) showed laboratory TLS criteria, according to Cairo-Bishop definition: ≥ 12 ALL (10, leucocytes >100×10^9/l), 2 ALL and 7 NHL. Biochemical data: hyperuricemia in 18 (1 increase of ≥25%), 5 hyperpotassemia (3, ≥25%), 7 hyperphosphatemia (3, ≥25%) and 5 hypercalcemia (4 with decrease of ≥25%). One patient showed pseudohyperpotassemia (12.6 mEq/L). The most common clinical complications were acute renal insufficiency (4), neuro- logical symptoms/convulsions (3), and cramps/tetany (2). No arrhythmias or deaths. Eleven patients required admission to Pediatric Intensive Care Unit and multidisciplinary management with oncologists and nephrologists was necessary. Aggressive hydration and oral allopurinol was the standard for prophylaxis of hyperuricemia but urinary alkalinisation with bicarbonate was added in 7 and diuretics in 6 patients. Nineteen patients were treated with Rasburicase (1–4mg/m²/day). Two patients were administered aminoglutetate and in one case phosphorus chelating agents. No patient needed hemodialysis.

Conclusions: TLS was more frequent in disseminated high-grade lymphomas than in leukemia in this study. The laboratory Cairo-Bishop TLS criteria should be adapted to the patient age, especially in young children. Allopurinol and Rasburicase, even a single-dose, are useful to avoid complications related to hyperuricemia and renal failure but alkalinisation is rarely indicated. TLS prophylaxis and therapy are effective for avoiding clinical complications but they need to be individualized in children, especially fluid therapy and drugs. A multidisciplinary approach in pediatric critical care units in severe cases is important.

No conflict of interest.

Poster Session, Saturday 28 January 2017 Abstracts
a treatment challenge. Despite the improved prognosis of AML (M3) after the introduction of differentiating agents, patients with the rare combination of Fanconi anemia and M3 who didn't receive bone marrow transplantation withstand a dismal prognosis.

No conflict of interest.

1410 POSTER
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Background: Malignant tumors in children made 4% of all tumors. LOXO-101 is an orally bioavailable, potent, ATP-competitive, selective pan-TRK inhibitor. Here, we report response and durability data for patients with NTRK fusions enrolled in an ongoing Phase I dose escalation trial. Updated pharmacokinetic (PK) and safety data for all enrolled patients (pts) are also reported.

Methods: This is an ongoing, open-label, multicenter, 3+3 dose escalation Phase I study. LOXO-101 is administered orally as a once- or twice-daily dose for continuous 28-day cycles. Response is measured by RECIST. Plasma is obtained for PK analysis. Safety information is collected on all patients and reported regardless of their attribution to the study drug.

Results: As of March 25, 2016, 43 pts with solid tumors have been enrolled, including seven pts with NTRK fusions across five different tumor types. Six of the seven patients were evaluable for response and all six have demonstrated a clinical response to LOXO-101. Five of six patients (83%) have achieved confirmed RECIST partial responses. All seven patients remain on study with a duration of therapy from one to fourteen cycles. No objective anti-tumor activity has been observed in treated patients without an NTRK fusion.

Conclusion: In total, 43 pts have been treated across five dose levels. Maximum plasma concentrations of LOXO-101 were reached 30–60 minutes following dosing. The unbound drug levels of LOXO-101 appear sufficient for approximately 98% inhibition of TRKA/B/C at peak concentrations at all dose levels. LOXO-101 has been well tolerated. The maximum tolerated dose has not been reached, and the most common adverse events are Grade 1 and 2 fatigue (33%), constipation (23%) and dizziness (23%).

Conflict of interest: Ownership: N Nanda and M Cox are employees and stockholders of Loxo Oncology, Inc. Corporate-sponsored Research: R Doebel has received a research grant from Loxo Oncology Inc. Other Substantive Relationships: S Smith and S Cruikshank are paid consultants of Loxo Oncology Inc.

1461 POSTER
WWOX-deficiency promotes increased survival by enhancing homology-directed repair
B. Batar1, M. Schrock1, J. Lee2, T. Druck1, B. Ferguson2, J. Hwan Cho3, K. Akakpo1, H. Hagrass1, N. Heerema4, F. Xia2, J. Parvin5, M. Aldaz6, K. Huebner1. 1The Ohio State University, Cancer Biology and Genetics, Columbus, USA; 2The University of Texas, Epigenetics and Molecular Carcinogenesis, Smidville, USA; 3The Ohio State University, Radiation Oncology, Columbus, USA; 4The Ohio State University, Pathology, Columbus, USA; 5The Ohio State University, Biomedical Informatics, Columbus, USA

Background: The WWOX gene spans the common fragile site FRAXE160, and has been shown to be a tumor suppressor gene in some model systems. Loss or reduction in Wwox expression may correlate with the progression of variety human cancers. Our objective was to determine the mechanism that allows Wwox-deficient cells to survive DNA double strand breaks (DSBs).

Material and Methods: To define if Wwox expression may affect repair of induced DBSs, we investigated the effects of ionizing radiation (IR) and chemotherapeutic agents on Wwox-deficient vs sufficient cells. Early passage mouse embryonic fibroblasts (MEFs) were exposed to various IR doses and agent concentrations and plated for clonogenicity to analyze cell survival and proliferation. To elucidate the mechanism that underlies Wwox-deficiency associated radiation resistance, we performed pathway specific recombinant plasmid reporter assays.

Results: We observed a significant difference (p < 0.0001) in survival at doses 7.7 Gy and higher, with knock out (KO) lines KO3 and KO5 surviving 10-fold better than wild type (wt) cell lines WT4 and WT7. Survival curves for shWWOXA and shWWOXB transformed clones (breast epithelial cell lines, MCF10A) also demonstrated increased survival at 7.7 Gy and above (p < 0.005) vs the Wwox-sufficient shScrambled transfected cells. Furthermore, KO MEFs exhibited enhanced survival to 4 hr mitomycin (MMC) exposure at concentrations 1µM and higher (p < 0.0001), and an even greater resistance noted after MMC treatment plus ABT-888 (p < 0.0001). Also, we found that Wwox expression enhances non-homologous end joining (NHEJ) and alt-NHEJ, but impairs HDR and single strand annealing (SSA) and radiation resistance in Wwox-deficient cells is caused by enhanced HDR.

Conclusions: Wwox-deficient cells have improved survival to agents which induce DBSs. Wwox deficiency promotes enhanced HDR efficiency. Selectively inhibiting the HDR pathway in Wwox-deficient cells may ablate their radio-resistance and re-sensitize them to radiation, suggesting the
use of HDR inhibitors in conjunction with radiation for treatment of Wwox- 
deficient tumors.

No conflict of interest.

1462 POSTER
Common attributes in mutation carriers identified in a 32-gene hereditary cancer panel
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The use of multi-gene panel testing (MGPT) with next generation sequencing (NGS) to detect hereditary cancer syndromes has become increasingly common. MGPT has identified more individuals with increased cancer risk than traditional methods, including mutations in genes that were not suspected. Which patients should have MGPT and what results may be found are common questions among clinicians, and the likelihood of finding a mutation is heavily considered in determining who should have testing. Our study aims to assess and compare the mutation frequencies among patients on CancerNextTM, an NGS panel of 22–32 genes during the time studied.

De-identified clinical and demographic data from 11,363 consecutive cases submitted to Amybr Genetics for CancerNext testing between March 2012 and June 2016 were retrospectively reviewed. Mutation rates at diagnosis were compared for 9 cancer types using logistic regression analysis, controlling for other cancer diagnoses.

CancerNext testing showed a positive rate of 10% and 13% in unaffected and affected patient groups, respectively. Except for thyroid and gastric carcinoma, all cancer diagnoses were significantly more likely to yield a positive result than an unaffected patient (Table 1). Younger ages of diagnosis were associated with higher mutation rates in brain (p = 0.03), ovarian (p = 0.02) and breast cancer (p = 0.0002).

Table 1. Relationship between mutation positive rate and affected status by cancer type

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Positive rate</th>
<th>OR (95% CI)</th>
<th>P-value</th>
<th>Most common gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain/cancer</td>
<td>9/47 (19%)</td>
<td>1.8 (1.1, 2.9)</td>
<td>0.02</td>
<td>CHEK2</td>
</tr>
<tr>
<td>Breast</td>
<td>51/457 (11%)</td>
<td>1.2 (1.1, 1.4)</td>
<td>0.002</td>
<td>CHEK2</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>64/547 (12%)</td>
<td>1.3 (1.1, 1.6)</td>
<td>0.003</td>
<td>MLH1</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>10/74 (14%)</td>
<td>1.5 (0.8, 2.4)</td>
<td>0.17</td>
<td>CDH1</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>53/362 (15%)</td>
<td>1.7 (1.3, 2.1)</td>
<td>0.001</td>
<td>BRCA2</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>17/129 (13%)</td>
<td>1.9 (1.4, 2.6)</td>
<td>0.0001</td>
<td>BRCA2</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>10/62 (16%)</td>
<td>1.7 (1.1, 2.6)</td>
<td>0.008</td>
<td>CHEK2</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>7/89 (8%)</td>
<td>0.9 (0.6, 1.3)</td>
<td>0.60</td>
<td>PALB2</td>
</tr>
<tr>
<td>Uterine-cancer</td>
<td>26/216 (12%)</td>
<td>1.8 (1.4, 2.2)</td>
<td>2.3E-07</td>
<td>MSH2</td>
</tr>
<tr>
<td>All cancers</td>
<td>1108/8796 (13%)</td>
<td>1.3 (1.2, 1.5)</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

* When compared to those without that type of cancer.

Patients diagnosed with cancer had a higher detection rate, showing the utility of testing an affected individual whenever possible. Age of diagnosis was only significant in a few cancer types, which may suggest genetic testing in patients of wider age ranges than previously thought. The gene-specific breakdown supports previous studies on MGPT in commonly studied cancer types and highlights interesting new associations for brain, sarcoma, and thyroid cancer. Additional work is needed to further delineate which factors impact CancerNext detection rates and by how much.

Conflict of interest: Other Substantive Relationships: Full time employee of Amybr Genetics.

1463 POSTER
Preparation of cytological effusion samples by the “plasma-thromboplastin” method and its application detecting malignancy and neoplastic primary site
R Vieira Martins de Siqueira1, L. Matos Rodrigues de Brito1, T.M. Mendes Lousa de Castro1, G. De Carvalho Caldas1, F. Pirani Caniero1, L. Maciel de Souza Vianna1, 1Faculdade de Medicina, Laboratório de Patologia Molecular do Câncer, Brasília – DF, Brazil

Introduction: Despite the cell block being considered a diagnostic method of wide applicability in routine practice, the indication of each method according to the different types and aspects of cytological samples is not well established. This study aims to evaluate the applicability of the plasma-thromboplastin (PT) method in pleural, peritoneal, pericardial, cerebrospinal fluids, bronchoalveolar lavage, urine and aspirated cystic lesions. Also, it was intended to apply widely used antibodies in clinical practice of immunocytochemistry (ICC) to detect malignancy and neoplastic primary site through the profile of protein expression.

Methods: Conventional smear, cell block and ICC were prepared for each cytological sample (n = 299). To the malignancy and primary site study, 226 samples were selected (excluding bronchoalveolar lavage, urine and aspirated cystic lesions). The expression of at least two malignancy markers was considered as carcinoma diagnosis criteria. Identifying the primary site, the positive result was with the presence of at least one marker suggestive of the primary site. The result was considered negative when at least one marker suggested a non-agreeing primary site. The markers applied were Epithelial related antigen, claudin 4, anti-mesothelium antibody, estrogen receptor, specific prostatic antigen, CDX2 transcription factor, cytokeratin 7 and 20, thyroid transcription factor 1. The current or previous history of carcinoma (diagnosed by histopathological study) was acquired on patient medical files or on the laboratory archives.

Results: The PT method was applicable in samples without or with small amount of sediment, including bloody ones, representing 88.3% of the total. Samples with large amount of sediment and/or anticoagulant (11.7%) were prepared by agar method. Adequate cellularity and cellular distribution with preservation of their morphology were observed in both methods. The ICC staining pattern was similar to that usually observed in conventional smears and the diagnosis had an agreement of 98.9% between both methods. Among the 226 samples analyzed, 18.14% had cancer (41/226) and these cases were confirmed by the method applied. The proportion of analysis and results are given in the table.

<table>
<thead>
<tr>
<th>Site</th>
<th>Number</th>
<th>Probable sites:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously known primary site</td>
<td>22(41)</td>
<td>Breast</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ovary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stomach</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lung</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breast/Ovary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervical</td>
</tr>
</tbody>
</table>

Conclusion: The PT method is applicable in most samples, has high diagnostic agreement with conventional smears and may decrease the false-negatives of cytological analyses. Also, the identification of metastatic carcinoma’s primary site through the analysis of ICC markers can be performed in most samples, but demands a wide panel of antibodies.

No conflict of interest.

1464 POSTER
Immunological and first anti-tumor data of the TLR9 agonist dSLIM2006
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Introduction: TLR9 agonists are potent activators of the immune system via induction of cellular and humoral responses. Preclinical and ongoing clinical studies support the use of TLR9 agonists for immunotherapeutic approaches. ODN2006 is a single-stranded oligodeoxynucleotide containing non-methylated CG-motifs (CpG-ODN) for TLR9 activation, which was used in clinical studies (ProMune, PF3512676, CPG7909). However, it is chemically-stabilized by phosphorothioates (PTO) in its phosphate moieties – and this modification produces off-target effects in immune cell populations that result in unfavorable risk-to-benefit ratios.

Methods: To avoid the off-target effects of PTO-modification but maintain the sequence, a corresponding molecule consisting of natural DNA was designed – dSLIM2006: dSLIM2006 belongs to the dSLIM® family of TLR9 agonists and is protected from exonucleolytic degradation by its covalently-closed dumbbell-shaped structure. It contains the immunomodulatory sequence of ODN2006 in both of its loops. The immunomodulatory properties of dSLIM2006 in comparison to ODN2006 were analyzed employing in vitro assays using human peripheral blood mononuclear cells (PBMC).

In addition, a pilot in vivo study was used to investigate the anti-tumor effect of dSLIM2006 in the syngeneic murine colon carcinoma CT26 model.

Results: The immunomodulatory benefit of dSLIM2006 completely differs from the linear Cpg-ODN ODN2006: Activation of PBMC with dSLIM2006 resulted in increased secretion of the cytokines IFN-alpha, IP-10, and IFN-gamma compared to ODN2006. Furthermore a broader activation of immune cells within PBMC was detected with an up-regulation of the activation markers of dSLIM2006 CD69 on monocytes as well as CD69 of T cells. In addition, dSLIM2006 shows a comparable increase of CD86 expression in B cells. The immune activation profile of dSLIM2006 strictly depends on the availability of CG-motifs and its natural
S150 Abstracts

Poster Session, Sunday 29 January 2017

Phosphatidic acid backbone. First data from the CT26 colon carcinoma model showed that dSLIM2006 reduces tumor growth and prolongs the survival of mice.

Conclusions: dSLIM2006, a member of dSLIM family of TLR9 agonists, broadly activates the immune system in vitro. The use of dSLIM2006 in a murine CT26 tumor model resulted in a reduction of tumor growth and therefore this TLR9 agonist has the potential for development as an immune surveillance reactivator for the treatment of cancer.

Conflict of interest: Ownership: BW is a shareholder of Malogen AG. Advisory Board: BW is a member of the advisory board of Malogen AG. Other Substantive Relationships: BV, KK, DO and MS are employees of Malogen AG.

1465 POSTER Preliminary clinical results of a metabolism-based method to detect circulating tumor cells

F. Del Ben¹, M. Turetta², E. Biscontin¹, G. Brisotto¹,³, G. Celetti⁴, G. Sciles¹,², Centre di Riferimento Oncologico CRO IRCCS, Dept. of Translational research, Aviano, Italy; ²Anatomic Pathology Institute, University of Udine, Medical and Biological Sciences, Udine, Italy; ³Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; ⁴Institute for Molecules and Materials- Radboud University, Dept. of Physical Chemistry, Nijmegen, Netherlands; ⁵Princeton University, Dept. of Chemistry, Princeton, NJ, USA

Background: Cancer imaging is the gold standard for monitoring cytotoxic cancer treatments, but has several limitations, the major ones being delayed diagnosis (due to a limit in tumor size-detection) and toxicity (due to ionizing radiation). Additionally, in the context of new molecular targeted therapies and, in particular, immunotherapy, clinical responses as measured by imaging are often dissociated from survival. New therapy-monitoring methods are an unmet clinical need in oncology. The number of circulating tumor cells (CTC) in blood is correlated with the progress of metastatic cancer, and is emerging as a minimally-invasive diagnostic tool for therapy monitoring and recurrence detection. A CTC assay could be a serially repeatable, early-predictor of therapy response in traditional therapies and a candidate marker of effective immune response in immunotherapy.

In a previous work (Del Ben, Turetta et al., Angew. Chem. Int. Ed. Engl., 2016) we demonstrated a label-free technique for CTC detection based on their altered metabolism, by measuring the secretion of H+ or lactate production of individual, viable tumor cells compartmentalized in microfluidically prepared micro-droplets. We present here additional clinical data and current challenges.

Methods: Clinical samples (2 mL of whole blood collected in EDTA-tube) were lysed and CD45-depleted using Miltenyi LD columns and beads. Droplets containing single cells are generated by microfluidic water-in-oil emulsification. Cells are suspended in culture medium, together with a ratiometric pH-sensitive dye (SNARF-5F). Droplets are incubated at 37 degrees Celsius for 30 minutes and reinjected for fluorescent pH measurement. A triggered camera collects pictures of selected drops.

Results: According to selected cut-off (n = 6.4) we detected significantly more events in metastatic breast (median 41/mL, range [5–3125], n=6) and lung cancer (49/mL, [28−87], n=4) vs healthy donors (3/mL, [1−9], n=7), p<0.005. In breast cancer, we demonstrated the presence of both EpCAM(−) and EpCAM(+) acid-producing cells, while CD45 showed dim or no expression.

Conclusion: We observed a significant difference between patients and healthy donors, with the number of events/mL comparable to existing literature on CTC. To further validate the technology, we set up a comparison study against Veridex CellSearch® and ongoing clinical trials on breast cancer focused on validating our metabolically activated CTC as a surrogate of survival. We are currently looking for collaborators conducting immunotherapy in order to test our system as a marker of effective immune response.

Conflict of interest: Ownership: Cytofind Diagnostics B.V. (innovator); start-up, ca. 15% ownership. Board of Directors: Cytofind Diagnostics B.V. (Chief Scientific Officer, 0.2 FTE).

1466 POSTER Upregulation of MicroRNA-1182 activates the apoptotic pathway p38/MAPK in MDA-MB-435 melanoma cells following reprogramming with transcription factors Oct3/4, Klf-4, Sox-2, c-Myc

K. Kutlu¹, H. Taheri¹, A. Yilmazer¹, ¹Ankara University Institute of Biotechnology, Basic Biotechnology, Ankara, Turkey; ²Ankara University Engineering Faculty, Biomedical Engineering, Ankara, Turkey

Background: Micro RNAs (miRNAs) are small non-coding RNAs, which work as the main epigenetic regulators of the cell metabolism. The miRNA expression levels show differences between normal and tumour cells and generally tumour suppressor miRNAs are down regulated in cancer. In addition to cancer development and progression, miRNAs play an important role during cellular reprogramming and cell fate conversion through forced expression of oncogenic transcription factors. We hypothesized that induction of cellular reprogramming via four reprogramming factors (Oct3/4, Klf-4, Sox-2, c-Myc) should change the miRNA expression profile of cancer cells and hence open up a new therapeutic strategy. We first compared the miRNA expression levels in MDA-MB-435 melanoma cells after transfection with Oct3/4, Klf-4, Sox-2, c-Myc, and identified candidate tumour suppressor miRNAs which could be important for tumorigenesis of the transfected cells.

Materials and Methods: MDA-MB-435 melanoma cells were cultured, and then transfected with Sendai virus vectors encoding the four reprogramming transcription factors Oct3/4, Klf-4, Sox-2 and c-Myc. After 27 days of culturing following transfection, microRNAs were isolated from both naive and transfected cells and miRNA levels were analyzed by Agilent miRNA Micro Array. With the help of GeneSpring software, gene targeting and pathway analysis were also performed in order to identify key genes or microRNAs, which could play important roles in tumorigenesis following reprogramming factors.

Results: A significant difference in miRNA expression profile was observed between naive and transfected melanoma cells. Following gene targeting and pathway analysis, we identified mir-1182 as a tumour suppressor miRNA. Upregulation of mir-1182 activated an apoptosis signalling pathway p38/MAPK and caused inhibition of metastatic gene MMP14. In addition, it was shown that some cancerous pathways were inhibited.

Conclusions: This study showed that miR-1182 can act as a tumour suppressor miRNA after transfection with four reprogramming factors. As a proof-of-concept the p38/MAPK signalling pathway, this miRNA has been shown to be involved in regulation of cellular apoptosis in response to DNA damage or oxidative stress. Therefore, activation of mir-1182 following induction of cellular reprogramming may represent a novel therapeutic strategy for the treatment of melanoma.

Conflict of interest.

Poster Session (Sunday 29 January 2017)

Rare Cancers – NET

1516 POSTER Mutational status of Yin Yang 1 gene in rare sporadic insulinomas: the Indian scenario with a review

K. Irshad¹, V. Jyotsna², K. Chosdol¹, S. Agarwal³, S. Pal². ¹AIIMS, Biochemistry, New Delhi, India; ²AIIMS, Endocrinology & Metabolism, New Delhi, India; ³AIIMS, Pathology, New Delhi, India, ⁴AIIMS, Gastro-intestinal Surgery, New Delhi, India

Background: Insulinomas are infrequent pancreatic neuroendocrine tu- mors (PNETs). Although extensive literature is present on the pathogenesis of other PNETs, the genetic causes underlying insulinoma are unclear and need investigation. Recently, three independent studies in the Chinese and Western Caucasian subjects reported a recurrent somatic mutation p.T372R in Yin Yang 1 gene (YY1 T372R) in insulinomas. It was shown to increase insulin secretion by β-cells. However, the status of this gene variation remains unknown in patients of other ethnicities. Hence, here we analyze YY1 T372R mutation in Indian insulinoma patients. We also review other mutation potential genes that have been documented in literature and so far with respect to etiology and population genetics in PNETs, including insulinoma.

Material and Methods: 17 patients diagnosed and operated for insulinoma during 2010 to 2015 at the All India Institute of Medical Sciences were recruited retrospectively. Records of patients’ family history and clinical parameters were collected. Formalin-fixed paraffin-embedded tumors were used to isolate genomic DNA that was subjected to PCR amplification of YY1 exon 5, followed by Sanger sequencing. The obtained nucleotide sequences were aligned against the known sequence of YY1 exon 5 from Ensemble database.

Results: All patients under study presented with clinical symptoms and biochemical diagnosis of insulinoma. On analyzing the sequence of YY1 exon 5 amplicon, we observed the absence of C to G mutation at YY1 exon 5, in all the 17 (100%) insulinoma tumors analyzed. Thus, as compared to the mutation frequency reported in Chinese patients, our results revealed genetic heterogeneity at the studied locus in insulinoma cases belonging to Indian subjects.

Conclusions: Ours is the first report on the status of YY1 T372R in insulinoma cases of Indian origin. On comparison with the Chinese cohort, our results point to genetic heterogeneity in the pathogenesis of insulinoma.
among Indian patients. This genetic difference observed between two population groups within the same continent might be attributable to increased population heterogeneity and admixture of ethnicities among Indians. Therefore, it necessitates the analysis of other documented/novel mutations involved in the genesis of insulinoma.

No conflict of interest.

1516A

NETs: Less common – still misunderstood
N Jervis1, C. Bouvier2. 1NET Patient Foundation, Patient Advocacy and Support, Leamington Spa, United Kingdom; 2NET Patient Foundation, Co-founder and CEO, Leamington Spa, United Kingdom

Neuroendocrine Tumours (NETs) have long been considered rare cancers, with a high percentage of late diagnosis and incurability. Rare, less common, cancers pose a unique set of challenges: late or incorrect diagnosis, accessing clinical expertise and appropriate treatments, paucity in available patient information and difficulties in carrying out clinical studies due to the small number of patients. According to the definition of the project Surveillance of Rare Cancers in Europe (RARECARE), rare cancers are those with an incidence <10/100,000/year. However, recent work, supported by the NET Patient Foundation, undertaken by Public Health England reports an almost doubling of incidence of NETs, compared to previous figures, of 8:100,000 (prevalence of 35–40:100,000). So whilst, by definition, no longer rare – issues experienced by those with a NET remain the same.

Materials and Methods: A critical review of the first published global survey of NET patient experience and subsequent UK survey was undertaken – with comparison made with the UK National Cancer Patient Experience Survey (NET patients were not included). Further information was obtained by undertaking a thematic analysis of calls received by the NET Patient Foundation (the only UK NET patient charity) over the past 12 months.

Results: Key themes identified included late diagnosis – with NET Patients reporting significantly more frequent visits to primary care prior to referral for investigation, delayed referral on to NET specialist centres, with more than 60% having metastatic disease by time of definitive diagnosis. A perceived lack of awareness and knowledge amongst both the general population and medical community about NETs – the exception being where patients were seen at a NET specialist centre. NET patients appear to be less likely to receive information on their disease, treatments, support groups and charities than those with common cancers (<50% compared with >80%).

Conclusion: Despite improvements reported in patient experience for more common cancers, NET patients, alongside others with less common cancers, face a diagnostic and treatment deficit in care related to limited awareness, lack of knowledge, delayed accurate and timely diagnosis and therefore more difficulty in accessing appropriate care.

No conflict of interest.

1517

Pancreatic glucagonoma associated with necrotic migratory erythema: case report and clinical review
D. Cardoso1, A. Cardoso1, F. Cardoso Filho1. 1General Hospital of Fortaleza, Surgery Department, Fortaleza, Brazil

Background: Glucagonoma is the rarest pancreatic neuroendocrine tumor (PNET) which is often heralded by paraneoplastic phenomena, with estimated incidence of 1 in 20 million. Necrotic migratory erythema (NME) is a rare skin disorder and the hallmark clinical finding in glucagonoma syndrome (GS). It is present in almost 70% of patients. The key features of the GS are NME and diabetes mellitus (DM). Its diagnosis requires elevated serum glucagon level and imaging confirming pancreatic tumor. Tail of the pancreas is the most common site, and generally large due to late detection. Late diagnosis is common, mainly because of the extreme rarity of the tumor. Approximately half of patients will have metastatic disease by the time the diagnosis is made, and the most common site is the liver. Because its slow growth, even patients with metastasis may achieve long survival.

Case presentation: Male, 56 yo, had diffuse erythematous lesions in lower trunk, inguinal region, and lower limbs for nine years without remission after multiple admissions, and medical treatments. Abdominal ultrasound was requested, evidencing a mass on pancreatic topography. Abdominal CT was performed and hyperdense mass was confirmed on body-tail pancreatic of 10.0x9.0 cm with mild degree of contrast enhancement. Laboratory tests: presence of anemia, abnormal glucose tolerance test, reduced albumin and total protein levels, and amino acids quite diminished.

Surgery was indicated, and preoperative nutrition rich in amino acids were introduced, and thromboembolism prophylaxis. Two weeks later the skin lesions healed completely. Body-caudal pancreatectomy and total splenectomy were performed with spleen autotransplantation in greater curvature. Pathology in the institute showed a pancreatic endocrine tumor with strong cell IHC showed expression of glucagon and chromogranin A in tumor cells (diagnosis of glucagonoma). In the postoperative period there was an improvement of glucose tolerance curve and normalization of serum levels of glucagon were observed, as well as evidence of spicular metabolism in the scintigraphy. Patient received outpatient follow-up for 10 years, without clinical complications.

Conclusion: Glucagonoma syndrome is a paraneoplastic syndrome with a characteristic triad composed by: pancreatic tumor secreting glucagon, DM, and NME. Early recognition and correct diagnosis of NME is important because it can be the only manifestation of the GS. Other clinical features include weight loss, anemia, cholestasis, diarrhea, neurologic and psychiatric symptom and signs, and thromboembolic phenomena. Complete resection of the tumor is the best treatment. Patients who underwent resection had longer median survival than patients who did not receive surgery, even when diagnosed with later stages of disease.

No conflict of interest.

1518

Predictive value of baseline hematology parameters on outcome of 177Lu-DOTATOC-PRTT
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Background: In external beam radiotherapy it has been well established that improved tissue oxygenation increases therapy efficacy, likely mediated by oxygen derived free radicals. Additionally, emerging evidence suggests immuno-stimulatory effects of radiotherapy through activation of lymphocytes. In peptide receptor radiotherapy (PRTT), the relevance of tissue oxygenation and immuno-stimulation have not been evaluated to date. Therefore, we compared baseline hematology parameters with PRTT efficacy.

Material and Methods: After baseline hematology and laboratory evaluation, 56 patients with metastasized, progressive and DOTATOC uptake positive neuroendocrine tumors (NET) (50% gastroenteral, 26.8% pancreatic, 23.2% other primaries) were consecutively treated with 177Lu-DOTATOC and analyzed retrospectively. Patients received on average 2.1 (range 1–4) cycles of 177Lu-DOTATOC as 7.0GBq (median) doses at 3-monthly intervals. Efficacy was analyzed based on RECIST and best response was classified as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD) in relation to baseline hematology parameters.

Results: Hematology parameters are presented as mean ± standard deviation. The non-parametric Kruskal–Wallis test was used to detect significant differences. Post-hoc analysis with the least significant method was used to evaluate differences between groups. For all parameters with P<0.01, the PD group was significantly different from all other groups.

Conclusions: The significant positive correlations between PRTT outcome and baseline hemoglobin content, baseline erythrocyte cell count and baseline lymphocyte cell count are compatible with a cascade of free radical damage followed by immune activation. As the lymphocyte and neutrophil cell counts result from a differential white blood cell count, it is surprising that we find an inverse correlation between PRTT outcome and neutrophil cell count. No correlation between PRTT outcome and leukocytes or platelets was found. Our results suggest that optimization of hemoglobin content prior to PRTT may be beneficial for therapy efficacy.

No conflict of interest.
Proffered Papers (Saturday 28 January 2017)

Rare Cancers – Sarcoma

1568

ORAL

Pathological fracture and prognosis of high-grade osteosarcoma of the extremities. An analysis of 2,847 consecutive cooperative osteosarcoma study group (COSS) patients

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Background: The objective of this study was to investigate potential correlations between pathological fractures (PFs) and prognosis of patients with high-grade osteosarcoma of the extremities treated between 1980 and 2010 and registered into the COSS-database. Intended treatment included pre- and postoperative chemotherapy and surgery. Univariate survival analysis was performed with Kaplan–Meier-Analysis and compared with Log-Rank-Test and multivariate analysis of the different variables and of the overall survival curves identified that the management of RPS in sarcoma-specialized centers could be associated with a lower locoregional relapse rate. However, it is not clear if for RPS, clinical outcome is more influenced by hospital case volume (HCV) or by surgeon case volume (SCV). The aim of this study is to explore the relationship between the case volume related to the hospital or the surgeon and the quality of surgery in a macroregion of Northern Italy.

Material and Methods: We retrospectively collected data about 2 regions of northern Italy, Piedmont and Aosta Valley, about patients with a diagnosis of RPS during the period 2006–2011 and analyzed OS, care center characteristics according to high or low HCV and SCV and quality of surgical treatment. Patients from different cancer centers were divided, into 2 groups according to a cut-off of 50 sarcomas new cases seen per year. In the first group there were two institutions: 1. HVCCC, a high volume comprehensive cancer center with a sarcoma-committed surgical team (high HCV and high SCV) and a regular RPS-multidisciplinary meeting; 2. HVTC, a high volume tertiary care academic hospital. In the second group there were all other hospitals, defined as secondary care low volume regional hospitals (LVSCH).

Results: Data from 22 hospitals and 138 patients with a diagnosis of RPS from 2006 to 2011 were identified. The division into subgroups according to care center was: HVTC 47 cases (34.1%), HVCCC 25 cases (18.1%) and LVSCH 66 cases (47.8%).

There was a statistically significant difference between HVCCC and HVTC regarding R0 vs R1/R2 distribution (In HVCCC was 85% vs 12%, in HVTC, 49% vs 32%; p = 0.0133). In LVSCH important surgical and histopathological issues were frequently missing: grading, tumor size, surgical margins, tumor fragmentation and primary/recurrent tumors. In both logistic regression models concerning tumoral integrity and surgical margins only the “care center” item demonstrated a statistically significant correlation. The Cox regression model analysis showed a trend of significance concerning a best survival linked to the caring institution and to the primitivity of the lesion.

Conclusions: Among centers with high-volume case (HCV), the analysis of different variables and of the overall survival curves identified that the surgeon’s activity volume (SCV) and a dedicated multidisciplinary board (MDT) may significantly influence the quality of treatment; we can presume that the lower quality of surgery due to less experienced surgical teams or the absence of a dedicated MDT in HVTC could have influenced clinical outcomes. Outside reference or tertiary care centers, the quality of management of RPS could be low because tumor integrity and surgical margins quality are not completely documented.

No conflict of interest.

1569

ORAL

Different quality of treatment in retroperitoneal sarcomas according to hospital-case volume and surgeon-case volume: a retrospective analysis in Italy

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Background: Few available retrospective data and existing guidelines state that the management of RPS in sarcoma-specialized centers could be associated with a lower locoregional relapse rate. However, it is not clear if for RPS, clinical outcome is more influenced by hospital case volume (HCV) or by surgeon case volume (SCV). The aim of this study is to explore the relationship between the case volume related to the hospital or the surgeon and the quality of surgery in a macroregion of Northern Italy.

Material and Methods: We retrospectively collected data about 2 regions of northern Italy, Piedmont and Aosta Valley, about patients with a diagnosis of RPS during the period 2006–2011 and analyzed OS, care center characteristics according to high or low HCV and SCV and quality of surgical treatment. Patients from different cancer centers were divided, into 2 groups according to a cut-off of 50 sarcomas new cases seen per year. In the first group there were two institutions: 1. HVCCC, a high volume comprehensive cancer center with a sarcoma-committed surgical team (high HCV and high SCV) and a regular RPS-multidisciplinary meeting; 2. HVTC, a high volume tertiary care academic hospital.

Results: Data from 22 hospitals and 138 patients with a diagnosis of RPS from 2006 to 2011 were identified. The division into subgroups according to care center was: HVTC 47 cases (34.1%), HVCCC 25 cases (18.1%) and LVSCH 66 cases (47.8%).

There was a statistically significant difference between HVCCC and HVTC regarding R0 vs R1/R2 distribution (In HVCCC was 85% vs 12%, in HVTC, 49% vs 32%; p = 0.0133).

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Conclusions: Among centers with high-volume case (HCV), the analysis of different variables and of the overall survival curves identified that the surgeon’s activity volume (SCV) and a dedicated multidisciplinary board (MDT) may significantly influence the quality of treatment; we can presume that the lower quality of surgery due to less experienced surgical teams or the absence of a dedicated MDT in HVTC could have influenced clinical outcomes. Outside reference or tertiary care centers, the quality of management of RPS could be low because tumor integrity and surgical margins quality are not completely documented.

No conflict of interest.

1570

ORAL

Exploring the potential for PD-1 blockade in sarcoma patients

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Background: The positive treatment effects of anti-programmed cell death-1 (PD-1) antibodies in adult tumors have increased the interest into the expression of PD-1 and programmed death-ligand 1 (PD-L1) in other malignancies. In order to further explore the potential of PD-1 checkpoint inhibitors in sarcoma patients, we assessed the expression of PD-1, PD-L1 and the presence of CD8+ cells in a large group of sarcoma patients.
Proffered Papers, Saturday 28 January 2017

Abstracts S153

Table 1 (abstract 1570). PD-1, PD-L1 and CD8 expression and clinical outcome in sarcoma patients

<table>
<thead>
<tr>
<th>N</th>
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<th>Survival</th>
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<tr>
<td></td>
<td>PD-1+ (%)</td>
<td>PD-L1+ (%)</td>
</tr>
<tr>
<td>OS</td>
<td>52</td>
<td>7 (13)</td>
</tr>
<tr>
<td>ES</td>
<td>22</td>
<td>6 (27)</td>
</tr>
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<tr>
<td>SY</td>
<td>23</td>
<td>6 (26)</td>
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<tr>
<td>DSRCT</td>
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</table>

Methods: Formalin-fixed paraffin-embedded tumor sections of primary osteosarcoma (OS, n = 52), Ewing sarcoma (ES, n = 22), alveolar rhabdomyosarcoma (ARMS, n = 42), embryonal RMS (ERMS, n = 80), synovial sarcoma (SyS, n = 29) and desmoplastic small round cell tumor (DSRCT, n = 9) patients were analyzed by immunohistochemistry for the expression of PD-1 (MRQ-22), PD-L1 (E1L3N) and CD8+ cells (C8/144B) and correlations with clinical outcome were determined.

Results: Table 1 shows the expression of PD-1, PD-L1 and CD8+ cells in all the examined tumor types. A subset of patients per tumor type showed either PD-1, PD-L1 or PD-1+/PD-L1+ expression. No correlation with clinical outcome could be determined for PD-1 expression alone in any of the tumor types. However, PD-L1 expression correlated significantly with better event-free survival (EFS) in ARMS patients and both PD-1+/PD-L1+ expression correlated with worse EFS in ES patients. In addition, all DSRCT samples showed PD-1 expression, of which 3 also showed PD-L1 expression.

Conclusion: PD-1, PD-L1, CD8 expression and clinical outcome in sarcoma patients is dependent on tumor type and expression is only seen in a subset of the patients. High levels of PD-1 expression, either alone or in combination with PD-L1 expression, were determined for the first time previously for DSRCT patients. Clinical association with worse EFS in ES and the high levels of PD-1, PD-L1 and CD8 expression in DSRCTs make further research into the efficacy of PD-1 blockade in ES and DSRCT patients of interest.

No conflict of interest.

1571 ORAL Diagnostic delay in primary osteosarcoma (OST) and Ewing sarcoma (ES) of bone in relation to metabolic activity on FDG PET/CT

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Background: Osteosarcoma (OST) and Ewing’s sarcoma (ES) are bone tumors that mainly affect adolescents and young adults. The rarity of these tumors, the reluctance of young patients to seek medical help and the prevalence of benign musculoskeletal symptoms in this age group all contribute to diagnostic delay. Survival is dismal once metastases have developed. Discordant results regarding the impact of delay on patient outcome have been published. Recently, Ferrari et al (PBC 2016) reported a negative linear relationship between outcome and delay in bone sarcoma, concluding that the intrinsic biology of the tumor outweighs the contribution of diagnostic delay to patient outcome. Here, we analyze the relationship between duration of delay and tumor metabolism depicted by FDG-PET/CT at diagnosis as a potential reflection of intrinsic tumor aggressiveness.

Patients and Methods: Forty-two patients (71.4% male) with a median age of 22 years at diagnosis (range 8–67 years) diagnosed between January, 2007 and April, 2016 in Radboudumc with osteosarcoma (47.6%) or ES (52.4%) of whom an FDG-PET/CT was made at diagnosis and who did not present with synchronous metastases entered the analysis. Diagnostic delay was defined as the interval between the onset of symptoms and histological diagnosis. Patients were grouped in those with short (<median) and long (>median) delay. Spearman’s correlations were calculated between diagnostic delay and maximum standardized uptake value (SUVMax) on FDG-PET/CT at diagnosis. Impact of diagnostic delay on overall survival (OS) in months was calculated with log-rank tests. The tests were performed in the group as a whole and in subgroups of OST and ES patients.

Results: The median interval between symptom onset and diagnosis was 4 months (range 1–36 months; OST median 4; ES median 3.5–136 months). The median SUVMax in all bone sarcoma patients was significantly different for short diagnostic delay: 8.9 versus 6.3 in the long delay group (r = 0.326 p = 0.037). In OST, SUVMax was 10.3 versus 7.0 (r = 0.392 p = 0.07) and in ES 7.6 versus 4.6 (r = 0.398 p = 0.082 for short versus long delay, respectively. Mean OS for the total group was 74.3 months (OST 61.5 months, ES 80.9 months); median survival was not reached in any group. No influence of delay on OS was identified in either subgroup or the population as a whole.

Conclusions: Our small cohort study demonstrates that tumor metabolism at diagnosis is inversely correlated with diagnostic delay, thereby supporting the hypothesis that diagnostic delay reflects a higher likelihood of a less aggressive phenotype for OST and ES.

No conflict of interest.

1572 ORAL Sarcoma in irradiated area (SARI): radiation-induced CD8 T-lymphocytes apoptosis as a potential predisposition factor: results of the SARI trial


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Background: Radiation-related sarcoma is a rare but serious event discussed during the implementation of new techniques and highlighted by radioprotection requirements. A prospective multicenter French trial including 502 breast-cancer patients suggested that radiation-induced CD8 T-lymphocyte apoptosis (RILA) can predict the risk of breast fibrosis. We studied the role of RILA as a predisposition factor to develop a sarcoma as a late event following radiotherapy for a primary cancer.

Materials and Methods: In a case control prospective study, a total of 120 patients suffering from sarcoma observed in an irradiated area were matched with 240 control patients. They have been enrolled in 13 centers working in the French Sarcoma Group. RILA, molecular profiles and genomic testing will be compared in this series. RILA was centrally assessed from blood samples using flow cytometry methods as previously described. This prospective study was registered in ClinicalTrials.gov website, number NCT01504360.

Results: Three hundred and forty seven patients were analyzed (118 case patients and 229 matched control patients) among 360 included patients (96.4%). A majority (74%) were initially treated by radiotherapy for breast cancer. 6.4% for head and neck carcinoma, 8.1% for pelvic tumors and 9.5% for other localizations. Median delivered radiotherapy dose was 50.0 Gy identical in case [8.0–150.0] and control patients [20.0–195.0].

No other stratification factors (age, sexe, location of the primary, delay...
after irradiation) were similar in the 2 cohorts. Median RILA values were significantly different between case and control patients with respectively 18.5% [5.5–55.7] and 22.3% [3.8–52.2] (p = 0.007). Around 20% of the case patients presented a RILA < 12% versus 10.5% in control patients. On the other hand, 59% of control patients had a RILA > 37% compared to 37% for case patients. The RILA test was significantly lower in the breast cancer population with sarcoma versus controlled patients (p = 0.0011).

Conclusions: This study suggested RILA as a robust parameter related to radiation-related sarcoma predisposition. This result has to be further completed by molecular and genomic testing to better discriminate risk or no risk population. Major consequences in clinical practice for frequent tumor types would be discussed as regard indication of radiotherapy.

Trial funded by the Programme Hospitalier de Recherche Clinique 2011

No conflict of interest.

1573

The impact of unplanned surgery and adherence to practice guidelines on outcomes of patients with osteosarcoma

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Background: Patients with rare cancer experience multiple pre-diagnostic consultations in primary care, leading to longer time intervals to referral specialists and state-of-the-art treatment. It is also well known that soft tissue sarcomas are more effectively treated in a specialist centre. Outside referral centre, the risk of unplanned (“whoops”) operation (surgical treatment without prior multidisciplinary team decision) is significantly higher, and it has an impact on overall survival. However, there are limited data related to the bone tumours.

Material and Methods: The aim of this study is to compare outcomes in three groups of osteosarcoma patients treated in the referral centre for adult sarcomas in Poland. We reviewed all osteosarcoma patients hospitalized between 1998 and 2016, who had a minimum follow-up of 3 years. There were 87% of patients with M0 disease, 25% with axial localisation, and 61% with primary tumour above 8 cm. All tissues were reviewed by the second pathologist experienced in sarcoma. We compared overall survival of patient using the Kaplan–Meier estimator and the Cox regression model.

Results: We analysed 299 patients referred to our centre: after an inadequate initial treatment (unplanned surgery) (group A: 46 cases), referred immediately after a diagnostic biopsy (group B: 102 cases), and referred directly, prior to any treatment (group C: 151 cases). Five year overall survival rate was 27%, 49%, and 51% in groups A, B, and C, respectively (p < 0.01). In multivariable analysis, unplanned operation was independently associated with risk of death (HR 1.5; 95% CI: 1.039–2.283). The model was adjusted for stage (M1 vs M0: HR 3.7; 95% CI: 2.479–5.450), localisation (axial vs extremities: HR 1.5; 95% CI: 1.039–2.283) and age (over 50 years vs younger, HR 1.4, 95% CI: 0.981–2.004).

Conclusions: Initial multidisciplinary approach is the main factor that determines local control and overall survival in patients with bone tumours, as much important as the known intrinsic prognostic factors such as stage, histological grade or axial localisation. The influence on outcome of initial multidisciplinary treatment decisions, which is made possible by referral to a specialist centre, is paramount.

No conflict of interest.

1624

Adjuvant radiotherapy with brachytherapy boost in soft tissue sarcomas

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Background: The standard primary treatment for soft tissue sarcoma (STS) is wide surgical resection, preceded or followed by radiotherapy. Purpose of this retrospective study was to assess the efficacy and safety of peroperative brachytherapy (BRT) plus postoperative external beam radiation therapy (EBRT) in a large patients cohort.

Material and Methods: BRT delivered dose was 20 Gy (with Low Dose-Rate or Pulsed Dose-Rate technique). EBRT was delivered with 3D-technique using multiple beams. The prescribed dose was 46 Gy to the PTV, delivered over 23 daily fractions. Neoadjuvant and adjuvant chemotherapy was used in patients with potentially chemosensitive histological subtypes. The primary aim of the study was to analyze overall survival (OS) and local control (LC) in a large patient population treated with surgery, perioperative BRT and adjuvant EBRT +/- chemotherapy (CHT). Secondary objective was to identify prognostic factors for patients outcome in terms of local control (LC), metastasis-free survival (MFS), disease-free survival (DFS) and overall survival (OS). Univariate analysis was estimated according to Kaplan–Meier method and log-rank test and multivariate analysis with Cox proportional hazard models.

Results: From 2000 to 2011, 107 patients (median age: 54 years, range 13–85; median follow-up: 100 months, range 48–176), presenting high grade primary or recurrent STS were treated with surgery, perioperative BRT and adjuvant EBRT +/- CHT. Five-year LC and OS were 80.9% and 87.4%, respectively. At univariate analysis a higher LC was recorded in primary vs recurrent tumors (p: 0.015) and in lower limb tumors vs other sites (p: 0.027). An improved DFS was recorded in patients with lower limb tumors vs other sites (p: 0.034).

Conclusions: The combination of BRT and EBRT is able to achieve satisfactory results. However, patients with recurrent or other than lower limb sited tumors show a worse LC. Prospective studies on combined modality treatment in the adjuvant setting of STS are still necessary to improve these results, particularly in patients with higher risk of relapse.

No conflict of interest.

1625

Clinical management of localized leiomyosarcoma: a single center experience

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Background: Among soft tissue sarcomas, approximately 5–10% are leiomyosarcomas, deriving from smooth muscle cells. The data of 74 leiomyosarcomas were collected and the impact on outcome of patients characteristics, tumor related factors and treatment modalities was analyzed.

Material and Methods: Seventy-four patients with leiomyosarcoma were treated from 1993 to 2013 at University of Florence. All patients underwent surgery and radiotherapy, chemotherapy was administered in high risk disease cases.

Results: The median age was 61 years (22–88). Fifty-three (71.6%) tumors were superficial. In fifty-nine (79.7%) cases the disease was localized at the extremities, the trunk was involved in 15 (20.2%)
cases. Grade 3 disease was found in 47 (63.5%) cases. Seven (9.5%) patients received neoadjuvant chemotherapy, twenty-three (31.1%) patients chemotherapy was administered in the postoperative setting. Wide excision was performed in 65 (87.8%) patients. All patients underwent radiotherapy: preoperative treatment in 5 (6.8%) cases and adjuvant treatment in 69 (93.2%) patients, for a median dose of 50 and 60 Gy respectively. Median follow-up was 60.2 months (range: 11.6–263.9). Local recurrence free survival (DFS-LR), distant metastasis free survival (DFS-DM), overall survival (OS) and disease specific survival (DSS) at 3 years were 87.9%, 70.3%, 85.2% and 82.4%, respectively. At statistical analysis only deep location affected DFS-LR (p = 0.03) and DFS-DM (p = 0.01). At univariate analysis deep lesion (p = 0.00012) and neoadjuvant chemotherapy (p = 0.017) were unfavourably correlated with OS: both tumor location (HR 4.5; 95% CI 1.9–14.1; p = 0.0001) and neoadjuvant chemotherapy (HR 5.8; CI 2.0–17.2; p = 0.0013) were independent predictors of poor OS at multivariate analysis. DSS was negatively influenced by KPS <70 (p = 0.011), deep sided lesion (p = 0.00012) and preoperative chemotherapy (p = 0.009); at multivariate analysis tumor size (HR 5.3; 95% CI 1.9–14.1; p = 0.00085) and preoperative chemotherapy (HR 6.8; CI 2.2–20.7; p = 0.00075) were independent predictors of impaired DSS.

Conclusions: In our series clinical outcome did not differ in operated ley- omiosarcoma patients receiving preoperative or postoperative radiotherapy. Deep lesions had a poor prognosis in terms of local and distant failure and survival. The administration of preoperative chemotherapy was correlated to a worst overall and specific disease survival; this could result from patient selection, since only patients who are not eligible for upfront surgery underwent preoperative chemotherapy.

No conflict of interest.
**1629**

**Prevention of chemotherapy-induced nausea and vomiting in patients receiving ifosfamide: High dose chemotherapy**

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**Background:** The chemotherapy regimens with high dose ifosfamide are highly emetogenic. The standard guidelines for chemotherapy-induced nausea and vomiting (CINV) prophylaxis are the combination of aprepitant (Emend\(^3\)) with a serotonin and corticosteroids. There are drug–drug interaction between aprepitant and ifosfamide, both substrates of CYP3A4. In the literature, this pharmacokinetic interaction increases the risk of ifosfamide induced encephalopathy.

The purpose of our study is to assess the efficacy of the CINV prophylaxis in high dose ifosfamide chemotherapy using corticosteroid plus palonosetron (Aloxi\(^6\)), a longer half-life 5-HT3 antagonist, instead of triple drug standard regimen.

**Material and Methods:** A single center prospective observational study was carried out in chemotherapy naïve patients with newly diagnosed sarcoma who receive high dose ifosfamide (6,000 mg/m\(^2\)) regimens from 01/07/2016 to 11/04/2016. All patients received the combination of palonosetron (0.25 mg, day 1 and every two days) and corticoids (day 1–3). Patient CINV risk factors (gender, age, smoker, history of motion sickness and NV pregnancy) were evaluated. Patients are hospitalized during the chemotherapy administration (D1 to D5) and outpatients completed a daily diary in which the degree of nausea (+ to +++), number of emetic episodes and no rescue antiemetic during acute, delayed and all phases. The secondary endpoint was no emetic episode or no rescue medication.

**Results:** Twenty two patients were included which corresponds to 50 chemotherapy cycles. The average number of cycle per patient is 2.2. The sex ratio (H/F) is 3. The median age is 50 years (range, 21–68). The complete response for acute emesis (24 h after chemotherapy) was 76%, for delayed emesis was 44%. During the acute emesis, rescue treatments were administrated in 26% patients. The complete response to both acute and delayed emesis was 58%. Palonosetron was well tolerated with constipation in 12%, no headache or QT disorders. Ifosfamide induced encephalopathy was observe in one patient.

**Conclusions:** The results show a good tolerance and effectiveness of corticoid and palonosetron regimen in high dose ifosfamide induced nausea and vomiting. Other highly emetogenic protocols could benefit from this therapeutic alternative. None of the 22 patients had encephalopathy. The incidence of this adverse effect is around 30% in the literature; therefore in order to highlight it and support the usefulness of Palonosetron the cohort must be increased in further studies.

**No conflict of interest.**

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**Poster Session (Saturday 28 January 2017)**

**Screening**

**1679**

**Screening of families with hereditary susceptibility to cancer of female reproductive organs**

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Literature review shows that hereditary forms of cancer consist 5−10% from the whole number of cancers. The purpose of this paper is secondary prevention and early detection of malignant tumors in families with high risk of cancer, which will reduce cancer morbidity and mortality in individuals with hereditary susceptibility.

**Objectives of the study:**

1. Identify families with accumulation of malignant neoplasms of female reproductive organs [endometrial cancer, ovarian cancer, breast cancer and multiple primary malignant neoplasms (MPMNI)];
2. formation of hereditary risk groups based on pedigree analysis, clinical, laboratory, genetic, molecular tests;
3. DNA testing for mutations of genes MLH1, MSH2, MSH6, BRCA1 in individuals with oncological risk genetically determined;
4. detection of early stages of malignant and benign tumors in families with high risk of cancer;
5. creation of Cancer Registry of families with hereditary susceptibility to cancer of female reproductive organs.

**Materials and Methods:** In this study we included data from 361 first-degree relatives of 145 female patients with endometrial, ovarian, breast and colorectal cancers. In this study we used methods, as: clinico-genealogical research, molecular testing, creation of data base Family Cancer Registry.

During the study we performed formation of 3 risk groups (high, medium, low), basing on a clinico-genealogical criteria. Clinical investigations of the 361 first-degree relatives from the 3 risk groups. We performed molecular testing of 25 relatives from the high risk group and as a goal of the study we create the Family Cancer Registry.

Our study shows that first-degree relatives have a two- to four-fold increased risk of acquiring cancer of female reproductive organs [endometrial cancer, ovarian cancer, breast cancer and multiple primary malignant neoplasms (MPMNI)] compared to the general population. Frequency among first-degree relatives affected with malignant neoplasms constituted 29.2 ± 2.53%.

Endometrial cancer was detected in 18 (4.9 ± 1.14%) relatives, ovarian cancer in 12 (3.4 ± 0.96%), breast cancer in 14 relatives (4.4 ± 1.78%), MPMN (the location of the first tumor in the body of the uterus) in 12 relatives and MPNN by 3.2% (the location of the first tumors in the ovaries) in 14 relatives by 4%.

**Conclusions:** Genealogical, clinical and genetic criteria are established by the survey in order to identify risk groups forming multilevel distinct hereditary oncology risk's variety and was proposed an algorithm of oncology screening process for individuals with hereditary cancer risk. A cancer registry was created for families with hereditary cancer risk, which is not only a database, but is also an operational registry, which makes possible a specialized monitoring of those families.

**No conflict of interest.**

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**1680**

**Role of FOBT in Assessment of Colonocarcinoma (FACT study)**

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Colorectal cancer (CRC) is the third most common malignancy in the world. In United Nation Meeting on Non-Communicable Disease, there have reported nearly 1.4 million new cases in 2012. This incidence seems low particularly in South Asian countries where screening tools are not readily acceptable Fecal Occult Blood Testing as a screening test in the population for flexible sigmoidoscopy (FS) or standard colonoscopy. Although since various studies have shown that FOBT offers better cancer detection rate 18% (12–24%) when used as a screening test as compared with the FS period at 9% (5–13%).

**Method:** This study was done between a period of 2006 to 2011 in a tertiary care hospital in the northern part of India to see the impact of readily acceptable Fecal Occult Blood Testing as a screening tool in the risk population. During this period we screened around 23978 patients of age group and maintained the demographic data and colonoscopy was offered to FOBT positive cases. Data maintained through for treatment received, recurrence, clinical status, survival, the cause of death. Follow-up was maintained at the rate of 95%.

**Results:** We found a total of 33 patients were FOBT positive. Follow-up colonoscopy revealed that 26 had carcinoma colon, 2 had diverticulosis, 2 were false positive. 17 cases were male while 9 were female. 2 cases have synchronous lesions while in 5-year follow-up one patient developed a metachronous lesion. Colectomy offered and histopathological assessment showed in situ tumour in 4 cases, localised in 5, regional direct in six, regional nodal in six and distant in 5 patients.

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ</td>
<td>98</td>
</tr>
<tr>
<td>Localized</td>
<td>92</td>
</tr>
<tr>
<td>Regional direct</td>
<td>82</td>
</tr>
<tr>
<td>Regional nodal</td>
<td>69</td>
</tr>
<tr>
<td>Distant</td>
<td>9</td>
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</table>

**Conclusion:** In summary, early detection of colon cancer saves lives when a program screens general risk population, FOBT is a good test that is able to reach more people, compare to gold standard colonoscopy that reaches fewer people. This particularly very helpful in south Asian countries because of cultural issues, large population and financial condition, less availability of expertise.

**No conflict of interest.**
**1681**

Comparative effectiveness of initiating colorectal cancer (CRC) screening (scr) at age 45

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**Background:** The incidence of CRC in age group 45−50 is rising based on SEER data. We investigated the outcomes of lowering Scr age to 45 from a societal perspective.

**Materials and Methods:** A Markov model was built to represent the natural history and incidence of CRC in the US general population (GP). Individual level simulation was used to compare 14 Scr strategies (ST). Effectiveness (E) in years (LY), costs in US ($) inclusive of CRC Scr and treatment were measured and discounted at 3%. Incremental cost effectiveness ratios (ICERs) were calculated.

**Results:** Primary comparison (PC) used a cohort of GP aged 45−75 with scr at age 45 (@45) or 50 (@50). This design paralleled a randomized trial approach. A secondary comparison (SC) used a cohort of GP aged 45−75 for @45 and a cohort of GP aged 50−75 for @50. This measured the E and $ of each starting age in the population it targeted. Sensitivity analyses (SA) were performed.

**Results:** In PC colonoscopy (CS) @50 ranked 1 with the highest E and the lowest $ & ICER followed by CS @45 (ranked 2) with an ICER of $23,074. In SC, CS starting @45 ranked 1. In PC and SC all remaining STs were dominated. In PC when CS was removed from Scr options, Fecal Occult Blood Test (FOBT) @45, CT Colonography (CT) every 10 years @50 and CT every 5 years @45 dominated remaining STs with ICERs of $0, $5585, and $31,058, respectively. When CT and FOBT were removed from Scr options, FOBT+FS @45 and DNA @45 dominated remaining STs with ICERs of $0 and $850,790, respectively. Results remained stable in SA.

<table>
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<th>STs</th>
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<th>SC</th>
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<tr>
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<td>1</td>
<td>4518</td>
<td>16.15</td>
</tr>
<tr>
<td>FOB T</td>
<td>2</td>
<td>4518</td>
<td>16.15</td>
</tr>
<tr>
<td>FIT</td>
<td>3</td>
<td>3759</td>
<td>16.19</td>
</tr>
<tr>
<td>FIT + FS</td>
<td>4</td>
<td>3848</td>
<td>16.19</td>
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<tr>
<td>FIT + FS</td>
<td>5</td>
<td>3810</td>
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**Conclusion:** This model supports the effectiveness and cost-effectiveness of beginning Scr for CRC @45 with ICER of <$50,000. When the dominating STs were sequentially removed, STs beginning @45 remained cost effective. Of note, DNA was not a cost effective with an ICER of $850,790 after CS and CT were removed from calculations.

**No conflict of interest.**

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**1682**

Clinicopathological characteristics and treatment of breast cancer among elderly patients at Tokyo Metropolitan Cancer Center

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**Background:** Increasing the budget for the health care of elderly persons is a serious issue in Japan, where life expectancy is the longest in the world and all citizens are covered by social insurance. Breast cancer (BC) is the most common malignancy among Japanese women, hence biennial mammogram screening is available to all women aged >40 years(y), but the upper age limit for this procedure is not regulated. The reported rate of Japanese women aged 65−74 y who undergo breast screening is 20.0%, but whether this presents a good opportunity to diagnose BC among elderly patients remains unknown. Moreover, whether elderly patients with BC should undergo standard treatment is also unclear.

**Materials and Methods:** We retrospectively investigated clinicopathological characteristics and provided treatment options for patients aged >70 y who were diagnosed with BC between January 2010 and December 2015 at the Tokyo Metropolitan Cancer Center Komagome Hospital.

**Results:** Among 1,683 patients, 441 were aged >70 y at diagnosis and 41 others with synchronous or metachronous bilateral breast cancers were excluded from analysis. Thus, 400 patients were included in the final analysis. The age ranged from 70−96 (median, 76) y and 355 (89%) patients had comorbidities. Symptomatic patients numbered 277 (70%), 64 (15%) were identified by breast screening, and 59 (15%) were incidentally diagnosed while undergoing follow-up CT assessment for another disease. The sizes of the primary tumors were T1a/1b/2/3/4A/B/C/D in 34/157/148/14/34 patients, and regional lymph node status was N0/N1/2/N3 in 325/44/14/17 patients, respectively. Clinical stages were 0/I/II/III/IV in 34/153/147/36/30, patients, respectively. Tumors were ER-positive (>10%) and HER2-positive (IHC 3+ and/or FISH >2.0) in 313 and 41 patients, respectively. Among 370 patients with clinical stage 0−III tumors, 347 (94%) underwent curative surgery, and 232 (85%) with ER-positive BC and 17 (45%) with HER2-positive BC underwent adjuvant (adj) hormonal therapy and adj anti-HER2 therapy, respectively. Fifty (68%) patients aged >80 y who had ER-positive cancer underwent adj hormonal therapy, whereas only two underwent adj chemotherapy or anti-HER2 treatment. Among patients with T4 tumors who required multidisciplinary treatment in general, only 5 (20%) could undergo curative surgery with systemic treatment. At a median follow-up of 26 months, 37 patients had died including 15 for whom another disease was the cause. Only one patient with BC identified by breast screening died due to BC.

**Conclusion:** BC is most commonly diagnosed among elderly individuals who are asymptomatic, since screening identified only 15% of BC in this population. Patients with advanced BC were unable to undergo multidisciplinary treatment. Therefore, a more effective procedure is needed to diagnose early-stage symptomatic BC.

**No conflict of interest.**

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**1683**

Comparing best practice in pathways to breast cancer diagnosis for Indian women in the UK and India: a documentary analysis

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**Background:** This paper involves a presentation of emerging findings from a documentary analysis research study of breast cancer information documents for Indian women in the UK and India.

**Material and Methods:** We analysed publicly available documents such as existing leaflets including self-examination instructions and wider breast care information (e.g. symptoms, detection) material. Electronic copies found through internet research as well as hard copies of documents were analysed. We conducted a scoping review of existing relevant literature including (i) studies of available cancer information material and (ii) intervention studies including culturally appropriate information. A score sheet was then developed with 13 higher-level items that had been identified from the literature as “best practice”, i.e. culturally sensitive and relevant content for Indian women.

**Results:** Preliminary results indicate key differences and similarities between India and the UK. In terms of similarities, both illustrations and relevant content for Indian women. This may diminish how
inviting and appealing the written materials are for Indian women and could consolidate attitudes around breast cancer being a Western disease.

In terms of differences, it is common in the Indian literature for information on breast cancer to be presented in combination with cervical cancer within the same document. Women with low levels of literacy are particularly confused. Furthermore, doctors are named in full in the Indian literature portraying a more inter-personal Dr-patient relationship in India. The documents from India also had a more motivational narrative. This includes use of motivational terms that are very personal and direct and are inadvertently related to the stigma of breast cancer in these communities. Included in our analysis were documents that advertised public breast cancer awareness events that tied in with cultural and religious festivals, which was not evident from the UK documents.

Conclusions: Recommendations for service providers in the UK include designing written information that relates to the way in which Indian women understand the Dr-patient relationship and accept and process information in relation to stigma around breast cancer. Furthermore, existing cultural and religious celebration events could potentially be forums for raising awareness in the wider community. They will be familiar for these women and be ‘safe places’ for learning about early detection. Service providers in India could present breast cancer information separately to that of other cancers. This would eliminate the risk of misperception, particularly for women with low-level literacy. Service providers in both the UK and India could do more to ensure that images included in documents relate to Indian women so that they can identify with the information.

No conflict of interest.
positive predictive value of positive screening (before further assessment) was 8.7%. Compared to screen-film mammograms, digital mammograms resulted in a higher cancer detection rate (but a lower detection rate by a second reader), as well as a slightly higher proportion of DCIS. Marked geographical variations in the screening programmes are observed.

Conclusions: The national screening database managed by the French national contains 10 years of records on screening results. Performance indicators indicate a good quality program, which provides the conditions for a reduction in breast cancer mortality in France. Appropriate epidemiological tools to evaluate the impact of the French organized program remain to be defined. Methodological challenges, amplified by a high uptake of opportunistic screening in France, will have to be overcome.

No conflict of interest.

Proffered Papers (Sunday 29 January 2017) Supportive Care

1734 Correlation between symptoms, endoscopic features and treatment response in immunotherapy induced colitis

M. Geukes Foppen1, E. Rozeman1, S. Van Wilpe2, C. Postma2

Supportive Care

ORAL

No conflict of interest.

Proffered Papers, Sunday 29 January 2017 Abstracts S159

Between August 2010 and March 2016 a total of 93 patients were diagnosed with immunotherapy-induced colitis at the Netherlands Cancer Institute. Four patients had two different episodes of immunotherapy-induced colitis. Median age was 58 years (range 30–88 years) and 55% of patients were female. Fifty-six percent of episodes were due to anti-CTLA-4, 20% due to anti-PD-1 and even 44% for the combination of anti-CTLA4 and anti-PD1, one of the most frequent immune-related adverse events. In current treatment algorithms for diarrhea and colitis, patients are treated symptomatically or with corticosteroids based on the severity of their symptoms according to CTCAE criteria. Addition of infliximab is advised for patients with steroid-refractory colitis. The precise role of diagnostic endoscopy is not clear. The aim of this study was to analyze the correlation between symptoms, endoscopic features and treatment response in immunotherapy induced colitis.

Materials and Methods: Patients treated with checkpoint inhibitors, who underwent an endoscopy and/or were treated with corticosteroids for diarrhea, were retrospectively identified. Endoscopies were assessed according to Mayo and van der Heide scores. Correlations between symptoms and endoscopic features were calculated using the Spearman correlation.

Results: Between August 2010 and March 2016 a total of 93 patients were diagnosed with immunotherapy-induced colitis at the Netherlands Cancer Institute. Four patients had two different episodes of immunotherapy-induced colitis. Median age was 58 years (range 30–88 years) and 55% of patients were female. Fifty-six percent of episodes were due to anti-CTLA-4, 22% due to anti-PD1 and 22% due to the combination of anti-CTLA4 and anti-PD-(L)-1. All patients had symptoms of diarrhea; 17% of patients had grade I, 38% grade II and 45% grade III. Seventy-one percent of patients underwent a colonscopy and 26% a sigmoidoscopy. In 3% of patients no endoscopy was performed. In 15 events (16%) the presence of ulcers was diagnosed, using only clinical tumour profile (favourable, moderate, unfavourable), presence of visceral and/or brain metastases and Karnofsky performance score (KPS; 100–0). This study was performed. This is a methodology that analyzes texts on a word-by-word level and counts words that belong to psychology-related categories. Conclusions: From the start of the AYA community in October 2010 until August 2016, 305 patients have joined the community (70% female; mean age at diagnosis = 25.6 years); treated in 43 hospitals in the Netherlands. Thirty users of the patient community completed questionnaires and indicated that the use of the community resulted in acknowledgements and advice regarding their problems (56%) and the feeling of being supported and having valuable contacts with peers (63%). Almost half of the users felt less lonely, 78% experienced recognition in stories of other AYAs and 26% of them felt more self-confident in their own strengths and resources. Fourteen AYA patients gave informed consent to analyze their anonymised content. Content analysis of the discussion forum revealed that the online discussions most frequently addressed emotional expression, emotional support and insight.

Conclusions: The Dutch online community AYA4 provides peer support in a secured digital environment as an important care in this young patient group in order to express their feelings, exchange information and cope with their disease. Further growth of AYA4 is expected since more hospitals in the Netherlands have only recently joined the Dutch AYA platform.

No conflict of interest.

1735 An easy-to-use prognostic model for survival in patients with cancer and symptomatic metastases of the long bones

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Background: Expected survival in patients with metastatic cancer and symptomatic metastases of the long bones is a crucial factor to determine the appropriate palliative treatment to maintain optimal quality of life. Recently, a simple prediction model for patients with spinal bone metastases was developed, using only clinical tumour profile (favourable, moderate, unfavourable), presence of visceral and/or brain metastases and Karnofsky performance score (KPS; 100–0). This study aims to validate the abovementioned model for patients with symptomatic metastases of the long bones.

Methods: Patients treated for symptomatic metastases of the long bones between 2000 and 2013 at the orthopaedic and/or radiotherapy departments were identified (n = 1520; 45% male; mean age 65 ± 12.8 years). Radiotherapy was the primary treatment in 68.5% of the patients, while surgery was the primary treatment in 31.5%. All patient-data needed to build the model was registered. The original tumour profile was adjusted slightly for 2 tumour types. For breast cancer, the molecular phenotype was incorporated in the clinical tumour profile (receptor positive phenotype as favourable; triple negative as unfavourable). For kidney cancer, the clinical
tumour profile was adjusted if there was a solitary metastasis (solitary as favourable; not-solitary as moderate). Survival curves were estimated using the Kaplan–Meier method and accuracy was assessed with the C-statistic. 

**Results:** Median overall survival was 7.4 months (95% CI 6.8–8.1). Primary tumour was categorised into three clinical profiles: favourable (34%), moderate (27%), and unfavourable (39%). Visceral and/or brain metastases were present in 42%. KPS was 80–100 in 43% and 0–70 in 34%. The model distributed the patients as such: category A (12%), category B (30%), category C (30%), category D (22%). Median survival in category A was 30.4 months (95% CI 26.8–33.9), for B 12.9 months (95% CI 11.5–14.4), for C 5.1 months (95% CI 4.3–5.9), and for D 2.2 months (95% CI 1.8–2.5). Harrell’s C-statistic was 0.69.

**Conclusion:** Clinical tumour profile, presence of visceral and/or brain metastases, and KPS according to the previously proposed spinal metastasis prognostic model, provide significantly different prognostic categories for patients with cancer and metastases of the long bones. This indicates that the use of one simple survival for spinal and long bone metastatic cancer patients is possible, which facilitates and encourages its use in routine clinical practice.

1737 Feasibility of advanced practice nurse in lung cancer consultations during early treatment: a phase II study

A. Serena1,2,3, A. Dwyer4, S. Peters2, M. Eicher5,1
1 Institute of Higher Education and Research in Healthcare - University of Lausanne, Doctoral School, Lausanne, Switzerland; 2 Lausanne University Hospital, Oncology; Lausanne, Switzerland; 3 University of Applied Sciences and Arts Western Switzerland-School of Health Sciences Fribourg, Research and development, Fribourg, Switzerland; 4 Institute of Higher Education and Research in Healthcare - University of Lausanne, Research and development, Lausanne, Switzerland

**Background:** Lung cancer and its treatment impose significant physical and psychosocial burden on patients. New models of care are needed to support the increasing supportive care, decrease symptom burden and support symptom self-management. The Advanced Practice Nurse in Lung Cancer (APNLC) role specifically targets these patient needs through specific consultations, contribution to continuous quality development and interprofessional collaboration. To date this role is not well established in many European countries, including Switzerland. The primary aim of this pilot study was to assess the feasibility of APNLC consultations and the ability to collect patient-reported outcome measures (PROMs) during first-line treatment. The secondary aim was to describe changes in self-efficacy for managing lung cancer-related symptoms, symptom intensity/burden and unmet supportive care needs.

1738 The impact of an automated, telephone-based coaching module on the adoption of an exercise program for cancer chemotherapy patients experiencing symptoms

K. Mooney1, S. Beck1, C. Echeverria1, G. Donaldson7, 1 University of Utah, College of Nursing, Salt Lake City, USA; 2 University of Utah, School of Medicine, Salt Lake City, USA

**Background:** Exercise has been shown to help reduce cancer treatment-related symptoms including fatigue, nausea, anxiety and weight gain. However, getting patients to adopt and maintain exercise during chemotherapy is difficult and can involve costly program development. The purpose of this study was to evaluate the effect of an automated symptom monitoring and coaching system that provided coaching about starting and maintaining a home exercise program for patients receiving chemotherapy at the time the patient reported fatigue, nausea, anxiety and/or weight gain.

**Material and Methods:** 180 patients in the intervention arm of a symptom monitoring study daily called an automated telephone-based system, Symptom Care at Home, and reported symptom severity levels including for fatigue, nausea, anxiety, and weight gain. When any of the 4 symptoms were initially reported, participants received automated coaching on the benefit of exercise for their reported symptom and were asked if they would like to set an exercise goal for the week including the number of times/week and minutes each time. Seven days later the automated system ‘remembered’ the goal and asked the participant if the goal had been met, then provided further coaching tailored to the participant’s reported level of success and encouraged setting a new goal for the next week. The primary outcomes of evaluation were the percent of patients who adopted the exercise program by setting one or more goals, the percent achieving one or more goals and whether higher exercise goal attainment produced significant symptom reduction.

**Results:** Participants had a mean age of 55 years. The majority were female with breast or lung cancer and had stage III/IV disease. Length of enrollment in the study averaged 77 days. 167 participants (93%) triggered the exercise coaching module with 103 (62%) setting 1 or more goals and 82 (80%) completing 1 or more goals. Thus, about half of those prompted to begin an exercise program successfully met goals. Participants set multiple weeks of goals, on average 6.3 times with the average goal set involving exercise sessions 3 days/week for 15–30 minutes. Those identifying as non-exercisers at study start (54%) were more likely to adopt goal setting. Participants who achieved a high percentage of goal attainment reported significantly lower symptom severity (p < 0.001).

**Conclusions:** Automated remote coaching of chemotherapy patients about the value of adopting an exercise program at the time they are experiencing symptoms is an efficient and effective approach to improving symptom outcomes for fatigue, nausea, anxiety and weight gain. Patients who describe themselves as non-exercisers are particularly willing to set goals. 

1789 The role of volunteers in quality palliative care delivery

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**Introduction:** Here in India almost 75% of cancer patient die a sad death of neglect due to lack of awareness about palliative care and low economic level. Surveys in India show that two third of cancer patient do not get proper care during the terminal phase of their life. Palliative care through volunteers can make a significant difference in this respect. 

**Objective:** To identify and try to solve, to the extent possible, the main difficulties in giving palliative care to the terminal cancer patients of the area. And evaluate the impact of volunteer’s direct care of palliative patients and their families.

**Methods:** Feedback from patients and their relatives regarding the palliative care they receive from nursing home and from volunteers and compare the two. Also feedback from volunteers regarding their positive and negative experience while delivering palliative care service. Then evaluate the data to compare and improve the quality of service.

**Results:** We carried out two studies. One study was undertaken in nursing home palliative care and another was in home setting by volunteers. Both studies were in adult palliative care services. Since January 2015, 496 cases were studied to enquire about their experience in both home
based care and nursing home care. Both the studies fulfilled our quality appraisal criteria. One found that those families and patients who received home visits from volunteers were significantly more satisfied. The study highlighted the value of the role of volunteers in better satisfaction of palliative care patients and their families.

Conclusions: Further research is needed to evaluate the role of volunteers in palliative care and how it can be delivered appropriately and effectively. We also wish to compare our findings with similar studies elsewhere.

No conflict of interest.

1790 POSTER
Difficulties in providing palliative care for metastatic breast cancer patients in rural India (West Bengal) – experience of an NGO
A. Mannan1, 1Chef Caregiver, Palliative Care, Purba Medinipur, India

Background: In any developing countries state of West Bengal in India has a huge burden of metastatic breast cancer patients in advanced stage coming from rural area where awareness regarding the usefulness of palliative care in rather poor. Our goal is to give a pain free good quality of life in these advanced stage breast cancer patients. Objective of this study is to identify the main difficulties in achieving the above goal in a rural village setting in India.

Method: Advanced breast cancer patients in need of palliative care in various villages in of rural India were selected for this study. Their symptoms and managements in that rural surroundings were evaluated by an NGO (under the guidance of a senior palliative care specialist) working in that area. An attempt was made to identify the main obstacles in getting proper palliative care in a rural setting.

Results: Pain, fatigue are the main symptoms effecting these patients. In most patients pain and other symptoms control were grossly inadequate due to lack of properly trained manpower in the rural India. However regular homecare visits by a group of social workers were of immense help in the last few months of life. NGO team was well guided by a palliative care specialist.

Conclusion: There is a wide gap of trained manpower in this filled in rural areas of India. Dedicated groups from rural area itself need encouragement, repeatedly home visits, awareness built up, prior training to home care giver, so that difficult symptoms can be managed locally along with necessary social and psychological support to these patients.

No conflict of interest.

1791 POSTER
Palliative care in Egypt: the experience of the Gharbiah Cancer Society
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Background and Context: The need for palliative care in middle and low resources countries, including Egypt, is emerging. The Gharbiah Cancer Society (GCS) is a nonprofit, nongovernmental hospital, located in Tanta, the Capital of the Gharbiah governorate in the mid-Nile Delta. The Society provides acute care to patients with cancer including surgery, chemo-, and radiotherapy. Review of 9 year-data of Gharbiah population-based cancer registry from 1999 to 2007 revealed 3480 cancer cases/year, with Age Standardized Rate (ASR) of 161.7/100,000 for males & 120.8/100,000 for females.

Aim: About 70% of cases present in advanced stages (III&IV) with liver metastases. The GCS started a comprehensive palliative care services in April 2011 with 10-bed inpatient unit and 6 days/week outpatient clinic. All palliative care equipment were provided by public donations.

Strategy/Tactics: Through collaboration with National Cancer Institute, Bethesda, Maryland and the San Diego Hospice and the Institute for Palliative Medicine and Middle East Cancer Consortium, a fellowship training program was developed for a medical oncologist in palliative medicine and End-of-Life Care training course for nurses.

Programme/Policy/Process: The program succeeded in convincing local health authorities to increase the recommended opioids dose and to allow more physicians to prescribe opioids for cancer pain. In a period of 24 months, symptom management and palliative care were provided to 195 patients with advanced malignancies. The opioids consumption was increased by 30 folds.

Outcomes/What was learned: The major challenges for the program were inadequate public and health professionals awareness of palliative care services and lack of vehicles and finances to cover home visits. The initial results of the program warrant allocating more resources for coverage of a large number of trainees and instituting a home visits program.

No conflict of interest.

1792 POSTER
Knowledge, attitude and practice and associated factors towards palliative care among nurses working in selected hospitals, Addis Ababa, Ethiopia
F. Zewdu1, T. Kassa1, M. Hallu1, R. Murugan2, D. Woldeyohannes3
1University of Gonder, Nursing, Gonder, Ethiopia; 2Addis Ababa University, Nursing, Addis Ababa, Ethiopia; 3Addis Ababa Science and Technology University. Public health. Addis Ababa, Ethiopia

Background: To provide quality care at the end of life or for chronically sick patients, nurses must have good knowledge, attitude and practice about palliative care (PC). In Ethiopia PC is new and very little is known about the type of services offered and the readiness of nurses to provide PC.

Methods: A cross sectional study design was carried out among nurses working in selected hospitals in Addis Ababa from January 2012 to May 2012. Systematic random sampling was used to select hospitals. Triangulation method was used: Frommelt’s Attitude Toward Care of the Dying (FATCOD) Scale, Palliative Care Quiz for Nurses (PCCN) and practice questions. EPI-INFO and SPSS software statistical packages were applied for data entry and analysis.

Result: Of the total 341 study participants, 104 (30.5%) had good knowledge and 259 (76%) had favorable attitude towards PC. Medical and surgical wards as well as training on PC were positively associated with knowledge of nurses. Institution, individuals’ level of education, working in medical ward and the training they took part on PC were also significantly associated with the attitude the nurses had. Regarding their knowledge aspect of practice, the majority of the respondents 269 (76.2%) had poor implementation, and nearly half of the respondents had reported that the diagnosis of patients was usually performed at the terminal stage. In line with this, physical and medical conditions were highly taken into consideration while dealing with terminally ill patients.

Conclusions: This study concluded that nurses had poor knowledge and knowledge aspect of practice, but their attitude towards PC was favorable. Recommendations are that due attention should be given towards PC by the national health policy and needs to be incorporated in the national curriculum of nurse education.

No conflict of interest.

1793 POSTER DISCUSSION
The spine instability neoplastic score (SINS) in the assessment of response to radiotherapy for bone metastases
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Background: Vertebral metastases are often causing pain and spine instability. Radiotherapy is of significant benefit for painful spine metastases but response to RT can be very variable, also in function of the degree of lesion instability. The Spine Instability Neoplastic Score (SINS) is a recent classification system for diagnosis of spinal instability caused by vertebral metastases. The aim of the study was to find a possible correlation of spine instability defined by SINS with pre-treatment pain and with response to radiotherapy.

Material and Methods: This study included 121 patients with spine metastases treated with palliative 3D conformal radiotherapy. Pain “at rest” and “breakthrough pain”, need for drug therapy in terms of “anti-inflammatory”, “weak opioids”, “strong opioids”, and SINS were assessed before and after radiotherapy. Statistical analysis performed by the correlation coefficient of Spearman and Kruskal–Wallis test.

Results: Pain relief after radiotherapy was observed in 50% and 58% of patients in terms of pain at rest and breakthrough pain, respectively. The correlation between pain before radiotherapy and SINS was not statistically significant for both pain at rest (p = 0.49) but the correlation between pain response after RT and SINS was statistically significant for both pain at rest (p = 0.007) and breakthrough pain (p = 0.047).

Conclusions: The degree of instability, classified according to SINS, to be predictive factor for pain response after RT. SINS might become a valid tool to identify those patients who can benefit the most from RT.

No conflict of interest.
1794
POSTER
Single dose or multifractionated reirradiation for painful bone metastasis
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Background: Pain relief is the main purpose of palliative radiotherapy in patients with painful bone metastasis. Many patients, who have been irradiated once, may need to be reirradiated. The aim of this study was to compare the effect on pain relief between single dose and multifractionated reirradiation in this category of patients.

Methods and Materials: Between January 2012 and May 2016, we reirradiated all 39 consecutive patients with in-field bone recurrence referred to the University Hospital Central ‘Mother Theresa’. The first irradiation dose varied from 27 to 30 Gy and all patients had complete or partial pain relief. We reirradiated 19 patients with a single 8 Gy dose, while 20 others were treated with multifractionated radiotherapy (5 × 4 Gy or 10 × 3 Gy), using 3D conformal radiotherapy. The median interval between two irradiations was 32 months (7–80 months). Anatomical locations of the retreatment were the vertebral spine (cervical, thoracic and lumbar vertebrae), humeral head and pelvic bones. Single dose reirradiation was used more in patients with lower Karnofsky Performance Status and shorter period between irradiations. Pain relief was assessed according to the Brief Pain Inventory score.

Results: Reirradiation was well-tolerated by all patients. While age, gender, cancer type and interval between irradiations were not significantly different between groups, patients undergoing multifractionated reirradiation presented a higher Karnofsky score (77.5% vs. 71.1%, p = 0.035) compared to single dose ones. After 2 months of follow-up, according to the Brief Pain Inventory score, patients presented partial (47.5%) or complete pain relief (52.5%). As expected, complete response was positively and significantly correlated with Karnofsky score and interval between irradiations, resulting respectively in Pearson correlation coefficients of 0.713 (p < 0.0001) and 0.314 (p = 0.049). On the other hand, single dose and multifractionated reirradiation showed no significant different effect on pain relief on independent samples t-test, correlation and logistic regression analysis.

Conclusions: Single dose and multifractionated reirradiation showed the same positive effect on pain relief. On the other hand longer distance between two irradiations and higher Karnofsky score predicted a better reirradiation outcome on painful bone metastasis. Based on such findings, single-dose reirradiation of 8 Gy for pain relief may be regarded as the standard reirradiation dose, given also its convenience in terms of health care costs and side effects.

No conflict of interest.

1796
POSTER
Perceived social support, psychological resilience and gender differences among cancer survivors
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Background: Resilience and Perceived Social Support (PSS) as psychological constructs in the recovery from cancer have been studied widely. They are important predictors giving insight into how different individuals deal with stressful situations in life. Studies have reported that different gender addresses the variables differently. This study aims to find out how well Perceived Social Support predicts the Psychological Resilience in male and female cancer survivors.

Materials and Methods: A purposive sample of 120 male and female cancer survivors, of age range 30–65 years (mean age 47.00 yrs) taken after screening to meet the inclusion and exclusion criteria of the study. Perceived Social Support was measured using PGI Social Support Questionnaire (Indian adaptation). Conner Davidson Resilience Scale (Indian adaptation) was used to assess the Psychological Resilience.

Results: The results indicated a significant positive co-relation between Perceived Social Support and Psychological Resilience in cancer survivors. In a cross-sectional study Perceived Social Support from family played a more important role for effective coping from diagnosis and treatment of cancer. It was found that Perceived Social Support in females differed significantly from males through analysis of T test. Significant gender differences for cancer survivors’ psychological resilience to fight against their disease was found whereby females were generally better resilient as compared to males.

Conclusion: This research revealed that there is a relationship between perceived social support and psychological resilience of cancer survivors. The results of this study have also shown a significant difference between perceived social support, psychological resilience and gender. Females perceived more social support than males and they also scored higher in psychological resilience than their male counterparts. Future research is required to gain greater understanding of men’s support needs. More importantly, efforts to increase social support and Psychological resilience might be useful to improve the quality of life among cancer patients.

No conflict of interest.

1797
POSTER
Effects of a psychosocial intervention programme on improving outcomes of patients with a stoma
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Background: Patients with stoma often experience physical, psychological and social challenges. Limited studies have examined the effects of psychosocial intervention on improving health outcomes on this group of patients. The purpose of this study was to develop a psychosocial intervention programme and examine its effects on the improvement of health outcomes of patients with newly formed stoma.

Material and Methods: This was a two-group pre- and post-tests randomized controlled trial. A total of 84 patients with newly formed stoma due to colorectal cancer surgery in a tertiary hospital in Singapore would be recruited. Participants were randomly assigned into either the intervention group or the control group. Outcomes measured include stoma care self-efficacy, acceptance of stoma, anxiety and depression and quality of life. Data were collected at four time points: before randomization and intervention (baseline), on the day of discharge (mid-intervention), at 4 weeks after discharge (immediately after the intervention) and at 4 months after discharge (3 months after the intervention). Repeated measures analysis of covariance will be used to analyse the data.

Results: Patient recruitment started in September 2015. At present 38 patients have (Intervention group n=20; Control group n=18) have been recruited. Data collection is ongoing and is expected to be completed by December 2016. Analysis of completed data will be performed in January 2017 and results will be presented at the conference.

Conclusions: We developed a psychosocial intervention programme for patients with newly formed stoma, which may improve patients’ stoma-related outcomes. The findings will provide direction for healthcare professionals about education and types of support that could be offered to patients concerning stoma care in the hospital settings, which will eventually improve their quality of life.

No conflict of interest.

1798
POSTER
Familial interaction patterns during the palliative phase of a family member living with cancer
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Background: When a person receives a cancer diagnosis; it influences the entire family and requires changes in the daily life for all family members. Current research highlights the individuals with cancer or their family members’ perspectives, but family systems nursing (FSN) studies are warranted. The aim in this study was to illuminate aspects of familial interactions when one member is in the palliative phase of his/her cancer.

Material and Methods: Narrative family interviews were conducted on 13 families living with cancer. Family interviews allow an interactional process to take place, thus capturing multiple perspectives that highlight how the family interacts and communicates The interviews were transcribed and analyzed according to a hermeneutic method.

Result: Analyses revealed the following: family interaction patterns were adjusted in response to changes in family life, which encompassed three different, but interrelated, patterns – (1) power dynamics in the family, (2) the “secret game” in the family, and (3) multifaceted closeness and distance in the family.

Conclusions: In conclusion, family interactions are complexed and it is difficult for one family member to be aware of everything that happens in the family; therefore, it is crucial to adopt a family perspective in palliative care to be able to meet the family’s needs. It is also essential for the healthcare facilitators to be aware of the complex, multifaceted, and new challenges that these families confront to obtain a greater understanding and feel secure to meet these families.

No conflict of interest.
Factors affecting anxiety and depression among breast cancer patients: a study from Northern India

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Background: The prevalence of psychological distress among breast cancer patients is high and they are at higher risk of developing severe anxiety, depression and potential mood disorders. In the present study, we conducted a prospective study to determine the socio-economic factors associated with anxiety and depression among breast cancer patients and to access the changes of psychological distress after the completion of treatment at 1 year of follow-up.

Material and Methods: This study was conducted among breast cancer patients enrolled in the Department of General Surgery, Sir Sunderlal Hospital, Banaras Hindu University, Varanasi, India. A total of 200 patients who were diagnosed from January, 2013 to December, 2014 were interviewed using the questionnaires of Hospital Anxiety and Depression Scale (HADS). HADS was administered at two time points: at time of diagnosis and 12 months after completion of treatment. The associated factors investigated concerned socio-demographics, socio-economic background and the cancer stage.

Results: Prevalence of anxiety and depression among the breast cancer patients was 37.0% (n = 74) and 28.0% (n = 56) respectively. We found strong association of anxiety with age group (p = 0.014), educational level (p = 0.034), monthly income (p = 0.001) and financial support (p = 0.041). However, marital status (p = 0.014), monthly income (p = 0.017), accompanying person (p = 0.005) and financial support (p = 0.002) were significantly associated with depression. Binary logistic regression analysis showed age younger than 50 years, those who earned less income, illiterate or low level of education, being single and receiving less financial support are more likely to have anxiety. For depression, those who earned less income, being single and receiving less financial support are more likely to have depression. At the 12 month follow-up, 184 patients were re-interviewed. We found significant improvement (P < 0.001) after 12 month follow-up in both anxiety and depression level (mean anxiety level improved from 11.4 ± 3.11 to 7.13 ± 3.63 and mean depression score improved from 8.67 ± 3.11 to 5.13 ± 4.51).

Conclusion: Study clearly shows that younger age group, low monthly income, having less financial support, low education level and being single were associated with anxiety and depression. For managing breast cancer patients, more care or support should be given to this type of patients as they are at high risk of anxiety and depression.

No conflict of interest.

Managing ethical considerations while researching vulnerable participant groups: glioma patient experiences of taking part in research interviews

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Background: At present, the evidence-base informing service provision and psychosocial care for patients with glioma is limited. The paucity in substantive patient-informed research and subsequent service provision may be due to the poor prognosis associated with a diagnosis of glioma and the difficulties in achieving double university- and hospital-based ethics committee approval as well as negotiating the conflicting standards of each committee. Concerns raised by ethics committees include the assumed ‘vulnerable-nature’ of the patient group, the possibility of impaired cognitive function and the potential for causing upset when discussing the difficult nature of the diagnosis. This government-funded study is the first of its kind in Ireland focusing on this patient-group.

Method: The core aim of this study is to generate a substantive theory detailing this patient-groups experiences across the disease trajectory. Repeated, in-depth, semi-structured interviews are being conducted throughout treatment and post-treatment to capture the processes undertaken by patients when managing the changes associated with treatment for glioma. Recruitment of approximately 20 patients is ongoing and has been facilitated with a specialist radiation-oncology hospital in Dublin over a 12-month period.

Results: Changes including the incorporation of a cognitive assessment tool, restrictions on interview location and length, directions for time and place of recruitment and strict limitations on confidentiality in the presence of emotional upset were incorporated in order to meet varying ethical standards required by both ethics committees. Despite concerns raised by the ethics committees, participation levels were high across the disease trajectory. 16 participants between the ages of 19 and 70 have been recruited. None of the participants to date have conveyed a significant level of emotional upset which required referral to supportive services.

Conclusion: In line with previous patient-informed studies, patients have reported therapeutic benefits derived from participation in research study. Patients reported that participation allowed them to process thoughts and emotions related to their diagnosis and treatment that they had not yet fully addressed. Patients were eager to provide advice and successful coping mechanisms and derived meaning and a sense of purpose from contributing to a study from which they would not directly benefit, but had the potential to benefit those in a similar position in the future. In this presentation I will further discuss the ethical and practical conditions for undertaking a qualitative research study of this nature within a clinical setting and provide findings from the context of this study. I will address their implications for further research relating to practice, service design and service provision in oncology settings.

No conflict of interest.
been recommended have therapeutic relationships, 73% reported painful intercourse and 91% found it unsatisfactory. 13%, not required, wanted psychological support.

Conclusion: Data show area of large and wide across emotional sphere. Since these women can live long, we should support them towards better QOL from their traumatic experience through specialist psychological support.

No conflict of interest.

1803 POSTER
A prospective study on quality of life among persons with lung cancer, before and after the chemotherapy treatment – evidence from South India
S. Katapalli1, A1 Iqbal Hospital, General Medicine, Thrissur, India

Background: Lung cancer is usually diagnosed at an advanced stage and survival has not improved in spite of several therapeutic advancements. Since most patients depend on palliative care, it is imperative to evaluate and maintain a satisfactory quality of life in them. This prospective study aimed to assess the quality of life related to health (QLRH) of patients with lung cancer after chemotherapy treatment.

Method: The QLRH was assessed using the questionnaires Quality-of-Life Questionnaire-Core 30 (QLQ-C30) and Lung Cancer Module (LC13), version 3.0.

Results: The sample was made up of 88 women and 99 men, with an average age of 68 years (51–87 years). After the chemotherapy treatment, the authors observed a clinically-relevant improvement in general quality of life, as well as in the symptoms of dyspnoea, insomnia, haemoptysis, cough, thoracic pain, pain in the arm/shoulder, and financial difficulty. There was a worsening on the functional scale which assesses role performance and symptoms of fatigue, nausea and vomiting, sensory neuropathy, pain in other parts, constipation, loss of appetite and alopecia.

Conclusion: Although the patients have an improvement of their QLRH and symptoms related to the lung cancer after the chemotherapy treatment, there was a worsening of the symptoms which resulted from the toxicity of the chemotherapy medications.

No conflict of interest.

1804 POSTER
Examination of the prognostic factors of CART (Cell-free and Concentrated Ascites Reinfusion Therapy) in cancer patients with malignant ascites

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Background: Malignant ascites (MA) is commonly observed in end-stage cancer patients. MA results in a deterioration of quality of life, causing discomfort and distension. Recently, CART has also been used for the management of intractable ascites as well as simple puncture in Japan. However, a methodology specifying the frequency, volume of removal, and reinfusion during each CART session has not yet been established.

Methods: Forty-seven patients who underwent CART between June 2013 and May 2015 were retrospectively examined. The primary endpoint was the relationship between the MA drainage volume during each CART session and patient outcome. Prognostic and predictive factors were also examined as secondary endpoints by dividing the patients into three groups according to the volume of MA removed during the initial session.

Results: A total of 42 patients with cancer were evaluated (16 men, 26 women). The mean age was 65 years (range: 38–89 years). The primary cancer sites were the pancreas, stomach, ovary, colorectum, liver, or unknown (9/9/4/4/4/4). The mean number of CART sessions was 1 (range: 1–10). The mean volume of MA removed was 4366 mL (range: 434–11523 mL). The drainage volume between the initial and subsequent CART sessions tended to decrease, but the difference was not statistically significant (P = 0.862). A comparison based on the volume of removed ascites revealed that the highest mortality rate within 14 days after CART was found in the group with the smallest volume of MA removal. In addition, a significant correlation between lower serum albumin levels and patient mortality within 7 days after CART was observed (P = 0.001).

Conclusion: No significant relationship between the drainage volume at the time of the initial CART and the interval and volume of subsequent sessions was found in our retrospective study. However, the serum albumin level might be a prognostic factor.

No conflict of interest.

1805 POSTER
The prognostic value of the comprehensive geriatric assessment (CGA) in elderly cancer patients (ECP) treated with chemotherapy (CT): a systematic review

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Background: CGA is commonly recommended in ECP.

Aim: To review the evidence on the role of CGA in identifying ECP likely to benefit from CT.

Methods: Medline, Embase, Web of Science, and Cochrane Library were searched using the terms “CGA”, “cancer”, “chemotherapy” and “predictive” or “prognostic”. Inclusion criteria: CGA used for prognostication, all patients

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<th>Outcome parameter</th>
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<td>Toxicity-outcomes</td>
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<td>Being limited in walking 1 block</td>
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<td>Need for assistance in taking medications</td>
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<td>Requiring assistance in mobility and housework</td>
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<td>GFI ≥4</td>
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<td>GVS ≥3</td>
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<td>Impaired ADL</td>
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<td>ADL ≥6</td>
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<td>TUG ≥50 s</td>
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<td>GDS-15 ≤2</td>
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<td></td>
<td>Impaired Physical, Role and Social functioning (QLQ-C30)</td>
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<td></td>
<td>WHO PS ≥1</td>
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<td>ECOG PS ≥2</td>
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<td></td>
<td>≥3 comorbidities</td>
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<td>PNI ≥10</td>
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<td>GFI ≥6</td>
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<td>KPS ≥60</td>
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<td>Frailty</td>
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<td>MMSE ≥27 and/or MoCA ≥26</td>
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<td></td>
<td>Depression</td>
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<td>≥6 medications per day</td>
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<td></td>
<td>Modified MMSE ≥77</td>
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<td>SPSP ≥3</td>
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<td></td>
<td>WHO PS ≥2</td>
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<td></td>
<td>GVS/GOSR ≥86.6</td>
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<td></td>
<td>QoL WAS ≥6</td>
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<td></td>
<td>GFI (≥1 positive item)</td>
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<td>MNA SF ≥7</td>
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Methods: Medline, Embase, Web of Science, and Cochrane Library were searched using the terms “CGA”, “cancer”, “chemotherapy” and “predictive” or “prognostic”. Inclusion criteria: CGA used for prognostication, all patients
Sheffield Hallam University, Faculty of Health and Wellbeing, Sheffield, A.Shrestha1, C.Martin 1, K.Collins 2, L.Wyld1, E.Ohlsson-Nevo1, I. Alkebro2.

Poster Session, Saturday 28 January 2017 Abstracts S165

Choosing quality over quantity of life and the factors influencing this decision.

Results: We retrieved 36 studies (27 prospective). The table presents prospective studies with significant results (n = 23). References and abbreviations will be shown on the poster.

Conclusion: CGA is a useful aid in predicting which ECPs are likely to benefit from CT or will experience CT-associated toxicity. Impaired performance and functional status are predictors of severe CT-related toxicity. An overall frail or vulnerable profile is associated with a higher risk of mortality. Comparison between studies is hampered by the use of multiple screening tools.

No conflict of interest.

1806 PAPER SPOTLIGHT

Validation of the assessment of cancer-related symptom scale

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Background: There is a need to assess cancer patients’ rehabilitation need during treatment and recovery and provide supportive care that can help improve the patients’ quality of life. The Assessment of Cancer-related Symptom Scale (ACSS) is a clinimetric questionnaire developed for systematically measuring the impact of cancer on physical and mental wellbeing. It is developed for a clinical setting to be a tool for oncology nurses to systematically assess the rehabilitation need of the the cancer patient. The questionnaire consists of 18 questions with a 4-point response scale. EORTC QLQ-C30 is a validated instrument for accessing health-related quality of life and consists of 30 questions.

Objectives: To evaluate the validity of ACSS.

Material and Method: After a qualitative evaluation of the understanding of the questions a total of 96 outpatients with 30 different cancer diagnosis completed both ACSS and QLQ-C30. The correlation between ACSS and QLQ-C30 was tested with Spearman’s rank correlation test.

Results: The understanding of the questions was good when tested on patients between 35 and 96 year. The missing value rates of 13 ACSS items were 0.0−2.1% (mean 0.5%). In comparison, the missing value rates for 23 similar items in QLQ-C30 were 0−6.3% (mean 3.4%). A strong (r ≥0.50) correlation was found between 13 items in ACSS and 17 selected similar items in QLQ-C30. Four items had medium (r ≥0.3) and two had small (r <0.1) correlations. The correlation between the functional scales and symptoms scales of QLQ-C30 and single items in ACSS were medium or strong (r =0.43−0.83).

Conclusion: The completeness of the data and the convergent validity of ACSS were better in comparison with QLQ-C30. The ACSS is a valid clinimetric questionnaire for assessment of the impact of cancer-related symptoms in patients with various cancer diagnoses.

No conflict of interest.

1806A POSTER

Quality of life versus length of life in cancer patients: literature review

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Background: Patients with cancer are faced with a difficult decision regarding treatment and there is often a requirement for the patient to make trade-offs between quality of life (QoL) and length of life (LoL). QoL is increasingly recognised as an important end-point of cancer treatment. Tumour-specific therapy can potentially prolong life; however, this may depend on the psychosocial aspects instead. The overall outcome may result in increased dependence on friends and family and further financial burden. The aim of this review is to understand whether cancer patients choose quality over quantity of life and the factors influencing this decision.

Methodology: A review of the literature was conducted using MeSH terms cancer, longevity or length of life, quality of life, patient preferences, decision making, trade off and health utility. Articles retrieved were between inception of databases to October 2016. Only articles published in English were included. Studies with in-depth analyses were included.

Results: Out of 4163 articles that resulted from the search, only 17 articles were included in the study. Patients reported QoL and LoL are both important factors to consider in treatment decision. Older patients were more likely to choose QoL over LoL, whereas, younger patients were more likely to undertake aggressive treatment to increase survival years. Preference for QoL and LoL was not influenced by gender, education, religion, children, marital status or the type of cancer. Those with strong family ties valued LoL. Patients with better health valued LoL and inversely, those with overall poorer physical status prioritised QoL more.

Conclusion: The patient’s treatment choices involve other issues besides physical health. They face an increased psychological burden regarding their individual outlook as well as their relationships with their friends and family notwithstanding any financial or other societal considerations. Although patients have expressed their choice regarding whether they choose QoL or LoL in cancer treatment, in-depth studies are required to understand physical and psychosocial trade-offs and compromises patients are willing to make concerning QoL or LoL.

No conflict of interest.
A nursing intervention to support cancer patients in dealing with chemotherapy-related symptoms at home (CHEMO-SUPPORT): a qualitative study of the patient experience


Background: CHEMO-SUPPORT, a nursing intervention to support cancer patients in dealing with chemotherapy-related symptoms at home, has demonstrated significant reduction in overall symptom distress. CHEMO-SUPPORT offers a counselling session at the start of treatment, a telephone counselling session during the first days at home, a new patient brochure and on-call and online availability of the CHEMO-SUPPORT nursing team. The current study aims at exploring how patients experience the intervention and its different components.

Material and Methods: All 71 respondents receiving the CHEMO-SUPPORT intervention completed a questionnaire on the helpfulness, strengths and weaknesses of the CHEMO-SUPPORT components. Semi-structured interviews were held with a purposeful selection of 9 patients. Helpfulness scores were analyzed descriptively. Interview data and questionnaire responses were analyzed using the Qualitative Analysis Guide of Leuven.

Results: Overall, helpfulness is highly rated with the highest score for the patient brochure (mean score of 8.5/10). While the interview data show that the importance ascribed to the intervention varies by the personal symptom experience, coping and expectations towards professional caregivers, all questionnaire respondents and interview participants appreciate the empathy and real concern the CHEMO-SUPPORT intervention displays. The intervention makes them feel reassured and empowered. At home, the brochure is their companion and the quotes from fellow patients are highly valued, as is apparent in both the interview and questionnaire data. The telephone follow-up demonstrates personal interest and offers opportunity to receive guidance on the symptoms they are experiencing.

Conclusion: While interview participants express their preference to self-manage their symptoms without disturbing professional caregivers, having a direct line to professional assistance feels highly reassuring.

Rethinking exercise identity – a qualitative study among sedentary cancer patients

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Copenhagen University Hospital, UCSF, Copenhagen, Denmark.

Background: Physically inactive cancer patients need targeted interventions to make them receptive to recruitment and participation in exercise interventions. The purpose of this study was to explore breast and colon cancer patients’ attitude and priorities concerning exercise pre-illness and during chemotherapy and concurrently participating in a 12-week multidimensional exercise programme.

Materials and Methods: Thirty-three patients referred to adjuvant chemotherapy at oncology departments were interviewed pre- and post-intervention using semi-structured interviews. Data was analysed using thematic analysis. Multimodal interventions including oncologist’s recommendations and exercise cancer nurse specialist’s counselling were offered prior to the patients’ allocation to two different twelve-week exercise interventions or control group.

Results: Pre-illness exercise had been excluded from patients’ daily lives due to perceptions of exercise as boring, lack of discipline and a stressful working-family life situation. Recommendations from oncologists and nurses inspired the patients to rethink their preconception and attitudes by accepting recruitment and participating in early initiated interventions during adjuvant chemotherapy. Despite the experience of extensive side-effects from chemotherapy, resulting in shorter or longer breaks, most patients demonstrated a high level of discipline and continued to perform exercise. This new self-discipline confirms the patients’ feeling of confidence and belief in their ability to realize and continuously prioritize
exercise behaviour in future. The majority expressed a desire of continuing in group training after the intervention period and planned to join various fitness or sports activities. Three patients experienced a high level of treatment complications resulting in hospitalization; hence they had limited exercise transformed from having no priorities in patients’ daily lives pre-diagnosis to highly prioritized during treatment; from failed exercise discipline to continuous participation. These findings can help guide clinicians and exercise cancer teams on how to integrate physical activity with cancer treatment in physically inactive cancer patients. Increasing the awareness of oncologists on the benefits of exercise during cancer treatment may aid in expanding the number of clinicians who recommend exercise as a supplement to drug-based treatments.

No conflict of interest.

1813 POSTER DISCUSSION

Optimal use of pegfilgrastim (a long-acting granulocyte-colony stimulating factor [G-CSF]) to manage chemotherapy-induced febrile neutropenia (FN) in haematological malignancies: consensus guidance recommendations


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Background: Chemotherapy-induced FN can cause treatment delays and dose reductions, with fatal consequences. Guidelines give recommendations on G-CSF for preventing FN, but guidance on long-acting pegfilgrastim is limited. We analysed expert consensus on guidance on optimal use of pegfilgrastim for preventing chemotherapy-induced FN in patients with haematological malignancies.

Materials and Methods: 1. Literature review to assess current data on pegfilgrastim and identify where guidance is needed.
2. Electronic survey and expert consensus meeting to develop guidance, using Delphi methodology with anonymous voting. Consensus reached if >75% of advisors (>75%) voted ‘agree’ or ‘strongly agree’ with each statement.

Results: 44 key papers were identified. 12 advisors answered the survey; 11 attended the workshop and voted to develop the following consensus statements:

- Curative intent: maintenance of dose-intensity using G-CSF to prevent dose delays/reduction should be standard of care.
- Treatment-associated FN risk ≥20%: G-CSF/pegfilgrastim from cycle 1.
- Treatment-associated FN risk <20%: G-CSF/pegfilgrastim if factors suggest real risk ≥20%.
- Pegfilgrastim and 11 days’ filgrastim have similar efficacy/safety. Pegfilgrastim is preferred to <11 days’ filgrastim due to convenience and compliance.
- Proposed biosimilar pegfilgrastim (LA-EP2006) seems to have a similar efficacy and safety profile as reference product (100% consensus).
- Multiple myeloma patients: pegfilgrastim can be used, but filgrastim may have more applications.
- Acute myeloid leukaemia (AML; induction therapy): consider filgrastim.
- AML (consolidation therapy with curative intent): pegfilgrastim may be prefered.
- Lymphoma/chronic lymphocytic leukaemia or myeloma (targeted treatment): pegfilgrastim or short-acting G-CSF can be considered.
- Palliative chemotherapy: convenience and compliance may favour pegfilgrastim.
- In this era of targeted therapies, additional trials with G-CSF are required.

Conclusions: Recommendations should be used with existing guidelines to optimise pegfilgrastim use in clinical practice.

Conflict of interest: Advisory Board: Professor Hus received speaker’s fees, travel grants, and/or acted on advisory boards for: Amgen, Celgene, Janssen, Roche, Sandoz GmbH. Corporate-sponsored Research: Professor Link received research funding, honoraria, acted on speakers’ bureau and/or consulted for: Amgen, Celgene, Chugai, Lilly, MSD Oncology, Mundipharma, Novartis, Pfizer, Hexal – Sandoz, Teva, Vifor Pharma. Other Substantive Relationships: Dr Aapro received honoraria and/or consulted for Amgen, Bayer, BMS, Celgene, Cephalon, Chugai, Clinigen, Eisai, GenomicHealth, GSK, Helsinn, Hospira, Ipsen, &J J. Kyowa, Merck, Novartis, OrthoBiotech, Pfizer, PierreFabre, Roche, Sandoz, Sanofi, Teva, Vifor, Dr Bocia consulted for Sandoz GmbH; Professor Choquet consulted for Sandoz GmbH; Professor Sliwa consulted for Sandoz GmbH.

1814 POSTER

Patient involvement in research agenda – an evaluation of the methods applied

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Background: Patient involvement in the clinical practice setting has expanded to include collaboration during the research process. This poster aims to present and evaluate a research model for patient involvement applied in the Patient Involvement in Research Agenda (PIRE) study. PIRE challenged the conventional research process by inviting patients with life-threatening cancer, relatives and patient organizations to join forces with clinical specialists and researchers to identify and prioritize future research issues within supportive care and rehabilitation in patients with high-grade glioma (HGG) and acute leukemia (AL) during the cancer trajectory.

Material and Methods: PIRE is an exploratory qualitative study that comprised two sets of three focus group interviews (FGIs); one set for HGG and the other for AL. Three separate diagnose-specific FGIs were conducted with patients, caregivers and specialists, respectively, to create a comfortable peer group dynamic within each FGI. Representative from the relevant patient support organizations were invited to participate in the FGIs for patients and caregivers. A semi-structured interview guide inspired by the James Lind Alliance method and guidelines for planning, carrying out, and evaluating the FGIs has been developed for each FGI. The FGIs were video/audio recorded, transcribed and thematically analyzed.

Results: FGIs were an adequate method to identify future research issues within supportive care and rehabilitation. Participants evaluated their contributions to be of importance and valued exchanging experiences with peers. Clinical specialists appreciated the time given for discussing their shared clinical practice, while researchers were provided with new, individual-oriented values and suggestions for new research to improve quality of clinical practice.

Conclusion: The design and methods applied in this study were helpful in identifying and prioritizing Danish research agenda within neuro-oncology and hematology. This study represents a research model for user involvement informing larger, multicentre international research programme aiming to involve various populations with life-threatening cancer diagnoses.

No conflict of interest.

1815 POSTER

Sensor-controlled scalp cooling in the clinical routine: an effective and safe method to prevent chemotherapy-induced alopecia in women with breast or female genital tract cancer

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Background: Chemotherapy (Ctx)-induced alopecia (CIA) is associated with severe psychological distress in many women involved. Although sensor-controlled scalp cooling (SCSC) is effective in preventing CIA, it is infrequently used in many countries due to physicians’ concerns regarding both safety and feasibility. This retrospective analysis was initiated to obtain detailed information about the effectiveness and safety of SCSC using the Paxman system (Paxman, Huddersfield, UK) in female patients (pts) exposed to CIA-inducing Ctx for breast cancer (BC) or genital tract malignancies in the clinical routine.

Material and Methods: 99 pts who underwent SCSC alongside with Ctx from 2014–2016 were identified from our database: BC, 76; epithelial ovarian carcinoma, 15; others, 6; cancer-pauusals, 48; postmenopausal, 51, 72 pts were treated in a curative intent, 27 were treated in a palliative setting; 66 pts were Ctx-native, 33 pts had a history of prior Ctx. The following Ctx regimens were used: anthracycline-based (A), 4, taxane-based (T), 29; At-based, 51; others, 15. Pts were subjected to SCSC during each Ctx cycle. CIA was quantified according to the Dean score (DS) determined 3 wks after the last Ctx cycle. Data were analyzed regarding feasibility indicated by the SCSC completion rate, quality of
No conflict of interest.

Method and Materials: Chemotherapy naive fifty patients who were planned to receive highly emetogenic chemotherapy protocol (CDDP >60 mg/m², Adriamycin >60 mg/m², Epirubicin >90 mg/m² or Ifosfamide >2 mg/m²) were enrolled. 25 patients were randomly grouped in group A(Standard) and 25 patients in group B(Aprepitant-containing regimen). Complete response no emesis, no rescue was 88% for acute period (24 hrs post chemotherapy) and 76% for delayed period (days 2-5 post chemotherapy) for 25 patients in arm A (Aprepitant-containing regimen). Complete response was 84% for acute period and 72% for delayed period for 25 patients in arm B (Olanzapine-containing regimen). There were no grade 3 and 4 toxicities. No patients who had complete response on cycle 1 developed nausea and vomiting on subsequent cycles. Olanzapine-containing regimen was comparable with aprepitant-containing regimen in control of CINV.

Conclusion: In this study, Olanzapine when combined with dexamethasone and granisetron was very effective at controlling acute and delayed CINV in patients receiving highly emetogenic chemotherapy. Olanzapine can be safe, effective and cheaper alternative for controlling CINV in patient receiving highly emetogenic chemotherapy.

No conflict of interest.

1818 Use of lidocaine 5% patches in post-thoracotomy and post-mastectomy cancer pain

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Background: Cancer pain still remains the challenge of the day. High dose opioids have various side effects and hence its time to bridge through newer options. This study was conducted to analyze the short-term efficacy and patients’ subjective perception of the use of lidocaine 5% patches for pain relief in post-thoracotomy and post-mastectomy cancer patients.

Material and Methods: This is a prospective randomized controlled clinical trial was done in 42 post-thoracotomy cancer patients who came to the palliative care outpatient clinic. The patients were allocated into two groups. In Group A patients lidocaine 5% patch was applied on scar after surgery and in group B placebo patch was applied. Demographic data, variables relating to the severity of the pain, and concomitant therapy both at the start and end of treatment, the need for interventional anesthetic techniques (IAT), patients’ subjective perception and treatment-related side effects were all recorded.

Results: 42 were included with a mean follow-up of 29 days. The treatment led to a statistically significant clinical improvement in pain severity. The VAS score was 3−4 in Group A and 7−8 in Group B (P = 0.04). In Group B, three patients required IAT to relieve the pain whereas in GROUP B 16 required IAT. Seventy five percent of patients were very satisfied with the therapy. No systemic or local adverse events were reported.

Conclusions: The addition of lidocaine 5% patches is effective in the short term for the treatment of neuropathic cancer pain accompanied by allodynia, whether deriving from a painful scar or chest wall tumor.

No conflict of interest.

1820 The use of an interactive cartoon web page to support communication between parents with cancer and their children

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Background: Each year about 6000 Danish children witness that a parent get diagnosed with cancer. To enhance the children's ability to deal with the illness of a parent and to prepare the children for the parent's treatment the webpage HC And www.hcand.dk/om_eller_far_kraeft was developed. The target group of the webpage is children in the age of 3−7 years. In this age group children learn and acknowledge by specific and tangible actions and therefore the webpage is designed from a child’s perspective to demonstrate how cancer is treated with either chemotherapy or radiotherapy. The purpose of this study was to evaluate the use of HC And and to examine if the use of the webpage had supported a better dialogue in the family about the disease.

Material and Methods: This combined qualitative and quantitative study, took place at Department of Oncology at Odense University Hospital from December 2015 to March 2016. In a cross-sectional design new cancer
Poster Session, Saturday 28 January 2017

1821

POSTER

Patient reported skin toxicity and experiences with barrier film on the breast during radiotherapy

P.K. Møller1, I. Habæk 2, B. Haislund 3, A.M. Iversen 4, K. Olling 5, M. Berg 6

Background: Radiation-induced dermatitis is one of the main acute toxicities among breast cancer patients although it has decreased over the last decade due to reduced prescribed radiation dose and CT based doseplanning with less and smaller hotspots. Herst et al 2014 from New Zealand investigated using a safetac-based barrier film (Mepitel® Film) on the skin of breast cancer patients compared to standard care and succeeded in reducing their rates of skin moist desquamation. This small study showed unequivocal that the interactive world of HC And could contribute as a positive tool to support communication between cancer sick patients and their children. The webpage could be used not only in the target group, but also for older children, as it would be beneficial if it was further developed for tablets and telephones.

Results: A total number of 14 parents, one grandparent, and 31 children were included in the study. The parents were 36–46 years old and the children were 3–15 years old.

The results showed that 15 (100%) of the parents and grandparent reported that the use of HC And had demystified the treatment and given the children a greater understanding and comfort of disease and treatment. Furthermore, HC And had supported a better dialogue in the family about the disease and the parents would certainly recommend other parents to use HC And for their young children. Also older children and siblings liked the webpage.

Conclusion: This small study showed unequivocal that the interactive world of HC And could contribute as a positive tool to support communication between cancer sick patients and their children. The webpage could be used not only in the target group, but also for older children, as it would be beneficial if it was further developed for tablets and telephones.

No conflict of interest.

1822

POSTER

State of the nutritional management of patients with cancer: a prospective study

A. Houda1, A. Zineb 1, B. Saber2, E.R. Hassan3, M. Bouchra 1

Background: The therapeutic management of cancer can have significant impacts on the nutritional status of patients leading to undernutrition and deterioration of their quality of life.

The aim of our study was to evaluate the nutritional knowledge, dietary habits of patients and demonstrate the need for oncology dietetics.

Material and Methods: This is a prospective observational study over a period of 4 months (from January to April 2016), including 61 patients under chemotherapy treatment at the National Institute of Oncology of Rabat. The Data collection was performed using an anonymous survey.

Results: The study population presented a mean age of 48 years with a standard deviation of 11.65. The extreme age was 19 and 76 years old, with female predominance (76%) treated for different cancer sites (breast, digestive, rectum, colon, lung, liver, ...). The assessment of nutritional status of our patients by calculating the body mass index (BMI) revealed 48% cases of malnutrition caused by chemotherapy; manifested as loss of appetite (42%), altered taste and smell (37%), nausea and vomiting (11%), swallowing problems (6%) and oral pain (4%). These last seem more relevant in the context of treatment protocols involving docetaxel, turnstables salts and 5-fluorouracil. For nutrition knowledge, only 18% of patients got advice concerning their diets from their doctors and only 7% of our patients were monitored by nutritionists at our institute. The study also showed that some patients kept away some foods: dairy products (22%), meat (48%), and eggs (9%) of their supplies. Consumption of medicinal plants during chemotherapy was observed in 13% of patients.

Conclusion: In order to improve the nutritional care of cancer patients, measures have been proposed, like improving the early medical care of malnutrition, the inclusion of nutritional management in the personalized plan of healing the sick, the establishment of an early and systematic consultation of dietary support, complementary to the medical consultation.

No conflict of interest.

1823

POSTER

Melanoma, riding the rollercoaster: a longitudinal Grounded Theory study of the experiences of melanoma patients and their carers

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Background: There are over 13,000 new cases of melanoma in the UK leading to over 2,000 deaths annually. Incidence rates continue to rise in most European countries with mortality rates remaining relatively stable meaning more patients need surveillance. Melanoma presents a complex pathway where diagnosis, curative treatment and palliative care can be required in quick succession. Support for melanoma patients and their carers in the UK is provided primarily by Clinical Nurse Specialists (CNS) who provide information, advice and support at all disease stages. Service provision is inconsistent regarding CNS availability, their skill set and provision of psychological support. To date little research has examined the support needs of patients with melanoma and their carers in order to direct input and ensure efficient use of resources. The aim is to explore the changing experiences and support needs of melanoma patients and their carers throughout the disease pathway.

Materials and Methods: The study employed a qualitative methodology using a constructivist grounded theory approach. Theoretical sampling was used to recruit 17 melanoma patients from outpatient clinics within a large teaching hospital in the UK. 11 carers and 11 Healthcare professionals (HCPs) participated with patient agreement. Patients and carers were interviewed in-depth, up to 8 times over 2 years and HCPs were interviewed on 2 occasions. Initial topics changed at subsequent time points as interviews took on an emergent design. Focus groups were conducted at the end of data collection to refine the theory.
Results: A Grounded Theory of the way melanoma patients and carers maintained their normal activities and roles was developed. This involved the process of re-thinking aspects of daily life while understanding what melanoma meant to them. Patients and carers experienced changes in terms of their roles, routines and relationships. Roles were maintained where possible but modified to avoid sun exposure. Routines included sun protection measures, self-examination and attending hospital for surveillance. The nature of a relationship determined how much information was shared or whether it was hidden. Relationships with HCPs were seen as different to personal relationships with information still central. HCPs, particularly CDS formed relationships with patients and actively sought to change aspects of patients’ and carer’s routines, such as sun protection. They also engaged in activities to maintain patients’ roles. Patients, carers and HCPs identified similar key time points with diagnosis being the most important.

Conclusions: Through a deeper understanding of the experience of melanoma patients and their carers, healthcare professionals can develop individualised care and contribute to positive experiences. Developing a therapeutic relationship from diagnosis is key to this.

No conflict of interest.

1824 Febrile neutropenia in adjuvant and neoadjuvant chemotherapy for breast cancer: a retrospective study in routine clinical practice from a single institution
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Background: Febrile neutropenia (FN) is one of the most critical and frequent side effect of chemotherapy. Despite many existing guidelines based on the use of granulocyte colony stimulating factor (G-CSF), FN still arises and cripples the quality of life and treatment of many patients. The purpose of this study was to assess in a routine clinical practice the incidence and the management of FN in chemotherapy regimen for early breast cancer.

Material and Methods: Every patient treated for primary breast cancer by chemotherapy in 2014 in the Institut Curie – Hôpital René Huguenin, was included prospectively. The incidence rate of FN and their management were reported. Factors associated with FN were studied with a Poisson regression with robust error variance.

Results: 524 patients received either neoadjuvant chemotherapy (N=130) or adjuvant (N=394). Most patients (80%) were treated with a combination of 5-Fluorouracil, Epirubicin, and Cyclophosphamide (FEC100 3 cycles) followed by Docetaxel 100mg/m² (3 cycles). 18% of patients received a primary prophylaxis (PP) for FN with G-CSF using pegfilgrastim in 64% of cases. 74% of patients over 70 years received a PP. Overall, the incidence rate of FN was 17%. Less than 5% of patients who received the PP suffered from FN. Recurrent FN after secondary prophylaxis occurred in 9% of patients. 47% of FN occurred after the first cycle and 30% after the fourth one, which correspond to Docetaxel 1/3-Trastuzumab, FEC100 chemotherapy regimen was associated with a relative risk of FN of 2.2 (p = 0.03). Among comorbidities, auto-immune or inflammatory diseases were associated with a higher risk of FN (RR: 2.56; p = 0.02).

There was no significant difference between adjuvant and neoadjuvant chemotherapy regarding FN. Management of FN was ambulatory in 72% of cases. Ambulatory patients with FN were treated mainly with the combination of amoxicillin-clavulanic acid and ciprofloxacin. Dose reduction or chemotherapy regimen modification were necessary in 25% of patients after FN. No toxic death was reported.

No conflict of interest.

Conclusion: Incidence rate of FN induced by adjuvant/neoadjuvant chemotherapy in early breast cancer is higher in routine clinical practice than in clinical trials. Prevention and management of FN in order to safeguard patient’s safety and quality of life are a major issue for both medical oncologists and supportive care physicians. Primary prophylaxis in patients at risk (elderly, comorbid patients) especially with FEC regimen is the key stone in managing this side effect.

No conflict of interest.

1825 POSTER DISCUSSION
Changes in cognitive impairment in ovarian cancer patients receiving chemotherapy: a pilot study
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Background: Post-chemotherapy cognitive impairment (PCCI) is a poorly understood side-effect reported by some chemotherapy patients with a potentially severe impact on everyday life. In the elderly cancer patient, cognitive disorders are often underdiagnosed. Ovarian cancer patients can benefit from chemotherapy even in the over 80 population. The effects of chemotherapy on general cognitive function have not previously been reported for ovarian cancer. The purpose of this pilot study was to investigate cognitive function in patients with ovarian cancer and the effects of chemotherapy on this.

Method: In this prospective audit, we used the validated Addenbrookes Cognitive Examination (ACE) version III. It assesses six key abilities of cognition with high specificity and sensitivity. Normative data for the UK suggest a cutoff score of 88–82 to predict dementia. Age-related deviation of the norm is minimal. Consecutive patients with ovarian cancer commencing any new line of chemotherapy were included. ACE was performed on each patient twice – on day 1 of their first treatment and at clinic upon completion of chemotherapy. Two versions of the test were used to avoid recognition. The results of the individual assessments were compared to investigate the effect of chemotherapy on cognition.

Results: 17 patients with ovarian cancer consented. Median age was 67 (range 50–86) 6 patients were chemo naive, 9 received single agent chemotherapy (5 only platinum). 15 had repeat ACE after chemotherapy; one patient (in whom clinically relevant dementia was suspected) withdrew her consent; another patient died from progressive disease. Results are shown in the table.

Seven (41%) patients initially scored below the normative cut-off for cognitive impairment which was previously formally undiagnosed, with a trend amongst previously treated patients (2/6 (33.3%) in chemo naive vs 5/11 (45.5%) in prior chemo). There was no significant age-related difference (mean ACE score 87 vs 86 for age <65 vs >65 years). A mean increase of 1.46 in ACE scores after chemotherapy was found. Subjectively all but one patient felt that treatment had negatively impacted on their cognition.

No conflict of interest.

Patient Age Line of chemo 1st ACE Pre chemo 2nd ACE Post chemo Difference

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Line of chemo</th>
<th>1st ACE</th>
<th>2nd ACE</th>
<th>Difference</th>
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<td>2.6</td>
<td>87</td>
<td>89</td>
<td>1.46</td>
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</tbody>
</table>

Conclusion: 7 out of 17 patients had undiagnosed cognitive impairment prior to starting chemotherapy for ovarian cancer. During chemotherapy most patients felt their cognitive function deteriorated, yet this could not be confirmed using ACE III. Selective testing of individual cognitive abilities in chemo naive patients may be more successful in understanding PCCI.

No conflict of interest.
Survivorship

ORAL

Impact of toxicities and neurocognitive impairment on the health related quality of life (HR-QoL) for survivors of medulloblastoma

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Background: We report our study evaluating the HR-QoL of medulloblastoma survivors previously treated at The Royal Marsden, investigating the relationship with reported long term toxicities and neurocognitive sequelae.

Materials and Methods: In this cross sectional study, HR-QoL was evaluated using PedsQL core and tumour surveys, with possible scores of 0–100. Child/Patient self-reports and/or Parent Proxy reports were collected from 52 paediatric and teenage & young adult (TYA) patients previously treated at RMH for medulloblastoma between 2004 and 2014. Late toxicities were graded in accordance with CTCAE v4.0 and correlated with PedsQL scores for most commonly occurring toxicities; tested using a t-test with a 5% significance level.

Additional neurocognitive testing using WISC-IV was undertaken on a selected subset of 20 children including assessment of working memory, verbal comprehension and perceptual reasoning. The association between the neurocognitive data and the HR-QoL plus core and tumour PedsQL scores, was assessed using Pearson’s correlation.

Results: Median age at diagnosis was 9.0 years (range 1–25 years), median time from treatment was 5 years (range 3 months to 10 years). 84.6% patients had received radiotherapy; 40 craniospinal irradiation. Mean (SD) HR-QoL scores: child reports 66 (17.6); parent proxy scores 57.6 (18.8). Most common toxicities identified on CTCAE included ataxia (82%), hearing impairment (59%), endocrine disorders (57%) memory impairment (44%), concentration impairment (40%) and visual disturbance (30%). Memory impairment showed significant association with both HR-QoL (p = 0.048) and tumour PedsQL (p = 0.024) scores. Ataxia showed significant association with both HR-QoL and tumour PedsQL score (p = 0.056). Median age of children undergoing neurocognitive assessment was 10 years (range 5–18). The mean scores all fell within average range and mean (SD) results were as follows: verbal reasoning 95.1 (24.4), perceptual reasoning 90.1 (19.7), working memory 92.9 (20.2) and general ability index 95.9 (21.8). Verbal comprehension and PedsQL tumour score have a moderate positive correlation and a similar trend was seen with working memory (Table 1).

Table 1. Correlation between PedsQL tumour and neurocognitive scores

<table>
<thead>
<tr>
<th>Correlation coefficient</th>
<th>P value</th>
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<tr>
<td>Verbal comprehension</td>
<td>0.51</td>
</tr>
<tr>
<td>Perceptual reasoning</td>
<td>0.38</td>
</tr>
<tr>
<td>Working memory</td>
<td>0.43</td>
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</table>

Conclusions: This study confirms the impact of neurocognitive sequelae and late toxicities on the HR-QoL of medulloblastoma survivors treated as children or TYA. Both reduced memory impairment and reduced verbal comprehension showed significant correlations with PedsQL scores. Further studies are required to fully understand the interplay between treatment strategy, late effects and HR-QoL in medulloblastoma survivors.

No conflict of interest.

Severe fatigue in adolescent and young adult (AYA) cancer patients: prevalence, impact on quality of life (QoL), and associated factors

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Background: Cancer-related fatigue is frequently reported in adult cancer patients during or after cancer treatment. Knowledge on the prevalence, impact and associated factors of severe fatigue in AYA cancer patients (aged 18–39 at diagnosis) is lacking. The current study determined the prevalence of severe fatigue in AYA cancer patients in comparison with gender- and age-matched population-based controls. In addition, factors associated with severe fatigue were examined.

Materials and Methods: Eighty-five AYA cancer patients consulting the outpatient clinic of the Department of Medical Oncology and/or the multidisciplinary AYA care team of a university medical center in the Netherlands completed questionnaires including the Checklist Individual Strength (CIS-fatigue), QOL-Cancer Survivors, Hospital Anxiety and Depression Scale (HADS), and the Cancer Worry Scale (CWS). Socio-demographic and treatment-related variables were collected by self-report and review of medical records.

Results: The vast majority of participants had been treated with chemotherapy (86%) and had completed treatment at the time of participation (92%). Prevalence of severe fatigue (CIS-fatigue score ≥ 35) in AYA cancer patients (48%, n = 41/85) was significantly higher in comparison with matched population-based controls (20%, n = 51/255; p < 0.001). Severely fatigued AYA cancer patients reported worse QOL (p’s < 0.05). Female gender, being unemployed, higher disease stage (III-IV) at diagnosis, higher CWS scores, and higher HADS scores were moderate to strongly associated with fatigue severity (all p’s < 0.05). Having had radiotherapy and being treated with palliative intent were weak but significantly associated with fatigue severity (p’s < 0.05).

Conclusions: Fatigue is an important symptom for cancer patients of all ages, but is especially challenging for those in the heart of their youth. Severe fatigue was highly prevalent in this group of AYA cancer patients, covering the lives of most whom were treated with chemotherapy. More than twice as many AYA cancer patients than matched population-based controls had severe fatigue. QOL is negatively affected by the presence of severe fatigue, stressing the importance of detection and management of this symptom in patients affected by a life-changing diagnosis of cancer in adolescence or young adulthood.

No conflict of interest.
Survivorship

1928 
Poster DISCUSSION
Survival rate of cervical cancer: a five year review at the National Center for Radiotherapy and Nuclear Medicine, Koorle-Bu Teaching Hospital, Accra, Ghana

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Background: Worldwide, cervical cancer is the second most deadly cancer, causing more than 273,000 deaths each year. Cervical cancer accounts for 2.1% of all deaths and 9% of female cancer deaths. The International Agency for Cancer Research estimated that in 2013, 3038 Ghanaian women developed cervical cancer and more than 80% Ghanaian women died of the disease. This high mortality is due to lack of information and knowledge as well as inadequate diagnoses and treatment. It was estimated that 6.67 million women over the age of 15 were currently at risk of developing cervical cancer in Ghana.

The study aimed at determining the five-year survival rate of cervical cancer patients who received radiotherapy at the National Center for Radiotherapy and Nuclear Medicine (NCRNM), Koorle-Bu Teaching Hospital, Accra, Ghana.

Methods: A quantitative retrospective cohort design was used for this study. Medical records of cervical cancer patients who received radiotherapy in 2007 were obtained from the records office. Descriptive statistics was used to determine frequencies and percentages of tumour stage, age and other factors and their effect on the overall survival rates of patients. The study was carried with ethical approval from Ethics and Protocol Review Committee, School of Biomedical and Allied Health Sciences, University of Ghana.

Results: A total of 100 cervical cancer patients were followed and 76 responded. Forty-one percent (41%) five-year survival rate was noted in the study. It was further noted that patients who received radical radiotherapy recorded 86.7% survival rate. The age range of the participants was between 30-90 years. The total of 56 patients received radical radiotherapy whilst the remaining 20 patients received palliative radiotherapy.

Conclusion: Patients treated at the radiotherapy department of the Koorle-Bu Teaching Hospital in 2007 have 41% survival rate compared to the USA, which is about 59% in African Americans and 69% in Hispanics. The overall survival rate was influenced by the age and stage at which patients presented. The poor rate of survival compared to other countries could be attributed to delayed presentation because of lack of access to screening, and poor awareness of the disease. Also, the absence of appropriate follow-up structure after the cervical cancer treatment may have influenced their life negatively.

No conflict of interest.

1877 
ORAL
Prevalence and associated factors of disability pension in Norwegian cervical cancer survivors

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Background: There are few studies of the work ability of cervical cancer survivors in Norway, persons younger than 67 years are entitled to disability pension if their work ability is permanently reduced with 50% or more. The aim of this study was to identify the prevalence of disability pension and associated factors among Norwegian cervical cancer survivors.

Material and Methods: 354 survivors of cervical cancer without another cancer or relapse, aged 33 to 65 years at survey and with a median time since primary treatment of 11 years (range 6–15), responded to a mailed questionnaire giving information about work ability and health-related issues. Cancer- and treatment related data were retrieved from the medical records.

Results: Median age at survey was 50 years. As to treatment modalities 22% had conisation only, 50% major surgery only, 17% had radiotherapy + eventual chemotherapy and 11% major surgery + radiotherapy (eventual chemotherapy). Twenty-four percent had disability pension, which was significantly higher than 11% among adult females of the general population. Compared to the paid work group, significantly more survivors from the disability pension group had been treated with radiotherapy and eventual cisplatin-based chemotherapy. Survivors of the disability group reported significantly more often low education, cardiovascular or musculo-skeletal diseases, poor self-rated health, chronic fatigue, and daily smoking. These survivors also had higher mean levels of neurotoxic side effects, anxiety, depression, and symptoms on the EORTC QLC C-30 questionnaire. The disability pension group also had significantly lower mean scores on all functional dimensions of the EORTC QLC C-30 questionnaire, and cancer specific symptom experience, and body image, but higher mean scores assessing lymphoedema, menopausal symptoms, and sexual worry. In the multivariable analysis having had radiotherapy with eventual chemotherapy only, older age, low education, high level of pain and neurotoxic side effects, and low level of global quality of life remained significantly associated with holding disability pension.

Conclusion: In long-term cervical cancer survivors the prevalence of disability pension was more than doubled compared to women of the general female population. Disability pension was significantly associated with older age and radiotherapy + chemotherapy only. Active approach to symptom burden could be relevant for improved work ability in such survivors.

No conflict of interest.

1930 
Poster DISCUSSION
Hearing loss after cisplatin-based chemotherapy (CBCT) in testicular cancer survivors (TCSs): less than previously described

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Background: Based on post-treatment audiograms (>12 kHz), but without pre-treatment assessments, 80% of TCSs have been described to have hearing loss (>20 threshold decibel [dB]) at any routinely assessed kHz frequency) after CBCT (Frisina: JCO 2016; 34: 2712).

No conflict of interest.
Aim: In >5-year TCSs to compare the prevalence of hearing loss before and after CBCT and to assess the degree of post-treatment hearing reduction.

Methods: 48 TCSs (median diagnostic age: 31 years) had audiograms (up to 8kHz) before (PRE) and median 10 years after (POST). CBCT: 10 of them also assessed at 12kHz. For each frequency, the number of TCSs with pre- and post-CBCT hearing loss was assessed, the difference representing the number of TCSs with new hearing loss developed after CBCT. For each frequency, median PRE vs. POST hearing threshold differences were also calculated. At the 10-year survey the TCSs also described their subjectively experienced hearing problems as "A little", "Quite a bit" or "Very much") by the validated SCIN instrument (Oldenburg: QoL Life Res. 2006 Jun; 15: 791).

Results: The PRE audiograms (<8kHz) of 17 TCSs (33%) displayed hearing loss at any kHz frequency. 10 years later, the prevalence had increased to 75%. The median PRE vs. POST dB differences increased with increasing frequency (Table). In 19 TCSs the POST audiograms revealed new hearing loss. 8 of 10 TCSs evaluated at 12kHz had developed new hearing loss 10 years after CBCT. At the 10-year survey 13 patients (27%) reported hearing problems (A little: 10; Quite a bit: 3).

<table>
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<th>kHz</th>
<th>PRE vs. POST difference (dB)</th>
<th>#TCSs with new hearing loss</th>
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<tr>
<td>0.25</td>
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<tr>
<td>0.5</td>
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<td>1</td>
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* Median. n = 10.

Conclusion: Pre- and post treatment audiograms are required to evaluate possibly CBCT-related ototoxicity in TCSs which seems lower than previously reported (~40%). Age-dependent hearing loss must also be taken into account before concluding on the role of CBCT for the development of post-treatment hearing loss. Considerable discrepancy exists between hearing loss assessed by audiograms and hearing problems experienced by the patient.

No conflict of interest.
Results: Five-year relative survival of colon cancer increased steadily over time from 41.1% (95% CI 39.6–42.6) in 1998–2001 to 44.2% (95% CI 42.9–45.6) in 2002–2005 and 47.4% (95% CI 46.1–48.6) in 2006–2009. Positive trend in survival was observed in all age groups and for both genders. The increase in 5-year relative survival was the most prominent in 20–49 age group where the survival rate for the three time periods was respectively 44.6% (95% CI 40.4–48.8), 47.3% (95% CI 43.2–51.3) and 52.4% (95% CI 48.2–56.4). The age group of 50–74 years had survival rates of 42.2% (95% CI 40.5–44), 46.1% (95% CI 44.5–47.7) and 49.6% (95% CI 48.2–51.1). The age group of 75+ years had increase in survival rate from 36.1% (95% CI 31.5–41) to 39.4% (95% CI 36–42.8) and 41.7% (95% CI 38.6–44.7) in 2006–2009. Furthermore, the analysis showed that survival decreased with age. The Bulgarian weighted five-year relative survival rate for women was respectively 41.4% (95% CI 39.3–43.5), 45% (95% CI 43.1–47) and 46.9% (95% CI 45.1–48.6). In comparison, survival rate among men was estimated to be 40.8% (95% CI 38.6–43), 43.5% (95% CI 41.6–45.4) and 47.5% (95% CI 46–49.6).

Background: Ovarian cancer remains an important health issue in current gynecologic oncology. It is the second most commonly diagnosed gynecologic cancer and the leading cause of death related to female reproductive system tumors. Cancer recurrence is present in 75% of patients after initial treatment. Markers used in diagnosis of ovarian cancer include CA125 and HE4. The specificity analysis shows greater effectiveness of HE4 than CA125 in identifying patients with malignant ovarian lesions. Studies show that elevated HE4 protein is a sensitive marker of ovarian cancer recurrence and it precedes elevation of CA125 by 5–8 months. The aim of this study is to evaluate the use of HE4 marker in prediction of the course of the disease in female patients with ovarian cancer who have finished the first line chemotherapy, considering concurrently accepted prognostic factors. Furthermore, another aim is to analyse the relationship between HE4 level and the diagnosis of ovarian cancer recurrence, considering its platinum-sensitivity. The study is also aimed to analyze trends in levels of HE4 marker during the second- and third-line chemotherapy in patients with recurrent ovarian cancer and its use in diagnosis of cancer progression during treatment, as well as the use of HE4 biomarker in prediction of therapeutic outcomes for recurrent ovarian cancer (duration of disease stabilization period, partial or total remission).

No conflict of interest.
differences in cognitive functioning according stage and neck dissection. Physical functioning was related with age and primary tumour surgery. Emotional scale was also related with surgery. Global quality of life was found to be worst in <65 years patients.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>65 years</th>
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<th>p value</th>
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<tr>
<td>Physical functioning</td>
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<tr>
<td>Global quality of life</td>
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<td>77.1</td>
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<tr>
<td>Neck dissection</td>
<td>100</td>
<td>83.3</td>
<td>0.099</td>
</tr>
</tbody>
</table>

Conclusions: Our study indicates that clinical and therapeutic characteristics impact on the quality of life of HNC survivors. We have found non-covered needs in physical, emotional and cognitive spheres.

Conflict of interest: Corporate-sponsored Research: We have received a grant from Vegenaft.

1937 POSTER SPOTLIGHT

Holistic needs assessment and care plans for women with gynaecological cancer – do they improve cancer specific health related quality of life? A mixed-methods study

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Background: Cancer and its treatment have lasting consequences for some. In the UK as part of a Broader Recovery Package, the holistic needs assessment (HNA) and care planning is proposed to address unmet needs of people treated for cancer.

The primary objective of this study was to test whether HNA and care planning by an allied health professional (AHP) improved cancer-specific quality of life for women following curative treatment for stage I–III gynaecological cancer. Secondary objectives compared changes between groups in functioning, symptoms, general self-efficacy and generic health related QoL, evaluated the impact on health and social care provision, conducted a cost-effectiveness analysis and explored the impact of HNA and care-planning.

Methods: Consecutive women were invited to participate in a randomised controlled study (HNA and care planning vs. usual care) at a UK cancer centre. Balancing factors were age, tumour site and primary treatment. Data were collected by questionnaire at baseline, three and six months. Women in the intervention group were offered consultations conducted using behavioural change principles with an AHP. Reviews were offered at three months. Outcomes were six-month change in EORTC-QLQ-C30 global score (primary), and in EORTC sub-scales, generic quality of life (SF-36), self-efficacy (General Self Efficacy Scale) (secondary outcomes).

The study was blinded for data management and analysis. Differences in outcomes were compared between groups. Health service utilisation and Quality Adjusted Life Years (from SF-6) were gathered for a cost-effectiveness analysis. Thematic analysis was used to interpret data from an exit interview.

Results: 150 women consented (75 per group), ten completing the intervention undertook an interview. For 124 participants (61 intervention, 63 controls) with complete data, no statistically significant differences were seen between groups in the primary end-point with a mean change in score favouring the control group of 1.5(95%CI −5.7, 8.7). The majority of those interviewed reported important personal gains they attributed to the intervention, which reflected trends to an improvement seen in EORTC functional and symptom scales. Themes from interview data were: dislocation: isolation, uncertainty and vulnerability at the end of treatment; space to be heard and understood by a ‘trustworthy’ independent professional; and moving towards to self-supported management.

Economic analysis suggests a 62% probability of cost-effectiveness at a £30,000/QALY threshold.

Conclusion: Care plan development using behavioural change principles, conducted by an AHP is cost-effective, acceptable and useful for some women treated for stage I–III gynaecological cancers. We suggest, on balance, this should be available for women following treatment and a similar approach tested earlier in the pathway.

No conflict of interest.

1939 POSTER DISCUSSION

What are cancer advanced nurse practitioners’ perceptions and experiences of introducing Holistic Needs Assessment (HNA) into clinical practice to address individual cancer patient’s needs?

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Background: Holistic Needs Assessment (HNA) is recognised as a key component in the recovery package, designed to address the long term needs, and improve both quality of life and patient reported outcomes for those living with and beyond cancer. Advanced Nurse Practitioners (ANP) working in cancer are designated key workers for cancer patients, to assist individuals from diagnosis and throughout the care pathway. Assessment and care planning is considered a fundamental aspect of their role. This study aims to explore the views and experiences of Cancer ANP introducing HNA into clinical practice.

Method: Following ethical approval cancer site specific ANP working within a single cancer centre were approached to take part. The views and experiences of 8 eligible ANP working within 6 tumour sites were explored using semi-structured interviews. Questions regarding barriersexperienced when introducing HNA and facilitators which had aided the introduction of HNA were used. Data was transcribed and then analysed using a thematic analysis approach.

Results: Whilst there was support for HNA, concerns were evident including identifying when and where HNA should be performed and having access to services to address identified concerns. The value of HNA assessments was noted, particularly when matters that may not have been recently discussed were raised. Barriers to introducing HNA included, identifying time within an already full job-plan, access to quiet, private rooms, and the confidence and ability of the ANP to address concerns. Items identified as facilitating its introduction included, a peer support network for sharing experiences, and knowledge, positive attitude and motivation to achieve personalised care.

Conclusion: The report concludes that further work be undertaken to fully understand the role ANPs should play in delivering HNA. The findings suggest Nurse leaders and clinical staff should identify opportunities for training and supervision for those planning to use an HNA tool. A multidisciplinary approach to defining the use of HNA within services should be considered to engage other health professionals.

No conflict of interest.

1940 POSTER DISCUSSION

Patient development of an electronic tool to empower adolescents and young adults with cancer

H. Pappot1, M. Hjerming2, G. Petersen3, K.A. Boisen4, C.U. Niemann5, L.L. Hjalgrim3, Kræftværkets User Network2, Rigshospitalet-University Hospital of Copenhagen, Department of Oncology, Copenhagen, Denmark; 2Rigshospitalet, Department of Hematology, Copenhagen, Denmark; 3Rigshospitalet, Department of Pediatric hematology and oncology-Department of Pediatric and Adolescent Medicine, Copenhagen, Denmark; 4Rigshospitalet, Center of Adolescent Medicine-Department of Pediatric and Adolescent Medicine, Copenhagen, Denmark

Background: In Denmark there are no adolescent and young adult (AYA)-specific departments for the 500 AYAs diagnosed with cancer each year. Based on this fact, the Danish Cancer Society and Rigshospitalet, University Hospital of Copenhagen, funded new AYA-friendly, in-hospital facilities in 2014: a youth sanctuary during cancer-treatment (Kræftværket). An AYA specific room designed with and for AYA-patients, aiming at facilitating and homing social networking among AYAs with cancer. However, the users of Kræftværket have requested additional tools for empowering their life with cancer.

Material and Methods: The objective of this study was to investigate the need for additional empowerment tools among AYAs with cancer to improve survivorship. In order to actively involve young people, a co-creation process with patients as the primary user and source was initiated. Twelve users of Kræftværket, aged 17–28 years including representatives from all over Denmark with different cancer diagnoses, gender and social
backgrounds participated. The development of ideas for empowerment tools happened in a joint venture with participation of a digital health service provider, members of the patient association YoungCancer and health professionals (nurse and doctor) from Krafftverket research-group. The co-creation workshop took place for 2 days outside the hospital in a non-clinical atmosphere and was facilitated by professional User Experience Specialists. The workshop focused on describing the AYAs life with cancer during and after treatment. Further issues were, to identify challenges/ problems and how to resolve these.

Results: The participants emphasized that tools for improvement of survivorship must be readily available both during and after treatment and it was suggested to develop a smartphone app. This app should be easy accessible with the possibility for anonymous use. Important content of the app was identified: (1) a forum for advice, support, information etc., (2) a library with e.g. storytelling (enabling mirroring), facts on and handling of side-effects, (3) an instrument for tracking/self-monitoring of e.g. side-effects and pain, (4) a list of links to information on e.g. patient rights/social security and (5) an agenda function integrating health/appointments, events, rehabilitation activities etc.

Conclusion: AYAs with cancer suggest a smartphone app to achieve empowerment during and after cancer treatment to improve survivorship. Fundraising to perform a user-involving research project with the development of the suggested smartphone app for AYA cancer patients is now ongoing.

No conflict of interest.

1941 POSTER

Post-transplant cancers negatively affect survival of kidney transplant recipients: Results from the Italian multicentric cohort study

D. Serraino1, P. Pissili2, F. Citterio3, L. Fratini4, 1Cro-National Cancer Institute, Epidemiology, Aviano, Italy; 2INMI L. Spallanzani-IRCCS, Epidemiology, Rome, Italy; 3Univ Cattolica S Cuore, Surgery, Rome, Italy; 4IRCCS Centro di Riferimento Oncologico, Medical Oncology, Aviano, Italy.

Background: It is well known that kidney transplant recipients (KTR) have a 2-fold higher risk of cancer than sex- and age-matched people in the general population, but data are available on the impact of post-transplant cancers (PTC) on survival of such people. The aim of the study was to quantify the role of PTC on the survival of KTR.

Materials and Methods: Observational, multicentric cohort study on 10850 KTR enrolled over all of Italy in 19 transplant centers between 1990 and 2010 (median age at transplant: 50.3 years, 64% men). At baseline (i.e., at transplant) information were collected on socio-demographic indicators and clinical data; vital status and the eventual diagnosis of cancer were updated at follow-up visits. Survival was computed from date of transplant to death, cancer diagnosis o date of last follow-up. Statistical differences were computed according to the Kaplan–Meier method. To death, cancer diagnosis or date of last follow-up. Statistical differences were computed according to the Kaplan–Meier method.

Results: 1367 KTR were diagnosed with 1 or more cancers during follow-up, including: 688 solid tumors, 623 skin cancers non melanoma. Overall, the post-transplant survival (PTC) on survival of such people. The aim of the study was to quantify the role of PTC on the survival of KTR.

No conflict of interest.

Proffered Papers (Saturday 28 January 2017)

Thoracic Cancer

1991 ORAL

First-line afatinib for advanced EGFR mutation-positive (EGFRm+) NSCLC: analysis of long-term responders in the Phase III LUX-Lung 3, 6 and 7 trials


Background: The reduced survival (upto 20% at 10 years after transplant) of transplant cancer patients negatively affects survival of kidney transplant recipients (KTR). AYAs with cancer suggest a smartphone app to achieve empowerment during and after cancer treatment to improve survivorship. The workshop focused on describing the AYAs life with cancer during and after treatment. Further issues were, to identify challenges/problems and how to resolve these.

Results: The participants emphasized that tools for improvement of survivorship must be readily available both during and after treatment and it was suggested to develop a smartphone app. This app should be easy accessible with the possibility for anonymous use. Important content of the app was identified: (1) a forum for advice, support, information etc., (2) a library with e.g. storytelling (enabling mirroring), facts on and handling of side-effects, (3) an instrument for tracking/self-monitoring of e.g. side-effects and pain, (4) a list of links to information on e.g. patient rights/social security and (5) an agenda function integrating health/appointments, events, rehabilitation activities etc.

Conclusion: AYAs with cancer suggest a smartphone app to achieve empowerment during and after cancer treatment to improve survivorship. Fundraising to perform a user-involving research project with the development of the suggested smartphone app for AYA cancer patients is now ongoing.

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1941 POSTER

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No conflict of interest.

1941 POSTER

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No conflict of interest.
17.5–24 days for rash/ acne; there were no discontinuations due to these AE.
Factors of atafinib dose reduction due to treatment-related AE was consistent with the LL3/6/7 overall populations; final atafinib doses of 20/30/40/50 mg were observed in 50/25/21/4% in LL3, 13/22/61/4% in LL6, and 32/21/47/0% in LL7. Conclusions: In the LL3/6/7 studies, 10–12% of atafinib-treated pts were long-term responders (treated >3 years). Among these pts, greater proportions of women (LL3/6 only) and Del19+ NSCLC were observed. In this analysis, atafinib conferred a long-term survival benefit of 3–5 years and was well tolerated, with predictable and manageable AE occurring soon after treatment onset.


Excess cancer rate was computed as the difference in lung cancer incidence rate in the intervention group. Excess cancer rate was computed as the difference in lung cancer relative risks (SRR), 95% confidence intervals (CI), and heterogeneity. Random-effects meta-analyses were performed to estimate summary mortality analyses show a SRR for lung cancer mortality of 0.90 (95% CI 0.74 to 1.10), among four trials, and a SRR for all-cause mortality of 0.94 (95% CI 0.89 to 1.00), among five trials. The NLST had a lower weight in the meta-analyses (>80%) and it was the only trial to report a significant lung cancer mortality reduction [RR: 0.80 (95% CI 0.73 to 0.93)]. Excluding NLST led to no reduction of all-cause mortality [SRR: 0.98 (95% CI 0.85 to 1.12)]. In the NLST, there was an excess of stage IA cancers in the screening group but the distribution of stage IB to IIIb cancers was similar in the two groups. The 87 fewer lung cancer deaths in the screening group were associated with the 32% (95% CI 20% to 43%) lower rate of stage IV lung cancers in this group as compared to the control group. The distribution of stage IA to IV cancers in the screening group diagnosed during the 4 years following LDCT screening was the same as in the control group. This is surprising because if screen-detected stage IA cancers were associated with previously undetected cancers, one would expect to diagnose these cancers at a higher stage in the absence of screening, one would expect to diagnose them at a more advanced stage in the absence of screening, one would expect to diagnose these cancers at a higher stage in the absence of screening.

No conflict of interest.

1993

Real-world treatment for malignant pleural mesothelioma: the Belgian experience

M. Rosskamp1, N. Van Damme2, H. De Schutter3, M. Slabbaert4, K. Henau2, M. Priet5, K. Nackaerts6, J.P. Van Meerbek3.1 Belgian Cancer Registry, Research, Brussels, Belgium; 2Belgian Cancer Registry, Program Coordinator, Brussels, Belgium; 3Belgian Cancer Registry, Registration, Brussels, Belgium; 4University Hospital of Ghent, Belgian Mesothelioma Registry, Gent, Belgium; 5University Hospital of Leuven, Pneumology, Leuven, Belgium; 6University Hospital of Antwerp, Thoracic oncology, Edegem, Belgium

Background and Introduction: Malignant mesothelioma (MM) is a rare but aggressive cancer most commonly originating from the pleura for which exposure to asbestos is a well-documented etiological factor. Diagnosis is sometimes difficult and treatment option is often limited to palliative combination chemotherapy, resulting in a median overall survival of 10.7 months (Belgium, 2007–2010). The study aims to provide an accurate treatment data on MM at the Belgian population level by combining information from the Belgian Cancer Registry (BCR) with additional data sources such as the pathology protocols, the Belgian Mesothelioma Registry, the health insurance companies (HIC) and the Multidisciplinary oncology team meeting (MDT) forms.

Material and Methods: The study cohort includes all pleural MM cases reported to BCR and diagnosed between 2004 and 2012 linked to HIC data (N = 1,984; 98.0% of all cases). Median age at diagnosis was 72 years, and a male predominance was noted (M/F ratio 5:1). Administrative HIC data contain information on all reimbursed cancer-related diagnostic and therapeutic procedures and pharmaceuticals. These IHC data served as main source for radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy. Data on radiotherapy and chemotherapy.

Timeframes around incidence date were used to assess first line treatment. Results: Preliminary analyses showed that for 71.3% of cases a MDT was done within 6 months after diagnosis ranging from 58.4% in 2004 to 82.9% in 2012. 72.2% of patients underwent tumour-directed treatment, defined as either surgery, chemo- or radiotherapy. As expected, the proportion of patients receiving treatment decreased with age at time of diagnosis. More than half of the patients (59.7%) received first line chemotherapy. Cisplatinum-pemetrexed regimen was the most frequently used schedule, with pemetrexed administration gradually increasing from its market approval in 2005 onwards. 822 patients (41.4%) received at least one episode of radiotherapy. More than 80% received their first irradiation within 3 months after diagnosis. Most were short series (1–10 fractions), presumably meant for palliation and/or prophylactic irradiation of insertion tracts.
Only few patients underwent radical surgery (4.8%). Neoadjuvant chemotherapy was administered in 73.7% and adjuvant radiotherapy (mostly long series) in 69.5% of surgically treated cases.

**Conclusions:** This study provides information on population-based management of MM in Belgium by using multiple data sources. Real-life treatment practices were revealed, suggesting that combining information from different data sources helps in overcoming the difficulties of single sources to estimate treatment patterns. Further investigations on referral practices, centre volumes and survival analyses are planned.

**No conflict of interest.**

**ORAL**

**Phase 2 study of lenvatinib in patients with RET fusion-positive adenocarcinoma of the lung**

V. Velcheti1, T. Hida2, K.L. Reckamp3, J.C. Yang4, H. Nokihara5, P. Sachdev6, K. Feit7, T. Kubota8, T. Nakada9, CE Dutcus, M. Ren9, T. Tamura8. 1Taussig Cancer Institute-, Cleveland Clinic-, Cleveland-, OH, USA; 2Aichi Cancer Center Hospital, Nagoya, Japan; 3City of Hope Hospital-, Lung Cancer and Thoracic Oncology Program, Duarte-, CA, USA; 4National Taiwan University Hospital and, National Taiwan University Cancer Center-, Taipei City, Taiwan; 5National Cancer Center Hospital-, Tokyo, Japan; 6Eisai Inc.-, Clinical Research, Woodcliff Lake- NJ, USA; 7Elisai Co., Ltd., Tokyo, Japan; 8St.Luke’s International Hospital-, Thoracic Center, Tokyo, Japan

**Background:** Adenocarcinoma, a type of non-small cell lung carcinoma (NSCLC), is one of the most common forms of lung cancer. RET fusions activate RET kinase and occur in 1% to 2% of these patients (pts). Lenvatinib (LN), a multikinase inhibitor whose targets include RET, may activate RET kinase and occur in 1% to 2% of these patients (pts).

**Material and Methods:** This open-label phase 2 study enrolled pts with RET-positive lung adenocarcinoma. Pts received LN 24 mg/d in 28-d cycles until disease progression or unacceptable toxicity. Notably, pts may have received prior RET-targeted therapy. The primary endpoint was objective response rate (ORR). Secondary endpoints included progression-free survival (PFS), overall survival (OS), disease control rate (DCR; complete response [CR] + partial response [PR] + stable disease [SD]).

**Results:** 25 pts with RET-positive NSCLC enrolled (KIF5B-RET: 13, other 12). 15 (60%) had >2 prior lines of therapy, 7 (28%) had prior RET therapy, and only 2 (8%) had no prior therapy. 16 (64%) were never smokers, 1 (4%) current smoker, 7 (28%) former smokers, and 1 (4%) unknown. Grade >3 toxicity occurred in the majority of pts. ORR was 16% (confirmed PRs). DCR was 76%. The table shows efficacy data by previous RET therapy. Median duration of treatment was 16 weeks (range: 2–117). Grade >3 treatment-emergent adverse events (TEAEs) were reported in 21 pts. 9 (36%) pts was possibly related to LN (pneumonia). TEAEs requiring drug withdrawal, dose reduction, and dose interruption occurred in 5 (20%), 16 (64%), and 19 (76%) pts, respectively. The most common TEAEs included hypertension (68%), nausea (60%), decreased appetite (52%), diarrhea (52%), proteinuria (48%), and vomiting (44%).

<table>
<thead>
<tr>
<th>Prior RET therapy</th>
<th>All pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n = 7)</td>
<td>No (n = 18)</td>
</tr>
<tr>
<td>ORR*, n (%)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Median PFS (95% CI), months</td>
<td>–</td>
</tr>
<tr>
<td>Median OS (95% CI), months</td>
<td>–</td>
</tr>
<tr>
<td>DCR, n (%)</td>
<td>6 (86)</td>
</tr>
<tr>
<td>CBR, n (%)</td>
<td>4 (57)</td>
</tr>
</tbody>
</table>

**CI:** confidence interval; **DCR:** disease control rate, defined as CR+PR+SD lasting >7 weeks; **NE:** not evaluable.

**All confirmed partial responses.**

**Conclusions:** LN showed promising clinical activity in pts with RET-positive NSCLC. For most pts, toxicities were manageable with dose modification. These results provide support for LN as a potential treatment for RET-positive NSCLC.

**No conflict of interest.**

**ORAL**

**Diagnostic performance of whole-body diffusion-weighted imaging compared to PET-CT plus brain MRI in staging clinically resectable lung cancer**

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**Background:** Precise staging of lung cancer is usually evaluated by PET-CT and brain MRI. Recently, whole-body diffusion-weighted magnetic resonance imaging (WB-DWI) can be applied for the staging of lung cancer. The aim of this study is to determine whether the diagnostic performance of lung cancer staging by WB-DWI is more accurate than that of PET-CT+brain MRI.

**Material and Methods:** PET-CT + brain MRI and WB-DWI were used for lung cancer staging before surgery. There were 59 adenocarcinomas, 16 squamous cell carcinomas and 6 other carcinomas.

**Results:** PET-CT + brain MRI correctly identified the pathologic N stage in 67 patients (82.7%), with overstaging in 5 patients (6.2%) and understaging in 9 patients (11.1%), giving a staging accuracy of 0.827. WB-DWI correctly identified the pathologic N stage in 72 patients (88.9%), with overstaging in 1 patients (1.2%) and understaging in 8 patients (9.9%), giving a staging accuracy of 0.869. There were no significant differences between the accuracies. PET-CT + brain MRI correctly identified the pathologic stages in 61 patients (75.3%), with overstaging in 4 patients (4.9%), and understaging in 16 patients (19.7%), giving a staging accuracy of 0.753. There were no significant differences between the accuracies.

**Conclusions:** Diagnostic efficacy by WB-DWI for lung cancer staging was equivalent to that by PET-CT + brain MRI.

**No conflict of interest.**

**POSTER**

**Profile of lung cancer in a developing country: single centre experience**

P. Gogia1, 2 Senior Resident, Radiation Oncology, New Delhi, India

**Background:** Adenocarcinoma is the commonest histological subtype of non-small cell lung cancer (NSCLC) in most of the Western countries. However, in India squamous cell carcinoma has been reported as the commonest histological type in most of the series. The aim of the study was to analyze the clinico-pathological profile, treatment outcome and survival of NSCLC treated at our centre.

**Materials and Methods:** We analyzed 364 NSCLC registered at our centre over a period of three years. They were evaluated for their clinical and pathological profiles, treatment received and outcome. We also analyzed epidermal growth factor receptor (EGFR) in 250 patients for which formalin-fixed, paraffin-embedded tissues was available. EGFR sequencing was performed with ABI PRISM 310 genetic analyzer.

**Results:** Median age was 55 years with a male:female ratio of 5:1. Seventy percent of patients were smokers. Adenocarcinoma was the commonest histological subtype after the pathology review. Among NSCLC, 75% cases were of stage IV. Forty percent of patients had mutation in one of the four exons characterized. Patients whose EGFR mutational status was not available at presentation before the start of treatment were started on chemotherapy. If EGFR mutational analysis was available and mutations
were present, the patients were started on either upfront tyrosine kinase inhibitor (TKI), 30%, or on chemotherapy arm were allowed to finish six cycles and then start with maintenance TKIs, 40%. The median progression free survival for patients with and without mutations was 12 months and 8 months. A median PFS of 16 months was seen in the mutation-positive group that received both chemotherapy followed by switch maintenance with TKIs versus 9 months in the group that received only TKI.

**Conclusions:** This analysis suggests that adenocarcinoma, the commonest histological subtype in India. Most of the patients present at advanced stage and outcome remains poor. The prevalence of EGFR mutations in this population of NSCLC patients was 42% with exon 19 mutation being the most common.

**No conflict of interest.**

**2047**

Malignant pleural mesothelioma (MPM) evaluation with 11C-methionine PET/CT before and after talc pleurodesis

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**Background:** Tumor assessment with conventional criteria based on contrast-enhanced computed tomography (CT) measurements is challenging in malignant pleural mesothelioma (MPM), because of its diffuse pattern of growth. 18F-FDG PET/CT has proved to be useful in detecting malignant pleural lesions, although unreliable results have been reported in patients receiving talc pleurodesis due to induced inflammatory reaction. In this study we aimed to define the role of 11C-methionine PET/CT in the characterization of MPM lesions before and after talc pleurodesis.

**Materials and Methods:** From September 2014 to February 2016, 30 consecutive patients referred to our Institution for talc pleurodesis in clinical suspicion of MPM were prospectively enrolled. Patients were evaluated at baseline (4 days post-procedural inflammation in case of large MPM lesions, whereas for other lesions) with two consecutive investigations: 11C-methionine PET/CT (experimental) and 18F-FDG PET/CT (standard).

**Results:** The interim analysis was completed in 15 patients (M:F=13:2; mean age 73 years) affected by MPM (12 epithelioid, 3 non-epithelioid). All tumors showed increased uptake of 11C-methionine at baseline: median SUVmean, SUVmax, metabolic tumor volume (MTV) and metabolic tumor burden (MTB = MTV x SUVmean), and statistically compared to pathological findings at videothoracoscopy.

**Conclusion:** 11C-methionine PET/CT offers a more accurate detection of MPM lesions and may be more effective compared to 18F-FDG PET/CT in the characterization of MPM lesions after talc pleurodesis.

**No conflict of interest.**

**2049**

Carcinomembryogenic antigen, C-reactive protein and lactate dehydrogenase measurement in pleural fluid of patients with malignant pleural effusion. A case-control study with multivariate analysis

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**Background:** Malignant pleural effusion (MPE) is common in patients with advanced lung cancer, mesothelioma or pulmonary metastases (PMs). Unfortunately, the pleural cytology (PC) sensitivity is usually low, and thus more invasive diagnostic procedures, including video-assisted thoracoscopic surgery (VATS)-guided biopsy, are often required. In all patients, the evaluation of specific gravity, pH, glucose and protein content of pleural fluid (PF), as well as the measurement of one or pleural markers is currently performed, with the aim of confirming (or excluding) a MPE. The goal of this study was to evaluate the accuracy of PC and carcinoembryogenic antigen (CEA), C-reactive protein (CRP) and lactate dehydrogenase (LDH) assay of PF of patients with a history of cancer and a PE suspicious for metastatic disease suggesting MPE.

**Materials and Methods:** We evaluated the results of PC and PF analysis of 40 patients with confirmed MPE (cases) and 57 sex- and age-matched controls with benign pleural effusion (overall median age 71, range 28-86 years). CEA, CRP, and LDH were measured using a chemiluminescent (CLIA) immunoassay, a human sandwich (quantitative) enzyme-linked immunosorbent assay (ELISA), and a colorimetric quantification assay, respectively. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) were obtained. The standard error (SE), the odds ratio (OR) and the relative 95% confidence interval (CI), and the p-value were also calculated.

**Results:** The measurement of specific gravity, pH, glucose and protein content of PF did not differ (p>NS) between cases and controls, while receptor) wild type cell line H838 and EGFR gene mutation cell lines (H1650, H1975, HCC827), and whether rhuEPO treatment affected growth and invasion of lung cancer cells. Moreover, the angiogenic effect of rhuEPO was also explored.

**Material and Methods:** The expression of EPO-R in lung cancer cell lines was measured by ELISA (Enzyme Linked Immunosorbent Assay). Proliferation of the lung cancer cells was monitored by a real-time cell monitor technology (InCell). The proliferation of lung cancer cells was analyzed in a 3D collagen gel cell culture model. Transwell invasion assay was also performed to detect invasion and migration of lung cancer cell lines in PBS, rhEPO and VEGF (vascular endothelial growth factor).

Matrigel plug in experiments was used to evaluate the angiogenic ability of rhEPO compared with VEGF and PBS in both nude mice and lung cancer cell lines H838 and H1975 bone nude mice models in vivo. Microvessel density (MVD) was checked in both of the above sections by using CD31 IHC staining.

**Results:** EPO-R can be detected in EGFR wild type lung cancer cell line H838 and small-cell lung cancer cell line H1339, while it was absent in EGFR gene mutation lung cancer cell lines H1650, H1975 and HCC827. Proliferation of EPO-R+ (H1650) cells was not affected by rhEPO treatment, interestingly, although EPO-R was expressed in H838 cells, it also did not affect proliferation of the cells, demonstrating that EPO-R is not necessary for proliferation of lung cancer cells in vitro. Invasion and migration of lung cancer cell lines were not promoted by rhEPO; rhuEPO significantly promoted HVEC tube formation in vitro and induced new blood vessel formation in nude mice models.

**Conclusion:** The role of rhEPO is beyond erythropoiesis, which also plays a strong role of angiogenesis and participates in the new blood vessel formation in lung cancer, implying that anti-EPO therapy may potentially act as one of the anti-angiogenic agents for cancer patients together with anti-VEGF treatment. Additionally, EPO-R may be co-expressed with EGFR, EPO-R mutation or chimeric receptor, and the role of EGFR and EPO-R in the mechanism of EGFR-TKI (tyrosine kinase inhibitors) resistance on the possibility of cross-talk signaling pathway may be further investigated.

**No conflict of interest.**
pleural CEA (37.2±100-3 vs. 1.6±1.4 ng/mL, p = 0.0008), CRP (5.8±8.5 vs. 11.9±7.4 mg/dL, p = 0.0003), and LHD (414.6±327.2 vs. 250.6±222.2 U/L, p = 0.004) were significantly different. The sensitivity, specificity and accuracy of PF cytology were 45.0%, 98.2%, and 75.3%, respectively. The multivariate logistic regression analysis excluded LHD from the model and the results are reported in the Table. The AUC for the combination of PC×CEA×CRP reached 0.894 (95% CI 0.830-0.958).

Table: Percentages of different clinico-pathological data among both cohorts.

<table>
<thead>
<tr>
<th>Females (n = 99)</th>
<th>Males (n = 95)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Median; IQR) years</td>
<td>51(46–60)</td>
<td>55(48–60)</td>
</tr>
<tr>
<td>Age &gt;53 years</td>
<td>39.4</td>
<td>53.7</td>
</tr>
<tr>
<td>Lt side lesion</td>
<td>39.2</td>
<td>35.5</td>
</tr>
<tr>
<td>Nodular pleural thickening</td>
<td>74.7</td>
<td>60</td>
</tr>
<tr>
<td>Inter-lobar fissure involvement</td>
<td>33.3</td>
<td>25.3</td>
</tr>
<tr>
<td>Mediastinal pleura involvement</td>
<td>40.2</td>
<td>34.7</td>
</tr>
<tr>
<td>Effusion</td>
<td>47.5</td>
<td>42.1</td>
</tr>
<tr>
<td>Osification/Calcification</td>
<td>3</td>
<td>5.3</td>
</tr>
<tr>
<td>Hemithorax contraction</td>
<td>34.3</td>
<td>45.3</td>
</tr>
<tr>
<td>Chest wall invasion</td>
<td>8.1</td>
<td>10.5</td>
</tr>
<tr>
<td>Pericardial invasion</td>
<td>1</td>
<td>7.4</td>
</tr>
<tr>
<td>Mediastinal invasion</td>
<td>9.1</td>
<td>4.2</td>
</tr>
<tr>
<td>Trans-diaphragmatic extension</td>
<td>0</td>
<td>5.3</td>
</tr>
<tr>
<td>Pulmonary nodules</td>
<td>18.2</td>
<td>20</td>
</tr>
<tr>
<td>Lymph nodes metastasis</td>
<td>33.3</td>
<td>41.1</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>2</td>
<td>7.4</td>
</tr>
</tbody>
</table>

Methods: This is a retrospective review of medical records of MPM patients who were treated in NCI, Cairo University, Egypt; diagnosed in the period between 2012 and 2015. Data regarding demographics, histology, tumor staging and CT finding were obtained from all patients. Pearson’s chi (χ²) test and Fisher’s exact tests were used for statistical analyses.

Results: 194 cases were included, 99 (51%) were females while 95 patients were males. Median age was 55 years (range 15–76). Most cases (62.6%) were Lt sided. Inter-lobar fissure was involved in 29.4% while mediastinal pleura in 37.5%. Effusion was present in 87% while only 4% had LHD from the model and the results are reported in the Table. The AUC for the combination of PC×CEA×CRP reached 0.894 (95% CI 0.830-0.958).

Conclusion: no conflict of interest.

2050 POSTER
KRAS driven expression signature has prognostic power superior to mutation status in non-small cell lung cancer

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Background: KRAS is the most frequently mutated oncogene in non–small cell lung cancer (NSCLC). However, no targeted agents are currently approved for treatment of patients with KRAS mutations. Moreover, the prognostic role of KRAS mutation status in NSCLC still remains controversial. Here, we hypothesize that the expression changes of genes affected by KRAS mutation status will have the most prominent effect and could be used as a prognostic surrogate signature in lung cancer.

Materials and Methods: We divided 555 NSCLC patients with simultaneous mutation and RNA-seq data into two cohorts – those with a genetic alteration in KRAS gene and those with wild type – and used Mann–Whitney test to identify the signature of genes showing altered expression between these cohorts. The mean expression of the top five genes was designated as a “transcriptomic fingerprint” of the mutation.

Results: Mutation of KRAS was most common in adenocarcinoma (98% of mutation in AC). Mutation status and KRAS expression were not correlated to prognosis. The transcriptomic fingerprint of KRAS include FOXRED2, KRAS, TOP1, PEX3, and ABL2. The KRAS signature had a high prognostic power in AC (HR=2.4, p=1.2E-12). Similar results were achieved when using the second and third set of strongest genes (HR=2.4, p=1.2E-12 and HR=2.5, p=4.4E-14, respectively). In addition, all cutoff values delivered significant prognostic power (p < 0.001). The KRAS signature also remained significant (p < 0.001) in a multivariate analysis including age, gender, smoking history and tumor stage.

Conclusions: Here we generated a “surrogate signature” of KRAS mutation status in NSCLC patients by computationally connecting genotype to a gene expression signature. Our results emphasize the importance of KRAS and prove that secondary effects can have a higher prognostic relevance than the primary genetic alteration itself.

No conflict of interest.

2052 POSTER
Sex differences in malignant pleural mesothelioma; National Cancer Institute (NCI) experience

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Background: Prior publication data proposed that malignant pleural mesothelioma (MPM) mortality rate was consistently lower for females when compared with males [Reid et al. Age and sex differences in malignant mesothelioma after residential exposure to blue asbestos (crocidolite). CHEST Journal 131.2 (2007); 376–382]. We sought to investigate sex difference in clinico-pathological data among our MPM patients.

Methods: This is a retrospective review of medical records of MPM patients who were treated in NCI, Cairo University, Egypt; diagnosed in the period between 2012 and 2015. Data regarding demographics, histology, tumor staging and CT finding were obtained from all patients. Pearson’s chi (χ²) test and Fisher’s exact tests were used for statistical analyses.

Results: 194 cases were included, 99 (51%) were females while 95 patients were males. Median age was 55 years (range 15–76). Most cases (62.6%) were Lt sided. Inter-lobar fissure was involved in 29.4% while mediastinal pleura in 37.5%. Effusion was present in 87% while only 4% had LHD from the model and the results are reported in the Table. The AUC for the combination of PC×CEA×CRP reached 0.894 (95% CI 0.830-0.958).

Conclusion: no conflict of interest.

2052A POSTER
Evaluation of the efficacy of cisplatin–etoposide and the role of thoracic radiotherapy and prophylactic cranial irradiation in large cell neuroendocrine carcinoma

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Introduction: In small-cell lung cancer (SCLC) the role of chemotherapy and radiotherapy is well established. Large cell lung cancer (LCNEC) shares several clinicopathologic features with SCLC, but its optimal therapy is not defined. We evaluated clinical response and survival outcomes of advanced LCNEC treated in first-line therapy compared with SCLC.

Methods: Seventy-two patients with stage III–IV LCNEC (n=28) and extensive-stage SCLC (ES-SCLC) (n=44) received cisplatin/etoposide with/thout thoracic radiotherapy (TRT) and prophylactic cranial irradiation (PCI).

Results: Comparing LCNEC with SCLC we observed similar response rate (64.2% vs 59.1%), disease control rate (82.1% vs 88.6%), progression free survival (mpFSS) (7.4 vs 6.1 months) and overall survival (mOS) (10.4 vs
10.9 months). TRT e PCI in both histologies showed a benefit in mOS (34 vs 7.8 months and 34 vs 8.6 months, both p = 0.0001). LCNEC receiving TRT showed an improvement in mPFS and mOS (12.5 vs 5 months, p = 0.02 and 28.3 vs 5 months, p = 0.004), similarly to ES-SCLC. PCI in LCNEC showed an increase in mPFS (20.5 vs 6.4 months, p = 0.09) and mOS (33.4 vs 8.6 months, p = 0.05) as in ES-SCLC.

Table 1. Characteristics of 72 patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
<th>LCNEC (N=28; 39%)</th>
<th>SCLC (N=44; 61%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (64.3)</td>
<td>28 (63.6)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10 (35.7)</td>
<td>16 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>65 (40−78)</td>
<td>64 (46−80)</td>
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<tr>
<td>ECOG performance status</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>15 (53.6)</td>
<td>24 (54.5)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9 (32.1)</td>
<td>12 (27.3)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (14.3)</td>
<td>8 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>4 (14.3)</td>
<td>4 (9.1)</td>
<td></td>
</tr>
<tr>
<td>Ever smoker</td>
<td>24 (85.7)</td>
<td>20 (90.9)</td>
<td></td>
</tr>
<tr>
<td>Clinical stage at diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I−II</td>
<td>6 (21.4)</td>
<td>2 (4.5)</td>
<td></td>
</tr>
<tr>
<td>IIIA/IIIB</td>
<td>7 (25)</td>
<td>14 (31.9)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>15 (53.6)</td>
<td>28 (63.6)</td>
<td></td>
</tr>
<tr>
<td>Site of disease</td>
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<tr>
<td>Intrathoracic</td>
<td>13 (46.4)</td>
<td>24 (54.5)</td>
<td></td>
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<tr>
<td>Extrathoracic</td>
<td>15 (53.6)</td>
<td>20 (45.5)</td>
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<tr>
<td>Brain metastasis at diagnosis</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (7.1)</td>
<td>4 (9.0)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>26 (92.9)</td>
<td>20 (90.9)</td>
<td></td>
</tr>
<tr>
<td>Surgery at diagnosis</td>
<td></td>
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<tr>
<td>Yes</td>
<td>6 (21.4)</td>
<td>2 (4.5)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>22 (78.6)</td>
<td>42 (95.5)</td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
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<tr>
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<td>1 (3.6)</td>
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<tr>
<td>Lobectomy</td>
<td>3 (10.7)</td>
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<tr>
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<td>2 (7.1)</td>
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<tr>
<td>Chemotherapy treatment, n (%)</td>
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<td></td>
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<tr>
<td>Medically courses received, number (range)</td>
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<td>6 (3−8)</td>
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<td>Consolidative TRT</td>
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</tr>
<tr>
<td>Yes</td>
<td>10 (35.7)</td>
<td>16 (36.4)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (64.3)</td>
<td>28 (63.6)</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (14.3)</td>
<td>17 (38.6)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24 (85.7)</td>
<td>27 (61.4)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: advanced LCNEC treated with SCLC first-line therapy has similar clinical response and survival outcomes to extensive-SCLC. No conflict of interest.

2053A POSTER Changing trends in lung cancer characteristics and evolution of its diagnostic and surgical modalities

V. Gupta1, S. Jeon2, 1Seoul National University Bundang Hospital, Thoracic and Cardiovascular Surgery, Seongnam-si- Gyeonggi-do, South Korea

Lung cancer has evolved from being a rare malignancy at the beginning of 20th century to a leading cause of death from cancer (14.1 million cases in 2012 and up to 24 million by 2035). Our aim was to find out the changing time trends in lung cancer, evolution of diagnostic and surgical procedures. The data was collected retrospectively at Seoul National University Bundang Hospital from 2003–2014. It was classified into surgery date, gender, age, smoking history, diagnostic method used and operative procedure performed. Histologic diagnosis was classified into adenocarcinoma, squamous cell carcinoma, small cell carcinoma, bronchoalveolar carcinoma, large cell carcinoma and others. Out of total 2,224 patients, 63.84% were male and 36.16% female. Incidence of adenocarcinoma (65.51%), squamous cell carcinoma (23.15%) and broncho-alveolar carcinoma were found in decreasing order of prevalence. 57.95% were smokers and 41.77% non-smokers. Adenocarcinoma was more prevalent in the never smokers and Squamous Carcinoma among the current and former smokers. Squamous Carcinoma and Small Cell Carcinoma showed preponderance in the male sex. Adenocarcinoma had its peak in the 60–69ys age group and Squamous Carcinoma’s peak was in the 70–79ys group. Over years, incidence of adenocarcinoma increased as compared to others. FNAB was the most common diagnostic technique and there was evolution from FNAB to Pre Op Tissue Conformation as the most common diagnostic technique over the years. Lobectomy was most common surgical procedure followed by wedge resection, segmentectomy, pneumonectomy and bilobectomy. During 2012–2014 VATS started and followed the same order as open thoracotomies. Such analysis of data improves our understanding and motivates to initiate extensive studies to explore further that will help us in devising strategies for prevention, early diagnosis and management of lung cancer. No conflict of interest.

2054 POSTER NOTCH2 and PTP4A3 gene copy number alterations are associated with prognosis and support novel therapeutic strategies for malignant pleural mesothelioma

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Background: Malignant pleural mesothelioma (MPM) is a rare but aggressive cancer, which incidence has constantly increased over the past two decades and is expected to peak in 2020–25. The overall prognosis is poor, and predictive biomarkers of drug activity are missing. Pharmacogenetic studies focused on candidate determinants of drug activity/metabolism, reporting controversial results. Given the heterogeneous and complex nature of MPM, it is likely that genomic aberrations changing the expression of several genes, might affect therapeutic response. Therefore, the aim of the present study was to identify genes whose copy number alterations (CNA) might predict the MPM prognosis.

Method: We retrieved official death certificate data for lung cancer (ICD-9 code: 162) dating from 2006 till 2010 based on the official information from the Institute of Statistics, Tirana, Albania. We calculated age-standardized mortality rates per 100,000 persons by sex in separate age groups and overall using the world standard population as reference. Annual percent change (APC) was computed by fitting a regression line to the rates using the calendar year as a regressor variable.

Results: Overall, lung cancer mortality (per 100,000 persons) was 11.4, 12.6, 15.1, 14.5 and 10.7 for the years 2006, 2007, 2008, 2009 and 2010, respectively. During these five years, lung cancer mortality has declined (APC = −5.2%) even though it is not significant (p trend = 0.6) which is attributed to the declining trend in men (APC = −6.2%, p trend = 0.5). Also, lung cancer mortality rates in men varied between age groups where a decreasing, not significant trend was observed in all age groups. Meanwhile, it was observed an increase trend in women (APC = 0.9%, p trend = 0.9). There was increasing significant trend in the women youngest age group (APC = 20.1% at age 20–49, p trend <0.05) whereas a decreasing, not significant trend was observed only in the oldest age group (APC = −5% at age 50−69, p trend = 0.7).

Conclusions: Lung cancer mortality has shown a decreasing but not significant trend in Albania during 2006–2010. However, these findings indicate that thanks to a comprehensive tobacco control program a decline began with the more favorable significant trend in men. Furthermore, our results suggest that public health strategies for lung cancer prevention should differ by sex in a developing country.
Material and Methods: Recurrent copy number alterations of chromosome fragments and genes were analyzed by high-resolution whole-genome sequencing in DNA obtained by paraffin-embedded samples from “discovery cohort” of 26 resected MPM patients treated with pemetrexed-based chemotherapy (8 with progressive disease (PD); vs. 18 with stable disease (SD) and 8 with partial response (PR)). Prognostic markers identified by Copy Number Variation analysis with Nexus, Control-FREEC and ReadDepth software were validated by PCR gene copy number and gene expression analyses both in the “discovery” and in two “validation” cohorts of pemetrexed-treated and untreated patients (N = 45 and 40). The role of emerging genes was evaluated through siRNA and pharmacological studies using proliferation, migration and apoptosis assays in MPM cells.

Results: As reported previously we observed copy number loss of CDKN2A (15q11-13) and 1p13 (77.6%) in 11 of the 18 patients when compared to normal controls (p < 0.05). The copy number gain of NOTCH2 was observed in 50% of samples of the patients who underwent progression, whereas losses of PTP4A3 gene were associated with clinical benefit (SD+PR). The prognostic relevance of NOTCH2 was confirmed by PCR analysis, as well as in the validation cohort. Moreover, Patients with high expression levels of both NOTCH2 and PTP4A3 had the worse prognosis (OS, 6 months), while no associations were found in pemetrexed-untreated patients. NOTCH2 silencing reduced MPM cell migration and enhanced apoptosis induction by pemetrexed, while a PTP4A3 inhibitor overcame pemetrexed resistance in MPM cells characteristic by high NOTCH2 and PTP4A3 expression.

Conclusions: These results support the role of NOTCH2 as a novel prognostic/predictive biomarker for MPM, prompting prospective randomized trials for its validation. Moreover, preclinical data suggest that NOTCH2 and PTP4A3 are oncogenes suitable for effective therapeutic targeting in pemetrexed-resistant MPM cells.

No conflict of interest.

2054A POSTER

The clinical significance of osteopontin (OPN) in non-small cell lung cancer and its biological impact on lung cancer cells

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Background: Osteopontin (OPN) is an extracellular matrix phosphoprotein secreted by a number of cell types in the body and implicated in a variety of physiological and pathological conditions. It has been reported that expression of OPN signiﬁcantly correlate with disease prognosis of certain tumour types. OPN has been identiﬁed as a biomarker for tumor progression in many human tumors. In NSCLC, the tumorigenic functions of OPN are incompletely understood. The current study sought to investigate the role of OPN in the progression in a cohort of NSCLC patients and the association with clinical implications and prognosis. The impact of OPN on the molecular and cellular functions of lung cancer cells were also evaluated.

Methods: OPN expression in human NSCLC tissue and plasma samples (n = 75) was analyzed using IHC and ELISA, respectively. The correlation between the levels of OPN and clinical characteristics were examined. Knockdown of OPN in NSCLC cell line A549 (positive for OPN) was carried out using shRNA targeting human OPN. An OPN overexpression cell model with the NSCLC cell line SMMC-1 (negative for OPN) was also established. The effects of OPN on the functions of these NSCLC cell models were determined using a variety of in vitro cell function assays.

Results: Signiﬁcantly higher tissue levels and raised plasma levels of OPN were observed in the cancer patients when compared to normal controls (p < 0.05 and p < 0.01 respectively). The OPN expression in plasma samples from patients with distant metastasis after surgical treatment was higher than that in those from patients who remained metastasis free (p < 0.05). Knockdown of OPN suppressed cell-matrix adhesion (p < 0.05), the in vitro migration (p < 0.05) and cell invasion (p < 0.05) in A549 cells. OPN overexpression in SMMC1 increased in vitro invasiveness, matrix adhesion and cellular migration (p < 0.05), when assessed using in vitro Matrigel invasion, matrix adhesion assay and electric cell-substrate impedance sensing, respectively.

Conclusion: Our study shows that OPN expression is increased in lung cancer and is associated with distant metastasis. OPN plays crucial roles in regulating the migration, adhesion and invasion of lung cancer cells. Together, these data suggest that OPN may mediate an oncogenic effect on NSCLC cells and indicates that OPN may be a potential therapeutic target.

No conflict of interest.
Treatment compliance and outcome in geriatric patients with locally advanced non-small cell lung cancer: Experience from India

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Objectives: To evaluate treatment compliance, toxicity and survival in geriatric patients (>65 years) with locally advanced non-small cell lung cancer (LA-NSCLC).

Materials and Methods: Departmental archive was collected for the details of demographics, treatment and outcome in elderly patients with LA-NSCLC (2008–2013) (n=96). Both progression-free survival (PFS) and overall survival (OS) were evaluated using Kaplan–Meier method. Acute and late morbidity was scored using common terminology criteria for adverse events version 4 Radiation Therapy and Oncology Group (RTOG) late morbidity scoring system.

Results: The completion rate was 65%. The rates of acute grade ≥3 hematologic and non-hematologic toxicities were 20% and 17%, respectively. Overall rate of late toxicity was 12.5%. Median PFS and OS were 7.4 months and 10.54 months respectively. Patients with multiple co-morbidities, poor socio-economic background and serum albumin level (<3.5 g/dl) were observed to have poor survival. Survival was lower for non-compliant patients.

Conclusion: Curative multi-modality therapy in elderly patients with LA-NSCLC is a challenging.

No conflict of interest.

Stereotactic body radiotherapy for medically inoperable early stage non small cell lung cancer: a retrospective single-center experience

R. Frakulli1, A. Arcelli1, E. Farina1, L. Ronchi1, A. Baldissera2, F. Salvi2, O. Martelli1, C. Degli Esposti1, D. Balestrini1, G. Siepe1, A. Milani1, S. Cammelli1, F. Monari1, M. Nretsa1, A.G. Morganti1, G. Frezza1.

1University of Bologna- Ospedale S. Orsola Mabipghi, Radiation Oncology Center- Department of Experimental-Diagnostic and Specialty Medicine- DIMEs, Bologna, Italy; 2Bellaria Hospital, Radiation Oncology Department, Bologna, Italy

Background: The purpose of this study was to analyze the outcomes of 110 patients (pts) with Stage I non-small-cell lung cancer (NSCLC), unfit for surgery, treated with stereotactic body radiotherapy (SBRT).

Materials and Methods: We retrospectively reviewed all pts with stage I NSCLC who underwent radical SBRT from April 2010 to August 2014. The total dose prescribed varied according to tumor size and maximum diameter. The median delivered dose was 56 Gy in 5 fractions (range, 54–60 Gy)/3–10 fractions), prescribed to 80% isodose. All pts underwent image guided radiotherapy (daily Cone Beam computed tomography [CT]).

Pts were assessed for toxicity once a week during the treatment and at each follow up (FU) visit after SBRT. Response rates were scored according to the RECIST guidelines versions 1.1 and for acute and late toxicity the CTCAE version 4.0 was used. Follow-up included physical examination and a chest CT scan +/- FDG PET/CT at 3, 6, 12 and 24 months, and thereafter annually after SBRT treatment. Response rates were scored according to the RECIST guidelines.

Results: 110 pts were included, 28 female and 82 male, median age was 78 years (range, 46–88). The median planning treatment volume (PTV) was 34.1 cc (range, 5.3–116.8). The median follow-up was 24 months (range, 2–60). Two- and 4-year local control rate, cancer specific survival, overall survival rate were 87.4% and 72.6%, 79.1% and 59.2%, 70.9% and 31.3%, respectively. No statistically significant difference was found in local control rates in terms of Biological Effective Dose (BED) (%100 Gy vs <100 Gy), lung comorbidity (yes vs no), or PTV (<34.1 cc vs >34.1 cc). No Grade 3 or greater acute and late toxicities were recorded.

Conclusions: Lung SBRT for early-stage NSCLC unfit for surgery resulted in satisfactory local control with minimal toxicity.

No conflict of interest.

Correlation of pre-treatment 18F-FDG PET/CT metabolic parameters with short-term efficacy of radiotherapy for non-small cell lung cancer

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Background: To investigate the correlation of 18F-FDG PET/CT molecular imaging metabolic parameters before radiotherapy and short-term curative effect of different pathological types NSCLC.

Material and Methods: 18F-FDG PET/CT images were collected from 61 patients with NSCLC from October 2014 to May 2016 in Shandong Cancer Hospital, 31 cases of adenocarcinoma and 30 cases of squamous cell carcinoma. First, GTV is delineated on the PET/CT fusion image with SUV values greater than 2.5; The secretion level of tumor metabolic parameters, including SUV volume histogram, maximum standard uptake value (SUVmax), mean standardized uptake value (SUVmean), metabolic tumor volume (MTV), total lesion glycolysis (TLG) and area under the curve of cumulative SUV volume histogram (AUC-CSH). Evaluation of radiotherapy response after four weeks of treatment. The correlation between metabolic parameters and short-term response was analyzed statistically.

Results: AUC-CSH, SUVmax, SUVmean, MTV, and TLG were all associated with short-term efficacy. Multivariate analysis, SUVmax was found as the independent prognostic factor of short-term efficacy, and in squamous cell carcinoma, the cut-off threshold of AUC-CSH was 0.4715, in adenocarcinoma, the cut-off threshold of AUC-CSH was used as an early predictor of treatment response in patients with NSCLC.

Conclusions: The metabolic tumor heterogeneity characterized may be valuable for predicting treatment response for patients with NSCLC. But there were differences between the different pathological types, different parameters should be used to predict short-term response for different pathological types.

No conflict of interest.

Global named patient use (NPU) program of afatinib in heavily pretreated advanced NSCLC patients who progressed following prior therapies, including erlotinib or gefitinib

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Background: Afatinib, an oral, irreversible ErbB family blocker, is approved in many countries for treatment of advanced EGFR mutation-positive NSCLC, as well as squamous cell carcinoma of the lung following platinum-based chemotherapy. An afatinib NPU program was initiated in 2010, after the Phase IIb/III LUX-Lung 1 trial demonstrated significantly improved progression-free survival and objective response rate (ORR) with afatinib versus placebo, in advanced NSCLC patients following failure of erlotinib and/or gefitinib and/or chemotherapy and/ORR of 1–2 lines of chemotherapy. This analysis of the NPU program provides real-world data for afatinib use in global clinical practice for NSCLC patients with no established therapeutic option.

Methods: Patients eligible for the NPU program had: advanced NSCLC; progressed after clinical benefit on prior erlotinib or gefitinib, and/or had an activating EGFR/HER2 mutation; exhausted all other treatment options (chemotherapy-naive patients were eligible if deemed unfit for chemotherapy); and were ineligible for actively recruiting afatinib trials. Physicians provided a pseudonymised data set for each patient participating in the program. Time to treatment failure (TTF, in months) was defined as the time from the start of afatinib to treatment discontinuation for any reason (including disease progression, intolerance and death).

Results: As of January 2016, data were available from 3966 NSCLC patients, from 41 countries across 6 continents. Patients were heavily pretreated, with ~50% receiving afatinib as ≥4-line treatment; almost all patients (3678/3699; 97.9%) received prior erlotinib and/or gefitinib. Among 2595/3966 (65.4%) patients with known tumour EGFR status,
2407 (92.8%) were EGFR mutation-positive. Median TTF for afatinib, calculated for 2862/3966 (72.2%) patients based on available data, was 4.4 months, and 4.3 months in each patient subgroup, consisting of any EGFR mutation, common EGFR mutations (e.g., Del19 or L858R), or uncommon EGFR mutations (e.g., T790M in 38% (720) in those with insertions in exon 20. No new or unexpected safety findings were observed.

Conclusions: A PFS analysis was undertaken after ~250 PFS events; primary analysis of OS was planned after ~213 OS events and a follow-up period of ≥32 mos.

Results: Events for OS analysis were met at the data cut-off of 8 Apr 2016. Median follow-up for OS was 42.6 mos. Median treatment duration was 15.4 mos; 77% (1749/2276) of pts with EGFRm+ NSCLC harboured any EGFR mutation. Notably, a 26% (26/100) ORR was reported in patients with NSCLC harboring uncommon EGFR mutations, including 19% (115/591) in T790M mutation-positive patients and 35% (720) in those with insertions in exon 20. No new or unexpected safety findings were observed.

Conclusions: This afatinib NPU program in nearly 4000 NSCLC patients who were refractory to several therapeutics, including School of Medicine and gefitinib, revealed encouraging effectiveness measures, such as TTF durations and tumour response rates for all patients, including those with NSCLC harboring common or uncommon EGFR mutations. Safety data were consistent with previous reports.


2060 POSTER SPOTLIGHT

Afinatin vs gefitinib in patients (pts) with EGFR mutation-positive (EGFRm+) NSCLC: overall survival (OS) data from LUX-Lung 7 (LL7)

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Background: The irreversible ErbB family blocker, afatinib, and the reversible EGFR TKI, gefitinib, are approved for first-line treatment of advanced EGFRm+ NSCLC. In the Phase IIb LL7 trial, afatinib (40mg/d) significantly improved progression-free survival (PFS; HR = 0.73 [95% CI 0.57–0.95] p = 0.017) and objective response rate (ORR; 70% vs 56%, p = 0.008) vs gefitinib (250 mg/d) in this setting. Here, we present the primary analysis of OS.

Methods: LL7 assessed afatinib vs gefitinib in treatment-naïve pts with stage IIB/IV NSCLC and a common EGFR mutation (Del19/L858R). Co-primary endpoints were PFS, TTF and OS. Other endpoints included ORR and adverse events (AEs). Primary analysis of PFS and TTF was
2061

Poster Session, Sunday 29 January 2017

Poster

Second-line afatinib vs erlotinib for patients with squamous cell carcinoma (SCC) of the lung (LUUX-Lung 8 [LL8]): analysis of tumour and serum biomarkers and long-term responders

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Background: In LL8, second-line afatinib (A) significantly improved OS and PFS vs erlotinib (E) in patients (pts) with SCC of the lung (N = 795). OS was significantly higher with A than E at 12 months (mos; 36 vs 28%; p = 0.016) and 18 mos (22 vs 14%; p = 0.001), suggesting prolonged benefit from A in some pts. Here we report exploratory tumour molecular analysis (n = 245), immunohistochemistry (IHC; n = 288) and VeriStrat® (VS) serum protein analysis (n = 675), assessing frequency of alterations in cancer-related genes and prognostic utility of the alterations. EGFR expression levels or VS status as predictive biomarkers. We also present post-hoc analysis of baseline characteristics and efficacy of A in long-term responders (LTRs; treatment [tx] for > 12 mos).

Methods: Tumour samples were analysed by FoundationOne® next-generation sequencing (NGS). EGFRv (by IHC) was defined as staining in ≥ 10% of cells. Serum samples were assigned as VS-Good (VS-G) or VS-Poor (VS-P) by mass spectrometry. Cox regression models were used to assess predictive potential of biomarkers for PFS/OS.

Results: In LL8 overall, ErBB family alteration frequency was low (short variants: EGFR 7%, HER2 5%, HER3 6%, HER4 6%; copy-number alterations: EGFR 7%, HER2 4%). No individual ErBB family alterations were predictive of PFS/OS. Benefit from A vs E was consistent in all molecular subgroups. EGFR expression was not predictive of PFS/OS benefit (Table). PFS and OS were improved (p < 0.0001) in the VS-G vs VS-P group. VS-G pts had significantly longer PFS (median 3.2 vs 2.0 mos) and OS (11.5 vs 7.9 mos) with A vs E; VS-P pts had no significant difference in PFS/OS with A vs E. There was no significant interaction between tx arms and VS classification. 15/998 pts treated with A were LTRs. Median tx duration was 16 mos (range 12.3–25.8). Pt characteristics were similar to LL8 overall (median age 65 yrs [range 54–81]; male 80%; Asian 13%; EGOG PS 0/1 40/60%; current/ex-smokers 83%). Median PFS/OS was 16.2 mos (range 2.8–24.0). NGS was undertaken in 9 LTRs; detailed will be presented at the meeting. ErBB family alterations were identified in 44% (LL8 overall 29%). IHC data were available for 1 EGFR+ pt. Of 14 LTRs assessed by VS, 86% were VS-G (LL8 overall 61%).

Conclusions: No biomarkers were identified that predicted benefit with A over E in LL8. A is a tx option in this setting irrespective of tumour characteristics. However, pt outcomes vary strongly dependent on VS status. In LTRs, pt characteristics were similar to LL8 overall, and A conferred OS benefit of nearly 2 yrs. The LTR dataset was too small to identify NGS/VS predictive signals.

Conflict of interest: Advisory Board: SMG: Boehringer-Ingelheim, Genentech/Roche, Astra-Zeneca; J-CS: Boehringer Ingelheim; GG: BMS, Pfizer, Boehringer Ingelheim, Astrazeneca, Lilly; EF: Boehringer Ingelheim, MSD, Eli Lilly, Roche, Pfizer, Novartis, BMS, Celgene. Other Substantive Relationships: Employment: NG, NK, CB, FS, EE, BL, Honoraria: EF: Boehringer Ingelheim, MSD, Eli Lilly, Roche, Pfizer, Novartis, BMS, Celgene. Speakers bureau: EF: BMS, Novartis, Roche.

2063

Poster

Safety and tolerability of nivolumab in an inner city minority population compared to clinical trials data

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Background: Nivolumab is a humanized Programmed death 1 (PD-1) inhibitor that is approved for first line treatment of malignant melanoma (MM) (in combination with ipilimumab, CheckMate-067 trial) and second line treatment of non-small cell lung cancer (NSCLC) (CheckMate-017 trial). CheckMate-017 was to confirm that nivolumab was non-squamous NSCLC (NS-NSCLC) and CheckMate-057 for non-squamous NSCLC (NS-NSCLC). renal cell carcinoma (RCC) (CheckMate-025) and Head & Neck cancers (HNC) (CheckMate-141). We undertook this study to evaluate the safety of nivolumab in a community minority based setting.

Methods: Cook County health and hospital system is the third largest public health care system in the United States. We screened all patients from our pharmacy database from January 2015 to August 2016 with an indication for Nivolumab. We included patients who had received at least one dose of nivolumab. We studied all adverse events (AE) by grade and compared with reported trials, studying NSCLC in detail since it was our largest group.

Results: A total of 44 patients were screened and 37 were included in the study (see table) including 23 NSCLC (4 squamous and 19 NS-NSCLC), 4 MM, 7 RCC and 3 HNC. Males comprised 70% of the patients with 49% African Americans (AA) and 22% Caucasians. Any AEs was seen in 32% with grade 3 or higher in 21%, including 3 grade 5 toxicities in 2 patients [1 with Tumor lysis (TLS) in melanoma on combination therapy and 1 with TLS and hepatitis in NSCLC], TLS has not been reported before in any nivolumab trials. Both TLS happened in week 3, day 18 and day 16 respectively.

All AEs in NSCLC were seen in non-squamous histology only. Comparing to CheckMate 057 in NS-NSCLC where they had 91% whites, our patients were 52% AA and 26% white. Any AE was seen in 32% of our NS-NSCLC versus 6% in CheckMate 057. Grade 3 or higher AEs were 37% versus 11% in the trial.

In our study 46% patients discontinued treatment due to AEs or progression with 53% of NS-NSCLC discontinuing compared to 5% in CheckMate 057.

Conclusion: Our study was clearly representative of an inner city minority population. Although limited by number, our patients had a higher rate of AEs with nivolumab compared to reported studies and a much higher rate of grade 3 or higher toxicities and drug discontinuation in NS-NSCLC. We also report 2 cases of TLS, an AE that has not been reported before with Nivolumab.

Nivolumab does not seem to be as well tolerated in the minority population compared to reported clinical trials and larger studies are needed to confirm this finding and identify patients at increased risk of AEs.

No conflict of interest.
2064


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Background: Non-small cell lung cancer (NSCLC) is one of the most common causes of cancer mortality in men and women, exceeding the combined mortality rates of breast, cervical and ovarian cancers in women, and colorectal cancer in men, and is thus likely to present a significant public health problem for years to come. The aim of this study was to explore the expression of cancer/testicular tumour-associated antigens (C/T-TAAs) MAGE-A1, MAGE-A3/4 and NY-ESO-1 in adenocarcinoma and squamous cell carcinoma of the lung, and to evaluate their association with the clinical-pathological features of surgically treated lung cancer patients.

Material and Methods: The study included 80 patients (40 patients with adenocarcinoma and 40 patients with squamous cell carcinoma of the lung) who had undergone surgery. The MAGE-A1, MAGE-A3/4 antigen expression was determined by an immunohistochemical method using monoclonal antibodies (mAb) 57B and the NY-ESO-1 antigen expression was determined with the addition of the B9.8.1.1 antibody (mAb).

Results: MAGE-A1, MAGE-A3/4 and NY-ESO-1 were expressed in 17.3%, 44.4% and 18.5% of NSCLC, respectively. A statistically higher immunohistochemical expression rate of MAGE-A3/4 was found in panclonocellular bronchial carcinoma (p < 0.001) and a significantly higher amount of tumour necrosis was observed in tumours with MAGE-A3/4 expression (p < 0.001), but no correlation with positivity lymph node metastasis was found. There was a statistically significant correlation between the MAGE-A1 expression in adenocarcinoma and the presence of tumour necrosis (p = 0.050). Furthermore, there was a significant correlation between the NY-ESO-1 expression and presence of lymph node metastasis in adenocarcinoma (p < 0.001), but not in squamous cell carcinoma.

Conclusions: Our results demonstrate that the MAGE-A3/4 and NY-ESO-1 expression was significantly associated with prognostic factors of poor outcome (presence of tumour necrosis and lymph node metastasis). As C/T-TAAs are important for inducing a specific immune reaction in lung cancer patients, there is an intention to form a subgroup of patients, whose treatment would be enhanced by specific immunotherapy.

No conflict of interest.

2065

Analysis of clinical and research implications of updating next-generation sequencing (NGS) libraries in the treatment options of lung cancer in a large cancer center

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Background: The routine use of next-generation sequencing (NGS) in clinical practice has increased the therapeutic options for many cancers. Multiple NGS assays are now commercially used. The genomic libraries used by these assays are continuously being expanded, resulting in increased detections of genomic alterations (GAs) leading to potential new treatments. The aim of this study was to identify the clinical and research implications of a database expansion in the detection of GAs in patients with lung cancer at a large comprehensive cancer center.

Materials and Methods: We retrospectively analyzed 72 consecutive patients with lung cancer that had NGS at the John Theurer Cancer Center between 01/2014 and 08/2016. GAs were identified using the FoundationOne assay (Foundation Medicine, Cambridge, MA). GAs, number of genomic-directed therapies and number of clinical trials were reviewed.

Results: Period 1 (P1) comprised 01/2014–09/2014, period 2 (P2) comprised 10/2014–08/2016. The NGS assay interrogated 236 genes and introns of 19 genes during P1, and was expanded to 315 genes and introns of 28 genes during P2. The 12 samples analyzed during P1 harbored a total of 44 GAs with an average of 3.6 GAs/sample (range 1–6). The 60 samples analyzed during P2 harbored a total of 330 GAs with an average of 5.5 GAs/sample (range 0–16). This represented an increase of 52% in GAs from P1 to P2. 35 GAs in 27 genes were detected in P2 that were not interrogated during P1. Based on new genetic findings, more clinical trials were made available for the patients on P2; an average of 10 vs 6 clinical trials (66% increase in available clinical trials).

Conclusions: Periodical updates on NGS and the expansion of genomic libraries are imperative for the detection of GAs, and available clinical trials for patients with lung cancer. Continued expansions of NGS are needed to improve genomic characterization, and increase in the personalized therapeutic options for our patients.

No conflict of interest.

Proffered Papers (Saturday 28 January 2017) Urology

2114

Feasibility and acceptability of follow-up care for prostate cancer in primary care

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Background: The number of prostate cancer survivors is high and will increase further due to the ageing population. Follow-up care for prostate cancer patients will therefore not be just a surveillance care but an increasing demand on health care. Capacity and costs. Increasing the role of the GP in follow-up care for prostate cancer patients may help to limit the increase in workload in secondary care and reduce health care costs. Before testing cost-effectiveness should first be tested in a smaller sample.

Materials and Methods: We tested the feasibility and acceptability of a new clinical pathway for patients with prostate cancer in a stable phase aged >65 years and with comorbidity. Follow-up care for prostate cancer was transferred to the GP and patients were followed for one year. We aimed to include 20 patients. Participating GPs and urologists jointly developed a care protocol. Patient satisfaction regarding GP care was measured (presence of tumour necrosis and lymph node metastasis) at 0 and 12 months after transfer of care from urologist to the GP with the subscale ‘personalized care’ of the Consumer Quality Index GP-care. Next, patients, GPs and urologists were interviewed about their experiences. We considered the clinical pathway successful if no patients were referred back to the urologist except for an increase in PSA, and the majority of patients and participating urologists and GPs were satisfied.

Results: Of the 20 patients included in the study, three were referred back to the urologist because of increasing PSA levels and one died (unrelated to prostate cancer). Most patients (73%) were satisfied with the transfer of care, indicated by a score of 3 or higher on the subscale ‘personalized care’. Participating GPs and urologists were confident in the ability of GPs to provide follow-up care and preferred to continue this.

Conclusion: The new clinical pathway was successful. This warrants a larger study to provide evidence for the (cost-)effectiveness of GP-led prostate cancer follow-up care.

No conflict of interest.

2115

Quality of life (QL) of muscle invasive bladder cancer (MIBC) patients (pts) receiving radiotherapy (RT) +/- chemotherapy (CT) in the BC2001 trial (CRUK/01/004)

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Background: BC2001 showed that addition of chemotherapy (SFU+MMC; cRT) to RT (55 Gy/20f or 64 Gy/32f) significantly improved rates of MIBC locoregional disease free survival from 54% to 67% at 2 years (James et al 2012) & reduced high dose volume RT (RHDV/RT) rather than standard RT (sRT) did not significantly reduce late side effects (Huddart et al 2013). Here we present QL outcomes.
Methods: Under the 2x2 partial factorial design, 458 pts were randomised to either RT (178) cRT (182) (CT comparison) and/or to sRT (108) or RHDVR (111) (RT comparison). Pts completed Functional Assessment of Cancer Therapy-Bladder (FACT-Bl) questionnaires at baseline, end of treatment (EoT), 6, 12, 24, 36, 48 & 60 months (mo) post RT. The mean change in bladder cancer subscale (BLCS) score (scale of FACT-Bl) between baseline and 12mo, was the primary endpoint. Secondary endpoints included change in total FACT-BL (TOTAL) & Treatment Outcome Index (TOI, sum of physical, functional wellbeing & BLCS domain scores). ANCOVA models were used to estimate treatment differences, adjusted for baseline score, alternative randomisation & fractionation schedule.

Results: Data were available for 331 (92%) & 204 (93%) pts at baseline & 181 (50%) & 107 (49%) at 12mo for the CT & RT comparison respectively. BLCS, TOI and TOTAL scores significantly declined at EoT (Overall mean change from baseline: BLCS = −5.1, p < 0.001; TOI = −9.3, p < 0.001; TOTAL = −8.2, p < 0.001) but recovered & were not significantly different to baseline from 6mo onwards. Changes in BLCS score at 12mo were: CT comparison: −0.6 (cRT) vs −0.4 (RT); adjusted difference: 0.18 (95%CI: −1.6 to 2.0, p = 0.84); RT comparison: 0.31 (sRT) vs 1.06 (RHDVR); adjusted difference: −2.01 (95% CI: −4.3 to 0.3, p = 0.09). Table 1 shows mean change from baseline (%Δ) at selected timepoints.

| Table 1: Change from baseline in QL scores |
|------------------|--|--|--|--|--|--|--|--|--|--|
| | Baseline | EoT 6mo | 12mo | 60mo | N | Median | N | Δ | N | Δ | N | Δ | N | Δ |
| **RT** | | | | | | | | | | | | | | |
| BLCS | 160 | 34.7 | 12.5 | −5.4* | 105−15.1 | 88−0.4 | 34 | −1.1 |
| TOI | 160 | 81.2 | 12.9 | −9.0* | 105−19.6 | 86 | 0.9 | 34 | −0.1 |
| TOTAL | 160 | 125.9 | −8.5* | 106−1.6 | 86 | 2.7 | 34 | −0.5 |
| **cRT** | | | | | | | | | | | | | | |
| BLCS | 169 | 33.6 | 13.5 | −5.1* | 114−0.5 | 89 | −0.6 | 54 | −1.3 |
| TOI | 167 | 79.6 | 13.0 | −10.6* | 113−0.3 | 88 | 0.8 | 50 | −0.5 |
| TOTAL | 168 | 123.8 | −9.4* | 115 | 0.9 | 87 | 53 | 1.3 |
| **sRT** | | | | | | | | | | | | | | |
| BLCS | 98 | 32.4 | 66 | −4.4* | 64 | 0.3 | 52 | 0.3 |
| TOI | 97 | 78.8 | 65 | −7.1* | 63 | 1.2 | 52 | 0.0 |
| TOTAL | 99 | 120.8 | 67 | −3.7 | 64 | 2.9 | 53 | 2.1 |
| **RHDVR** | | | | | | | | | | | | | | |
| BLCS | 102 | 34.1 | 79 | −4.6* | 60 | −0.2 | 52 | 1.1 |
| TOI | 101 | 79.9 | 78 | −9.5 | 59 | 1.7 | 52 | 1.8 |
| TOTAL | 102 | 119.9 | 76 | −8.5 | 61 | 4.4 | 53 | 5.7 |

Negative values represent worse outcome.

*Significant at the 1% level.

Conclusions: After an initial decline at EoT, pts receiving sRT or RHDVR, with or without synchronous chemotherapy report QL outcomes similar to those experienced prior to treatment. No statistically significant evidence of difference in QL between the treatment groups in either the CT or RT comparisons was seen between 6 and 60mo post-treatment.

No conflict of interest.

2117 Overall survival results from the phase 3 trial of cabozantinib vs everolimus in advanced renal cell carcinoma (METEOR)


ORAL

2118 Patient mobility for radical prostatectomy in the English NHS: its impact on service configuration and technology integration

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Background: In England, 1 in 3 men who have a radical prostatectomy (RP) for localised prostate cancer are prepared to travel beyond their nearest hospital for their surgery, especially men who are younger, fitter and more affluent. We investigated the impact of potential competitive factors on patient mobility and configuration of prostate cancer surgery in the NHS.

Material and Methods: Using national administrative hospital data, patients who underwent a RP between 2010 and 2014 (n = 19,253) were mapped according to their place of residence and where they had their surgery. In this way, we could identify for each RP centre the number of “movers” (patients for whom that RP centre was nearest but who had their treatment elsewhere) and “arrivers” (patients for whom another RP centre was nearest, but who had their surgery at that centre) identified as having a net gain or net loss if the difference between arrivers and movers was statistically significant based on the conditional method for testing a difference between poison means. For each centre we determined whether it provided robotic surgery before 2010 (“established robotic centre” – n = 10), we evaluated the media profile of its urologists using a UK newspaper review of prostate cancer surgery, and we calculated a spatial competition index (SCI) for each centre using a scale from 0 (most competitive environment) to 1 (least competitive) based on the number of additional RP centres and eligible RP patients that were within 30 min and 60 min drive time.

Results: Of the 65 (35%) RP centres in the English NHS had a significant net gain of patients in the study period. These centres were more likely to be established robotic centres (odds ratio 15.4, p < 0.001) and to employ urologists with an established media profile (odds ratio 37.5, p < 0.0001). Of the 37 RP centres (57%) which had a significant net loss of patients, 11 (29.7%) have closed since 2011. External competition was significantly stronger for centres that “closed down” (median SCI 0.461) than in those that remained open (median SCI 0.680, p = 0.02).

Conclusions: Hospitals providing prostate cancer surgery attract more patients if they were known as centres that provide innovative surgical technology and employ surgeons with a strong media profile. It is likely that – even without evidence on better outcomes – these competitive factors have contributed to the large-scale investment in equipment for robotic surgery (e.g. 30 new surgical robots were acquired between 2011 and 2012). English NHS, was nearest but who had their surgery at that RP centre). A centre was defined as a “robotic centre” − n=10), we evaluated the media profile of its urologists using a UK newspaper review of prostate cancer surgery, and we calculated a spatial competition index (SCI) for each centre using a scale from 0 (most competitive environment) to 1 (least competitive) based on the number of additional RP centres and eligible RP patients that were within 30 min and 60 min drive time.

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group and number of prior VEGFR TKIs (1 or >2). The study was designed to detect a HR for OS of 0.75 (80% power, 2-sided α = 0.04).

Results: A total of 658 patients were randomized from Aug 2013 to Nov 2014. As of 31 Dec 2015, with a minimum follow-up of 13 months, 74 (22%) patients remained on cabozantinib, 9% of patients remained on cabozantinib, and 124 (35%) patients were on placebo. The median age at time of AS initiation was 72 years (57–88). Within ten years from start of AS, 10% of men aged 50 and 50% of men aged 70 with no comorbidity at initiation will transition to WW. The median time on AS was 5 years. Our prevalence simulation suggested that the number of men on WW who were previously on AS only stabilizes after 30 years.

Conclusions: Changes from AS to WW were predicted to become common in men with very low-risk PCa who were elderly at time of AS initiation. Men remained on AS for a median of five years. The possibility of a change from AS to WW should be part of the treatment pathway discussion with a man considering AS as a treatment option. Clear guidelines on follow-up, including criteria to decide when AS should change to WW and how this should be managed in different healthcare systems, are thus needed.

No conflict of interest.

Poster Session (Sunday 29 January 2017)

Urology

2169

POSTER

Specialties in pathomorphology of moderately differentiated urothelial tumors of upper urinary tract

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This research included morphological analysis of histological preparations of 157 patients with urothelial carcinoma and in 42 cases (26.7%) of which the moderately differentiated tumor was identified. We conducted a comprehensive morphological research of urothelial cancer of upper urinary tract by using complex of general histological, morphometrical, histochemical and immunohistochemical methods which allows us making several generalizations. The basic differential morphological features of moderately differentiated urothelial cancer of renal pelvis are following:

- the emphysemic damage of renal pelvis with prevalence of tumor nodes having papilar character and a presence of sectors with squamous differentiation of tumor cells
- moderate cellular and nuclear polymorphism with average indexes of section length of nuclei of tumor cells and nuclear-cytoplasmic ratio are 6.58±0.083 respectively that grow in the areas of squamous differentiation with increasing the section length of nuclei of tumor cells up to 6.94±0.01% and nuclear-cytoplasmic ratio up to 2.93±0.074;
- moderate proliferative activity of cells with indexes of pathological figures of mitosis on average is 8.7±0.21%, mitosis index − 11.6±0.0082 respectively with the invasion of tumor cells into blood vessels, wall of renal pelvis and into ureter, kidney and surrounding cellular tissue;
- an uneven distribution and dissemination the sectors of necrosis in tumor tissue with a specific volume of necrosis lesions on average is 0.2011±0.0082;
- prevalence of intensive anti-tumor immune response formation with formation of large infiltrations with relatively high indexes of immunocompetent cells in stroma on 1mm² (117.18±23.79) and medium number of cells in the one field of view (23.41±4.03), which presented mainly with lymphocytes (63.0±1.62%), macrophages and neutrophils (4.59±0.31%, 4.83±0.21% respectively), with presence of not high number of plasma cells (2.84±0.10 %), tissue basophils (1.83±0.17%) and eosinophils (1.80±0.01%).

No conflict of interest.

2170

POSTER

Induction of V2X para-renal carcinoma in rabbits: generation of animal model for loco-regional treatments of solid tumors

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Background: Animal models of para-renal cancer can provide useful information for the evaluation of tumor response to loco-regional therapy

Methods: Using population-based data on cancer characteristics, age and comorbidity in PCBaSeLung, a state-transition model was created to estimate the probability of treatment changes between pre-defined treatments to predict transitioning from AS to WW.

Results: Our predictions indicated that 48% of men with very low-risk PCa starting on AS eventually changed to WW. This proportion increased with age at start of AS and comorbidity. Within ten years from start of AS, 10% of men aged 50 and 50% of men aged 70 with no comorbidity at initiation will transition to WW. The median time on AS was 5 years. Our prevalence simulation suggested that the number of men on WW who were previously on AS only stabilizes after 30 years.

Conclusions: Changes from AS to WW were predicted to become common in men with very low-risk PCa who were elderly at time of AS initiation. Men remained on AS for a median of five years. The possibility of a change from AS to WW should be part of the treatment pathway discussion with a man considering AS as a treatment option. Clear guidelines on follow-up, including criteria to decide when AS should change to WW and how this should be managed in different healthcare systems, are thus needed.

No conflict of interest.
2172 Prognostic factors in germ cell cancer – a population based study

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Background: The prognostic factors in germ cell cancer (GCC) are not totally settled. The International Germ Cell Cancer Collaborative Group Classification (IGCCCG) and the American Joint Committee on Cancer (AJCC) staging are the current prognostic guidelines available in the clinical practice but some authors suggest the need to review these models in a contemporary population. Our aim was to validate the established prognostic classifications in a recent population cohort and test new factors that may impact the outcomes.

Methods: Portuguese registry population-based retrospective study of GCC patients (2008–2012). Brain GCC was excluded. Outcomes assessed were overall survival (OS) and progression free survival (PFS). Survival was calculated by Kaplan–Meier method. Patients age, IGCCCG, AJCC staging, tumor size and vascular invasion were evaluated. Health care indicators as time between first GCC symptom to diagnosis, diagnosis and start of chemotherapy and compliance to GCC treatment guidelines were also tested. Log-rank test and Cox regression models were used for uni and multivariable analyses.

Results: 406 GCC patients were included with a median age of 32 years (range 16–84). Histology was 50% seminoma and 48% non-seminoma (2% unknown) and 13% had vascular invasion. By stage, 54% were I, 18% II and 15% III (13% unknown). According to the IGCCCG, 81% had good, 5% intermediate, 7% poor prognosis (7% unknown). Median time from first symptom to diagnosis was 2.1 months (range 0.1–58.2) and from diagnosis to start of chemotherapy was 4.2 months (range 0.05–16.4). There was 31% of non-compliance to treatment guidelines. The 5-year OS was 95% (95% CI 93–97%) and PFS was 86% (95% CI 82–90%). At the multivariate level, only IGCCCG and older age had adverse impact in both OS and PFS (p = 0.010 and p = 0.006, respectively). A trend for a negative impact on OS with non-compliance to treatment guidelines. The longer time from diagnosis to chemotherapy in advanced stages was significantly associated with worse PFS.

Conclusions: In our population, we confirmed the prognostic relevance of the IGCCCG and age but not AJCC staging. Older age has been recently described as a prognostic factor but additional investigation is needed. Health care indicators didn’t seem to majorly influence the outcome of GCC patients.

No conflict of interest.

2173 Small renal mass biopsies: An effective tool in avoiding unnecessary surgery

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Background: There has been in increasing incidence of Small Renal Masses (SRMs) over the past decade in keeping with the global increasing incidence in RCC seen over the past decades. Studies have shown that between 20%–30% of small renal masses are benign, but as yet we are unable to reliably distinguish between benign and malignant disease radiologically. Renal biopsy has been established as a safe and reliable technique to obtain information on the pre-treatment histology of renal masses. However adoption by the urological community as a standard approach to guiding treatment remains low, as the available evidence is for high volume centres.

Objective: We proposed to validate the safety, accuracy and reliability of renal biopsy in our centre. And to evaluate the effectiveness of using biopsies to guide treatment decision for small renal mass biopsies.

Materials and Methods: We conducted a retrospective study of patients who underwent SRM biopsy between 2013 and April 2016. Patients were included if they had been maintained electronic patient record system (Clinical Portal) and our pathology database (Telepath). Diagnostic and concordance rates will be presented as proportions.

Results: A total of 208 renal biopsied SRMs were included in the analysis and the comparison with other high volume centres can be seen in Table 1. Of those biopsied masses, the initial biopsy was diagnostic in 88% (n = 183) of cases, of which 16.43 (n = 34) were found to be benign. Only 1 patient had an adverse event 0.5% requiring a blood transfusion for post biopsy bleeding (Clavien-Dindo Grade II).

No conflict of interest.
Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Years</th>
<th>No of tumours</th>
<th>Mean age</th>
<th>Non-diagnostic</th>
<th>Diagnostic</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our study</td>
<td>2013–2018</td>
<td>208</td>
<td>74</td>
<td>12%</td>
<td>88%</td>
<td>16.3%</td>
<td>71.6%</td>
</tr>
<tr>
<td>Richard et al.</td>
<td>2011–2015</td>
<td>373</td>
<td>7.6</td>
<td>13%</td>
<td>87%</td>
<td>18%</td>
<td>82%</td>
</tr>
<tr>
<td>Jeon et al.</td>
<td>2008–2015</td>
<td>442</td>
<td>2.3</td>
<td>11.1%</td>
<td>88.9%</td>
<td>21.3%</td>
<td>67.6%</td>
</tr>
<tr>
<td>Richard, Jewett, Bhat et al</td>
<td>2001–2013</td>
<td>529</td>
<td>2.5</td>
<td>10%</td>
<td>90%</td>
<td>23.4%</td>
<td>66.6%</td>
</tr>
<tr>
<td>Prince et al.</td>
<td>2000–2014</td>
<td>413</td>
<td>Not reported</td>
<td>17.4%</td>
<td>82.6%</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Leveridge et al.</td>
<td>2000–2009</td>
<td>345</td>
<td>2.5</td>
<td>19.4%</td>
<td>80.6%</td>
<td>16.6%</td>
<td>64%</td>
</tr>
<tr>
<td>Menegue et al.</td>
<td>1998–2009</td>
<td>268</td>
<td>2.5</td>
<td>20%</td>
<td>80%</td>
<td>20.8%</td>
<td>59.2%</td>
</tr>
</tbody>
</table>

Concordance rates have improved with time and recent series from Richard et al. in Toronto have shown concordance rates of 90%. Our series has a 100% concordance rate for biopsy with surgical histology. We did not routinely report grading on renal biopsy so we cannot confirm if this level of concordance would apply to grading of tumours.

Conclusion: The present study provides further evidence of the benefit of renal biopsy. With the increasing use of imaging, an increasing number of SRMs are being diagnosed. The majority of SRMs are still being treated with up front definitive treatment, which results in over treatment. Consequently, for patients in whom definitive treatment is being considered, we believe that biopsy of SRM is a way to reduce over treatment, the cost of treatment and, more importantly, limit treatment-related morbidity.

No conflict of interest.

2175

Relevance of pVHL expression in biological profile of renal cell carcinomas

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Background: Von Hippel Lindau (VHL) is the tumor suppressor gene; alterations in gene product (pVHL) of which leads to development of Renal Cell Carcinoma (RCC). pVHL functions through transcription dependent nuclear-cytoplasmic trafficking for it’s action. Present study is an aim to evaluate and correlate the frequency of pVHL expression with different Renal Carcinoma subtypes, stages and grades.

Material and Methods: A total of 78 cases of RCC which included three subtypes viz. clear cell, papillary and chromophobe were analyzed for pVHL expression using polyclonal antibody to pVHL (pVHL30/pVHL19). Age of the patients varied from 05 to 70 years with a mean age of 54.5±12 years. Of these 70 cases expressed positivity. Among these 55, 11 and 04 were expressions. TNM staging wise, exclusive nuclear expression was shown a predominant predilection for advanced stages viz. 23% and (06%) expressions. Failure to achieve statistical significance was achieved for most of the results.

Conclusions: To conclude, the results emphasize that VHL gene mutations leading to structural alterations in pVHL have significant relevance in biological profile of Renal Cell Carcinomas.

No conflict of interest.

2175

Outcome of oligo-progressing metastatic renal cell carcinoma patients treated with locoregional therapy: A multicenter retrospective analysis

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Background: No survival outcomes about continuing the same targeted therapy beyond progression or switching to second line options are available in patients with metastatic renal cell carcinoma (mRCC) who progressed in one or more metastatic sites treated with locoregional treatments.

Patients and Methods: 55 mRCC patients were retrospectively analyzed. Post-first-progression free survival (PFPFS) and post-first-progression overall survival (PFPPOS) in patients who continued the same TT versus those who switched to another TT after locoregional treatment were analyzed via the Kaplan–Meier method and Mantel–Haenszel log-rank test. A Cox-regression model was applied to the data with a univariate and multivariate approach in order to analyzed possible predictive and prognostic factors of PFPFS and PFPPOS.

Results: The global median post-first-progression OS (mPFPPOS) and PFS (mPFPFS) were 37 months (95% CI 25.2–48.7) and 14 months (95% CI 6.9–21) respectively. Patients who continued the same therapy after a locoregional treatment on a site of progression had a significantly longer mPFPFS compared to patients who switched to another therapy (39 vs 11 months, p = 0.014). An advantage in mPFPFS was also observed in patients with a good risk score compared to patients of the intermediate risk group (p = 0.039) and in patients with bone metastases versus visceral metastases (not reached [NR] vs 31 months, p = 0.045). At multivariate analysis, change of treatment after first progression (p = 0.008, HR 4.140) and bone metastases as site of first progression (p = 0.041, HR 4.056) were independent predictive factors of poorer and better prognosis in terms of mPFPFS respectively. Considering mPFPFS, patients with Fuhrman grade 2 and ECOG PS of 0 or 1 had a longer mPFPFS compared to patients with a PS of more than 1 (14 vs 7, p = 0.065) and Fuhrman grade of 1, 3 and 4 (22 vs 4 vs 10 vs 6 months, p = 0.009) respectively. No statistically significant differences in terms of mPFPFS were observed between patients who continued the same treatment after disease oligo-progression and those who changed therapy (15 vs 7 months, p = 0.257).

Conclusions: Locoregional treatments represent an option for oligo-metastatic mRCC treated with TT. Continuing the same systemic treatment after radical locoregional treatment in one or more metastatic site appear to be an independent predictive factor of better outcome in this subset of patients. Bone oligo-progressing mRCC showed similar better outcome. Furthermore no difference in terms of progression free survival was found between patients who continued the same TT and patients who switched to another TT. No conflict of interest.
2176

PERIOPERATIVE CHEMOTHERAPY FOR BLADDER CANCER IN THE GENERAL POPULATION: ARE PRACTICE PATTERNS FINALLY CHANGING?

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Background: International guidelines recommend neoadjuvant chemotherapy (NACT) for patients with muscle invasive bladder cancer (MIBC). Our group (Booth et al Cancer 2014) and others have previously reported low utilization of NACT in routine practice. Here we report contemporary use of NACT and adjuvant chemotherapy (ACT) as well as medical oncology (MO) referral patterns during 2009–2013 in the general population of Ontario, Canada.

Methods: Electronic records of treatment were linked to the population-based Ontario Cancer Registry to identify all patients who underwent cystectomy for bladder cancer in Ontario 2009–2013; surgical pathology reports were obtained to identify cases with muscle-invasive disease. Utilization of NACT/ACT in the contemporary cohort is compared with previously published data from 2004–2008. Logistic regression was used to analyze factors associated with use of NACT/ACT. Physician billing records were used to identify pre-operative consultation with MO.

Results: During 2009–2013, 1307 patients in Ontario had cystectomy for MIBC. Use of NACT increased substantially from 6% in 2004–2008 to 19% in 2009–2013 (p < 0.001). Temporal trends within the study period suggest continued further uptake; NACT rates increased from 12% in 2009 to 27% in 2013 (p < 0.001). Factors associated with use of NACT include younger age (p < 0.001) and more recent year of surgery (p < 0.001). There was also substantial regional variation (range 4% to 30%, p = 0.007). ACT was delivered to 26% of patients in 2009–2013 which is comparable to practice in 2004–2008 (22%, p = 0.084). Use of ACT did not increase during the 2009–2013 period. Factors associated with use of ACT include younger age (p < 0.001), less comorbidity (p = 0.006), higher T stage (p = 0.001) and node positive disease (p < 0.001). Hospital and surgeon cystectomy volume was not associated with utilization rates of NACT or ACT. Use of any peri-operative chemotherapy (NACT or ACT) in 2009–2013 was 35% compared to 27% in 2004–2008 (p < 0.001). Pre-operative referral rates to MO remained stable during 2009–2013 but were substantially greater than 2004–2008 (30% vs 16%, p < 0.001). While pre-operative MO referral rates were stable during 2009–2013, the proportion of referred patients who received NACT increased significantly over time (from 42% in 2009 to 60% in 2013, p = 0.001). Post-operative referral rates decreased during 2009–2013 (from 42% to 27% p = 0.001); however use of ACT among referred patient increased over time (from 50% to 72%, p = 0.002).

Conclusions: After many years of practice lagging behind evidence, these data demonstrate that use of NACT in the general population has increased substantially in the contemporary era. Our results suggest that increased uptake has been driven by greater pre-operative referral to MO as well as greater propensity of MOs to deliver NACT among referred patients.

No conflict of interest.

2177

E- AND N-CADHERIN EXPRESSION IN PROSTATE CANCER AS A SIGN OF EPITHELIAL–MESenchymal TRANSFORMATION

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Background: Epithelial–mesenchymal transformation (EMT) is considered to be one of the first steps towards tumor metastases. Its markers may serve as additional diagnostic and prognostic variables. Aim of the work was to study ‘cadherin switch’ [decrease in E-cadherin (E-cad) and increase in N-cadherin (N-cad)] and its relationship to clinico-pathological features in prostate cancer (PCa).

Material and Methods: E- and N-cadherin expression was studied in 40 radical prostatectomy samples by immunohistochemistry. E-cad was evaluated with Aperio Image Scope software using average intensity of positive pixels (Iavg) as a marker of staining intensity. Cases with Iavg > median Iavg were considered as E-cad high. N-cad due to nonspecific granular cytoplasmic staining was evaluated semiquantitatively on a 0–4 magnification as a percent of cells with positively stained membranes regardless of staining intensity. Cases with >5% positive cells were considered N-cad high.

Results: 50% of cases were E-cad high and 35% N-cad high. Membrane expression of both cadherins was predominant, though cytoplasmic staining was also seen in a small number of cells. It was mostly low to moderate for E-cad and for N-cad low to strong cytoplasmic staining could be observed even in one case. Decrease in membranous E-cad was mostly homogenous while N-cad neoexpression in epithelial cell membranes (low to strong) was seen in single cells or their groups per acinus or in groups of acini. Such expression pattern may be due to N-cad expression at a later stage of EMT than decrease of E-cad and the progression of the process to this stage in a smaller proportion of cells. N-cad+ cells were also seen in benign glands, in some cases their number exceeding that in PCa. In Gleason 5 cancers growing as solid nests high E-cad was retained while in single cells admixed with stroma its level was low. In some cases higher E-cad was seen at the leading edge of a group of invading cancer cells proving its possible role in connection of collectively migrating cells. Neither E-cad nor N-cad correlated with Gleason score, TNM stage, PSA level or patients’ body mass index (p > 0.05). E-cad tended to be lower in high N-cad cases though not statistically significant (p = 0.123).

Conclusion: Signs of EN-switch could be seen in 71.3% of PCa cases, but the cadherin expression wasn’t connected to standard morphological characteristics of the tumor.

No conflict of interest.
2179 Use of diffusion weighted-MRI (DW-MRI) as a prognostic biomarker of survival and time to cystectomy in muscle invasive bladder cancer (MIBC) following organ conserving treatment

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Background: Neo-adjuvant chemotherapy (nCT) has known survival benefit in the treatment of MIBC and identifies responders who may then benefit from radical radiotherapy. Conventionally response assessment is with cystoscopy. DW-MRI quantifies water molecule motion within tissue using the apparent diffusion coefficient (ADC). As an imaging biomarker it has been related to treatment response in solid tumours. Its use as a prognostic marker in bladder cancer remains novel.

Method: 48 patients with confirmed MIBC suitable for nCT were recruited prospectively to an ethics approved protocol. DW-MRI was performed on a 1.5T system using b-values 0, 50, 100, 250, 500 and 750 mm/s prior to and on completion of nCT. Tumour was drawn on the 750 mm/s images and transferred onto the corresponding ADC map to record mean values. Absolute change in ADC (∆ADC) was calculated as the difference between post treatment and baseline ADC. Following final DW-MRI patients proceeded to cystoscopy + biopsy.

Results: 38 patients achieved response following nCT and 10 patients had poor response as assessed at cystoscopy + biopsy. Mean ∆ADC of 0.18 ± 10 × 10⁻³ mm²/s was identified as predicting neo-adjuvant chemotherapy response with sensitivity/specificity/positive predictive value/negative predictive value of 71.1%/80.0%/93.1%/41.2% respectively. Mean % ∆ADC of 18.0% was identified with sensitivity/specificity/positive predictive value/ negative predictive value of 57.9%/90.0%/97.7%/36.0% respectively.

Conclusion: DW-MRI may provide prognostic information in bladder cancer but further validation is needed.

No conflict of interest.

2180 Understanding prostate cancer biology using metabolomics and proteomics approaches: potentials in the improvement of the diagnosis, prognosis and identification of new therapeutic targets

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Background: Prostate cancer (PCa) remains a major health problem in men worldwide. The treatment of the disease is still a challenge for Urologists, as well as the establishment of a clear prognosis, which is compromised by the lack of specificity and sensitivity of the currently available markers. Therefore, it is imperative to unravel PCa biology to enable the identification of key molecular events and molecules that aid PCa diagnosis, prognosis and the discovery of new therapeutic targets. In this study we aimed to identify metabolic and proteomic alterations that enable the distinction between prostate benign and malignant tissue.

Materials and Methods: Biopsies from prostate tumours and adjacent benign tissue from the central zone of the gland were obtained from eight patients. Prostate specific antigen (PSA) blood levels, prostate carcinoma stage (TNM) and Gleason score were determined in all patients. Each sample was divided and analysed using two approaches: infrared spectroscopy and an antibody microarray, which allowed the analysis of expression and phosphorylation state of 800 signalling proteins. The list of differentially expressed/regulated proteins between normal and tumour conditions was then subjected to an extensive bioinformatics analysis to integrate all data and complement with already existing studies.

Results: Principal component analysis of spectroscopic signals derived from PCa biopsies and adjacent benign tissues revealed different spectra for each condition. Dysregulations in lipid metabolism, kinases of phospho-amino acids and protein phosphorylation were the most relevant alterations observed in PCa tissues. Moreover, 40 proteins were identified as differentially expressed between the two conditions and 13 proteins revealed alterations in their phosphorylation levels. The identification of known PCa-related proteins reinforce the fidelity of the screen. The analysis of protein-protein interaction networks and ontologies showed the disruption of cell singling events during prostate carcinogenesis.

Conclusions: Metabolomics and proteomics approaches can provide vast information about carcinogenic processes. The integration of different ‘omics’ approaches are increasingly important when moving to a personalised medicine era, which requires the understanding of a disease as a whole system. Here, we show that applying two distinct approaches to the same set of samples it is possible to retrieve a lot of complementar information, increasing not only the knowledge on prostate carcinogenesis, but also allowing the identification of key molecular alterations that may aid an accurate diagnosis/prognosis or the development of new therapies.

No conflict of interest.

2180A High-throughput mutational analysis of urothelial bladder carcinoma

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Background: Bladder cancer (BC) is a devastating disease characterized by high recurrence rates and elevated progression rate to invasive phenotype. Recent data indicates that BC heterogeneity may contribute to cancer progression and to false-positive biomarker identification. This heterogeneity is mirrored in the genomics features of BC, typically, identifying genetic aberrations, especially mutational hotspots, will inevitably contribute in biomarkers discovery and influence future therapeutic intervention.

Methods: formalin-fixed paraffin-embedded tissues (FFPE) from 96 patients with urothelial bladder cancer were included in the study. High-throughput mutational analysis was performed using Cancer Hotspots Panel (CHP) v2 on the Ion Torrent™ platform. Kaplan–Meier curve was used to evaluate the relationship between genes mutations and cancer-specific survival; p values were calculated using the log rank test.

Results: Our data indicated that BC patients harbour frequent mutations in TP53 (84%), PIK3CA (55%), KDR (40%), FGFR3 (39%), KIT (29%), APC (19%), PTEN (19%), CDKN2A (14%), ATM (12%) and SKP2 (11%). Lower frequency mutations have also been reported for the rest of the gene panel. Interestingly, only FGFR3 mutations were significantly associated with poor disease-specific survival (p = 0.018).

Conclusion: The current study was able to validate known mutations in bladder cancer and to identify other genes that are mutated at high frequency in BC patients from the Kingdom of Saudi Arabia. In addition, other, novel mutations were also identified that may prove clinically useful following validation.

No conflict of interest.

2184 Prognostic impact of nodal relapse in definitive prostate-only irradiation

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Background: Nodal pelvic irradiation (WPI) in prostate cancer patients has been extensively investigated with the aim of preventing metastatic spread of cancer cells through lymphatic drainages in prostate cancer patients eligible for definitive radiotherapy (RT); on the other hand, due to uncertain clinical benefit and increased toxicity, its use has substantially declined in the last decades in favour of prostate-only irradiation (PI). The aim of our study was to assess the predictive and patient-specific value of nodal relapse and their impact on outcome, in localized prostate cancer patients treated by definitive PI with or without neoadjuvant/adjuvant androgen deprivation therapy (ADT).

Poster Session, Sunday 29 January 2017
Background: To determine if setup errors during external beam radiation therapy (RT) for prostate cancer are influenced by the combination of androgen deprivation treatment (ADT) and RT.

Materials and Methods: We retrospectively analyzed data from 175 patients treated for prostate cancer [concurrent ADT plus RT, 35 patients (19%), neoadjuvant ADT plus RT, 51 patients (29%), or RT only, 51 patients (29%)]. Required couch shifts without rotations were recorded for each CBCT, and corresponding alignment shifts were recorded as left-right (x), superior-inferior (y), and anterior-posterior (z). The non-parametric Mann-Whitney test was used to compare shifts by group. Pearson correlation coefficient was used to measure correlation in couch shifts between groups. Prostate shift means and standard deviations were calculated and pooled to obtain mean or group systematic error (M), random error (S), and total error (T). The non-parametric Wilcoxon test was used to compare mean shifts by group. Significant positive correlation was observed between prostate volume and average prostate shift in the z-direction (r = 0.04, p = 0.7 for x-direction; r = 0.03, p = 0.001) and y-direction (r = 0.07, p = 0.7). Random and systematic errors for all patient cohorts and ADT groups were similar.

Conclusion: Hormone therapy given concurrently with RT was not found to significantly impact setup errors. Prostate volume was significantly correlated with shifts in the anterior-posterior direction only.

No conflict of interest.

2186 POSTER
Predictive factors of late-onset rectal mucosal changes after radiotherapy of prostate cancer
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Background: Vienna rectoscopy score (VRS) assessed one year after radiotherapy is a surrogate end-point of late rectal toxicity. The aim of this study was to investigate the association between treatment-related factors and 1-year VRS.

Material and Methods: We performed a retrospective analysis of prospectively collected data. Patients with prostate adenocarcinoma treated with curative or adjuvant radiotherapy (RT) underwent endoscopy one year after RT. Correlations between VRS >2 and treatment parameters were investigated by univariate and multivariate logistic analyses.

Results: One hundred-ninety patients (mean age: 69; range: 43–81) were considered eligible for the study. At the univariate analysis, patients treated with hypofractionation, radiosurgery boost and an EQD2 dose (≤3) >75 Gy had a significantly higher incidence of VRS ≥2 (p < 0.001) after 1-year of follow-up. At the multivariate analysis, radiosurgery boost was an independent risk factor of developing rectal mucosal lesions (VRS >2), yielding an OR of 4.14 (95% CI 1.2–13.8), while pelvic surgery was inversely associated with VRS ≥2 (OR: 0.39; 95% CI: 0.17–0.94).

Conclusions: Hypofractionation, followed by radiosurgery boost significantly increased the risk of developing late-onset rectal mucosal changes. Therefore, special care and preventive treatment strategies are needed when using this boost technique after hypofractionated RT.

No conflict of interest.

2187 POSTER
SHARP hypofractionated stereotactic radiotherapy is low and intermediate-risk prostate carcinoma patients = PSA outcome
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Background: Prostate cancer is one of the most common solid tumors in men worldwide. For patients with early-stage prostate cancer radical prostatectomy or radiotherapy is the standard approaches. Stereotactic body radiation therapy (SBRT) is a new radiotherapy method. The objective of the study was to report tumor control of prostate cancer patients treated with SBRT.

Materials and Methods: A single institution prospective clinical study was done among previously untreated, histologically confirmed localized prostate cancer patients. The patients received 33.5 Gy in 5 fractions (SHARP regimen). The prostate-specific antigen (PSA) levels were evaluated before SBRT and every three months.

Results: There were included 68 men to the analysis (age 55–83 years), Gleason score 3–8 (mean and median, 6), Pretreatment PSA level for all patients was 4–20 ng/mL (mean, 10.9 ng/mL; median, 10 ng/mL), a median PSA level for patients who did not receive androgen deprivation therapy was 7.53 ng/mL (mean, 8.55 ng/mL). All patients completed the treatment. The average and median follow-up was 39 months. No patients died during the observation period. Four years after the end of radiotherapy, the
median PSA levels were 0.28 ng/mL for all patients, 0.93 ng/mL for those who did not receive androgen deprivation therapy, 0.21 ng/mL for patients who underwent 6 months of hormone therapy and 0.08 ng/mL for patients who underwent 2–3 years of hormone therapy. The median nadir PSA level was 0.025 ng/mL (mean, 0.18 ng/mL) for all patients, 0.48 ng/mL (mean, 0.62 ng/mL) for patients without hormone treatment. Low PSA nadir (<0.5 ng/mL) was observed in 50% of patient without androgen deprivation therapy and in 80% of other patient. PSA failure (nadir plus 2 ng/mL) was observed only in four patients from those who did not receive androgen deprivation therapy during observation (25% of patients without hormone therapy, 6% of all patients). There were no patients with PSA failure in the case of patient who underwent 6 months or 2–3 years of hormone therapy.

**Conclusions:** Prostate cancer patients treated by SBRT had good local control rates at four years.

**No conflict of interest.**

### 2188

**POSTER**

**Retrospective analysis of radium-223 treatment for adults with progressive castration-resistant metastatic prostate cancer with symptomatic bone metastasis**

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**Background:** To evaluate the efficacy of radium-223 for patients with progressive castration-resistant metastatic prostate cancer with symptomatic bone metastasis.

**Material and Methods:** 14 patients with progressive castration resistant prostate cancer and symptomatic bone metastasis commenced radium-223 therapy between 16/7/15 and 2/3/16. All men had evidence of ≥2 bone lesions on isotope bone scan within 12 weeks prior starting treatment. None had visceral metastasis. 6 men had not received prior docetaxel.

**Results:** The median age was 65.5 years. Interim analysis show 4 (29%) experienced symptomatic skeletal events (SSE’s) during treatment. Median time to SSE was 3.37 months amongst these patients. 6 months overall survival was 71% v 82% in the ALSYMPCA trial. 36% patients have completed the full course of 6 cycles, with 4 (29%) showing an improvement in health cycle (Mean improvement 10.5%, p = 0.056). 13 (93%) experienced a drop in alkaline phosphate between cycle 1 and cycle 2 (p = 0.007). A measure of health cycle (0–100) was assessed at each visit with an improvement in mean from 66.54 to 77.00 (p = 0.724). 35% of those with SSE’s experiencing a rise in PSA. There was no correlation between performance status, haemoglobin or prior docetaxel use and an improvement in pain or health cycle.

**Conclusion:** Radium-223 has been shown in the ALSYMPCA trial to significantly prolong overall survival in patients with castration resistant metastatic prostate cancer with bone metastasis. Our study to date shows that there is significant reduction in alkaline phosphate on radium-223 which has been associated with an improvement in median overall survival (p < 0.0001). Longer follow up will allow us to assess the impact on median overall survival and SSE’s. The study is ongoing.

**No conflict of interest.**

### 2189

**POSTER**

**The nephron sparing surgery in localized renal tumor**

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**Purpose:** Conservative renal surgery has become the gold standard treatment for small and peripheral malignant kidney lesions or in cases of reduced renal function or bilateral lesions. Nephron sparing surgery provides effective therapy in patients with a solitary sporadic renal tumor 4 cm or less and in presence of normal contralateral kidney or in presence of an anatomic or functional solitary kidney. However, the optimal selection criteria for NSS have not yet been defined.

**Material and Methods:** We retrospectively analyzed our database relating to the use of NSS in 33 pts from 216 pts operated for renal tumor in the cohort study January 2000 through December 2015. The records for all patients were reviewed. All patients included in analysis were with a single renal mean tumor size 3.6 cm (range 3.2–4.3) and with a normal contralateral kidney. In our series, it corresponds to 26% of the performed partial nephrectomies, but in other series reaches from 20% to 32%.

**Results:** We have performed 33 nephron sparing surgeries in a total of 216 patients, 16 were female and 17 were male.

The patients’ mean age was 49 ± 9.5 years and in all patients the indication was elective. In 19 patients lesions were located in the upper pole, 13 in the lower pole. One case was with meso-renal location. The open approach was used in all cases. The mean tumor size was 3.6 cm (range 3.2–4.3). The pathologic findings demonstrate a RCC in 30 cases and benign lesions in 3 patients (9%).

The patient who shows delayed bleeding for two days subsequent nephrectomy was performed. In that case the tumor size was 4.3 cm with meso-renal location. The subsequent nephrectomy was positive for residual tumor (RCC).

The ultrasound was performed at one to three months postoperatively. CECT/MRI was used subsequently six-monthly for two years and then yearly. Radiological investigations shows no local recurrence, no metastasis. Also no one of these patients developed a tumor in the contralateral kidney after NSS. The mean follow-up by laboratory tests and US/CECT/MRI was 42 months (3.5 years). Patients experienced postoperatively no deterioration in renal function.

**Conclusions:** Our results suggest that appropriate patient selection criteria and technical surgical improvements are important factors for satisfactory functional long-term outcome. Open nephron sparing surgery and laparoscopic radical nephrectomy are relatively recent and significant developments for treating patients with renal tumor and they represent accepted standards of care in those with a small renal mass and normal contralateral kidney. The NSS has become a method of choice in our department in for patients with renal tumor size <4 cm. These data suggest that nephron sparing surgery (NSS) can be performed with safety and maximum preservation of renal function.

**No conflict of interest.**

### 2191

**POSTER**

**Frequency and sites of stage I renal cell carcinoma progression**

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**Background:** Renal cell carcinoma has relatively good prognosis when operated in the I stage. Conversely, the prognosis of metastatic disease is poor. Later stage at diagnosis is a known predictor of poor outcome, however, in some cases even stage I tumors progress with development of metastases in multiple organs, but predictors of stage I RCC progression are largely unknown.

The aim of the study was to analyze the frequency of stage I RCC progression and main sites of metastatic spread as well as some patients’ characteristics and time to relapse.

**Material and Methods:** Automatic search of stage I RCC patients with disease progression between 2006 and 2012 was performed in database of Minsk City Clinical Oncological Health Center. More detailed information was obtained from patients’ medical records.

**Results:** During the indicated period disease progression was registered in 78 stage I RCC patients (12.7% of all disease progressions). Men comprised 69.2% (n = 54), women 30.8% (n = 24), median age at diagnosis was 60 years (42–95 years). Radical surgery was performed in 70 (89.7%) cases (nephrectomy in 49 cases, radical resections in 21). Median time to progression was 37 months (1–159 months) with 20 (25.6%) of patients progressing more than 5 years after surgery. Both locoregional progression and distant metastases developed in these patients, with 22 (28.2%) of them having metastases in different sites diagnosed at the same time and 21 (26.9%) – at different times. Sites of metastases are listed in the table.

<table>
<thead>
<tr>
<th>Site</th>
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<th>%</th>
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<tbody>
<tr>
<td>Lung</td>
<td>39</td>
<td>50</td>
</tr>
<tr>
<td>Bone</td>
<td>22</td>
<td>28.2</td>
</tr>
<tr>
<td>Liver</td>
<td>11</td>
<td>14.1</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>11</td>
<td>14.1</td>
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<tr>
<td>Local recurrence</td>
<td>10</td>
<td>12.8</td>
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<tr>
<td>Adrenal gland</td>
<td>8</td>
<td>10.3</td>
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<tr>
<td>Brain</td>
<td>6</td>
<td>7.7</td>
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<tr>
<td>Kidney</td>
<td>4</td>
<td>5.1</td>
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<tr>
<td>Other sites</td>
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In some cases metastases to relatively rare sites were present, such as thyroid, ovary, nasal cavity, soft tissues. Different treatment modalities were used after progression immunotherapy and surgery (including palliative operations) being the most frequent. Survival time after disease progression varied significantly according to the number and sites of metastases and possibilities of treatment. It varied from 1 month to 4 years.
Conclusions: RCC, even diagnosed and treated at the earliest stage, can progress and develop multiple metastases leading to patient’s death. Progression may develop long after initial treatment, that emphasizes the necessity of long follow-up. As clinical course in the majority of stage I RCC patients is favourable further investigations are needed to search for factors predicting disease progression in this category of patients.

No conflict of interest.

2192 POSTER DISCUSSION
MRI-based peri-prostatic-fascia thickness measurements as tool to virtually predict postoperative erectile function after robot-assisted radical prostatectomy

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Background: Erectile dysfunction (ED) is a frequent complication associated with robot-assisted radical prostatectomy (RARP). It is generally assumed that nerve-sparing techniques help to preserve erectile function (EF). The aim of the study is to determine the correlation between thickness of the periprostatic fascia measured in preoperative MRI data, an intraoperative facia preservation (FP) score, and EF-outcome measurements performed after RARP.

Materials and Methods: One-hundred-and-six patients with localized PCa and normal EF prior to surgery were retrospectively included. Patients were divided into two groups: 1; ED and 2; no ED after RARP (ED defined as International Index of Erectile Function – Erectile Function outcome <19). Preoperative 3 tesla multiparametric MRI (mpMRI) score was analyzed using an ImageJ-macro (image processing program), developed for this study. For reproducibility assessment FT was determined in axial slices at apex, mid and base of the prostate in 12 circumferential positions in 20 of the 106 patients. Interobserver variability was determined with intraclass correlation coefficient (ICC).

In all patients FT was analysed at midprostate level of the preoperative mpMRI. In combination with the intraoperative FP score the total saved fascia could be determined. The predictive value of total saved fascia on postoperative EF was evaluated with receiver operating characteristic (ROC)-curve-analysis. Pathologic evaluation of the periprostatic fascia was performed on a subset. Results: FT assessment was most reproducible when midprostate level images were analyzed. Men with an above average FT were more likely to preserve EF (p = 0.05). The sum of saved FT-segments on MRI showed the highest area under the curve in a ROC-curve-analysis compared to other clinical parameters, such as FP score alone.

Conclusions: Preoperative measured in preoperative MRI is predictive for EF. Total Saved Fascia was the strongest predictor for EF after RARP. By calculating FT prior to surgery, a “virtual” prediction can be made regarding EF after nerve-sparing RARP.

No conflict of interest.

2193 POSTER
Retrospective study of modified video-endoscopic versus open inguinal lymphadenectomy

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Introduction: Inguinal lymph node metastases are traditionally treated with open inguinal lymph node dissection (OILND) for which the reported morbidity rate is high. Minimal invasive approach is an alternative that can be utilised to gain early post-operative recovery. The aim of this study is to compare the immediate postoperative and short-term outcomes of lateral video-endoscopic inguinal lymph node dissection (L-VEIL) vs OILND.

Material and Methods: We conducted a retrospective analysis of inguinal lymphadenectomies performed for various cancers (penile and vulval carcinoma, melanoma, others) at our institute between January 2012 and December 2015. Only cases with clinical N0 status and operable primary tumor were included in the study. Unlike standard VEIL technique, all three ports are placed lateral to femoral triangle in our L-VEIL technique.

We had 24 cases undergoing L-VEIL and 92 cases of OILND. Patient characteristics, operative outcomes, and 30-day morbidity were evaluated.

Results: Both the groups were similar in patient characteristics with no statistically significant differences in patient age, gender, body mass index, or clinical status. L-VEIL required longer operating time (94.5 vs 68.1 min, p = 0.08) but had less blood loss (23.3 vs 64.8 ml, p = 0.002). The wound dehiscence rate (0 vs 24%, p = 0.005), flap necrosis rate (2.7 vs 46%, p = 0.0006), hospital readmission rate (0 vs 13%, p = 0.005), and hospital length of stay (3 vs 8 days, p = 0.0002) were all lower in the L-VEIL group. The lymph node count was significantly higher (11.04 vs 8.38, p = 0.001) for L-VEIL compared with OILND.

Conclusion: L-VEIL is a feasible alternative for radical inguinal lymph node dissection that provides equivalent lymphadentectomy and reduced postoperative morbidity in comparison to OILND.

No conflict of interest.

2194 POSTER DISCUSSION
MRI guided biopsy in patients with previously negative TRUS biopsy or suspicion of non-low grade disease on multiparametric MRI: High yield with predominantly intermediate to high risk prostate cancer found

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Background: Prostate cancer is now the second most common cancer in men with an estimated worldwide incidence of 1.1 million in 2012. Most prostate cancers occur in men with elevated PSA levels who undergo transrectal ultrasound (TRUS) guided biopsies. However, in a fair proportion of men these biopsies will be negative. It is of importance to detect intermediate and high grade prostate cancer. Multiparametric (mp) MRI of the prostate in these men will be able to map the entire prostate and detect clinically significant prostate cancer with high accuracy. Subsequently, in bore MRI guided biopsy can directly target the perceived lesions. The purpose of the study was to analyze the learning curve and the accuracy of the procedure as well as determine the accuracy in detecting intermediate and high grade prostate cancer.

Materials and Methods: From November 2013 to June 2016, 66 patients with elevated PSA levels and with previously negative TRUS guided biopsy or low grade prostate cancer underwent a mpMRI of the prostate at the first field strength of 3 tesla, which included T2-weighted, diffusion weighted (DWI) and dynamic contrast-enhanced imaging. This was followed by direct MRI guided in bore biopsy of lesions scored as PI-RADS 3 or higher and/or suspicion of intermediate/high grade disease on DWI. These were the first procedures performed at the department. Two radiologists without prior prostate MRI biopsy experience performed all procedures. A maximum of three biopsy cores were taken from each targeted lesion. Biopsy histopathology with Gleason score reporting was the standard of reference. In patients who after confirmation of prostate cancer underwent robot-assisted laparoscopic radical prostatectomy (RARP), the results were also compared with prostate specimen histopathology.

Results: In four patients more than one lesion was biopsied. A total of 106 patients (34/71 (48%) biopsies in 30/66 (45%) of patients were positive for prostate cancer. A learning curve was observed in which the biopsy yield in the second half of patients was significantly higher than the first half of patients (36% vs 69%, p < 0.005). In 65% (22/34) of biopsies, the detected cancer was intermediate or high grade (Gleason 7 or higher). In 76% (14/16) patients who underwent RARP MRI guided biopsy correctly predicted the final prostatectomy Gleason score on prostatectomy as intermediate or high grade.

Conclusions: A clear learning curve was observed for direct in bore MRI guided biopsy, which suggests that at least 30 procedures have to be performed to provide a sufficient level of experience. A large majority (65%) of prostate cancer detected by MRI guided biopsy was intermediate to high grade. The MRI guided biopsy Gleason score correlated well with the final Gleason score on prostatectomy, thereby reducing undergrading and optimizing patient risk stratification.

No conflict of interest.

2195 POSTER
Lymphocyte count in surgically treated urological cancer patients is a sensitive marker of the status of the disease

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The connection between cancer and systemic inflammatory response is well established and documented. These processes lead to neutrophilia
and lymphocytopenia, which in turn causes increase in secretion of proangiogenic, growth, antiapoptotic factors, and depression of the intratumoral T-cell activity. Low levels of the lymphocytes may signify poor immune response to the development of the neoplasia, and vice versa. We postulate that in the course of the treatment the peripheral blood may reflect the overall condition of the patient, which could be used as a marker of the status of the disease.

**Purpose of the study:** To assess retrospectively the count of the lymphocytes in the peripheral blood of urological patients with malignancies at the different stage of the treatment process, and correlate it with the stage of the treatment process itself.

**Materials and Methods:** We studied the medical records and blood analysis at the moment of the admission of 830 urological patients who were treated at the Oncology Department of O. Bogomoletz National Medical University (Kiev) in 2014. We focused on the absolute count of lymphocytes in the peripheral blood, and ratio of lymphocytes/white blood cells (L/WBC). Statistical work-up included calculation of the Mann–Whitney criteria (Two-tailed test) for absolute lymphocyte count and L/WBC count that show that statistically significant differences with p = 0.001 in lymphocyte count in peripheral blood are only observed between cancer patients and healthy individuals, and between cancer patients and radically surgically treated ones. Statistically significant differences in L/WBC ratio are only observed between cancer patients and all other groups of comparison.

**Conclusions:** Absolute lymphocyte count in the peripheral blood is simple laboratory parameters providing valuable prognostic information on the status of the disease and patient. It accurately differentiates cancer patient from healthy treated one, from health individual and patient with benign pathology.

**No conflict of interest.**

**2196 POSTER DISCUSSION**

**Efficacy of cabozezantinib vs everolimus in advanced renal cell carcinoma with bone metastases: results from the phase 3 METEOR study**

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**Background:** Bone metastases (mets) are associated with poor outcomes in patients with metastatic renal cell carcinoma (RCC; McKay Eur Urol 2014). METEOR (NCT01865747) evaluated the efficacy and safety of cabozezantinib (cabo) vs everolimus (eve) in patients with previously-treated RCC. Overall survival (OS) was significantly improved with cabo with a median OS of 21.4 mo vs 16.5 mo for cabo vs eve and a hazard ratio (HR) of 0.66 (95% confidence interval [CI] 0.53–0.83, P = 0.0003) (Choueiri Lancet Oncol 2016). Progression-free survival (PFS) and objective response rate (ORR) were also significantly improved (PFS HR of 0.51, 95% CI 0.42–0.62, P < 0.0001). Cabo has previously shown activity in bone mets in preclinical and clinical studies (Dai CCR 2014 and Smith JCO 2014). Here we present outcomes in patients with bone mets from METEOR.

**Materials and Methods:** 658 patients were stratified by MSKCC risk group and the number of prior VEGFR tyrosine kinase inhibitors (TKIs) and randomized 1:1 to receive cabo (60 mg qd) or eve (10 mg qd). Clinical outcomes included PFS, ORR, OS, and safety. Exploratory endpoints included bone scan response (BSR) per independent radiology committee (IRC) in patients with bone scan lesions at baseline (Brown Nut Med Commun 2012), incidence of skeletal-related events (SREs), and changes in bone turnover markers.

**Results:** At baseline, 142 patients had bone mets and 112 also had visceral mets. Patients with bone mets had an MSKCC risk distribution that was consistent with that for the overall study population. PFS HRs for cabo vs eve were 0.33 (95% CI 0.21–0.51) for patients with bone mets and 0.26 (95% CI 0.16–0.43) for patients with bone and visceral mets. OS was also markedly improved with HR 0.54 (95% CI 0.34–0.84) for patients with bone mets (median OS of 20.1 mo [cabo] vs 12.1 mo [eve]) and 0.45 (95% CI 0.28–0.72) for patients with bone and visceral mets (median OS of 20.1 mo [cabo] vs 10.7 mo [eve]). The ORR per IRC with cabo was 17% for patients with bone mets vs 20% for patients with both bone and visceral mets. BSR per IRC was 18% with cabo vs 10% with eve. At least one SRE occurred in 12% (cabo) and 14% (eve) of patients, including 4 (cabo) and 8 (eve) cases of spinal cord compression. For patients with a history of SRE, at randomization, the incidence of post-randomization SREs was 16% (cabo) and 34% (eve) and included 0 (cabo) and 5 (eve) cases of spinal cord compression. Reductions in the bone markers P1NP and CTx were greater with cabo vs eve. The most common adverse events in patients with bone mets were consistent with those observed in the overall study population.

**Conclusions:** PFS, OS, and ORR in patients with bone mets were improved with cabo compared with eve and were consistent with results for the overall population. Bone metastasis-related endpoints supported the observed improvements.


**2197 POSTER SPOTLIGHT**

**Update of the international prognostic classification for first line metastatic germ-cell cancers. An international initiative**

L. Collette1, on behalf of the International Germ Cell Cancer Classification Group: “EORTC, Brussels, Belgium

**Background:** Since its publication in 1997, the International Germ Cell (GC) Consensus Classification Group (GCCCG) is used to risk stratify treatment of about 6000 patients with metastatic GC cancer. The classification was built based on data from patients treated before 1990 ie before the wide-spread use of Bleomycin-Etoposide-Platinum (BEP) chemotherapy. Since then, staging and supportive care also improved, and evidence suggests heterogeneous prognosis inside the intermediate or poor prognosis subgroups. The IGCCCG Group 2 Initiative aims to assess the performance of the prognostic classification using data from patients who received current standard therapies, and potentially improve its prognostic granularity.

**Material and Methods:** Individual data from patients treated between 1990 and 2013 with current standard first line chemotherapy (BEP or high dose) inside clinical trials, epidemiological databases or large consecutive series are collected worldwide through international partnership with major
centers and research organizations. A central data warehouse is built and will be analysed at the EORTC Headquarters (Brussels, BE). Models for the primary endpoints progression-free and overall survival will be built using pre-treatment and treatment information.

Results: Over 40 potential partner organizations were identified worldwide, totaling over 13000 patients. So far, 29 partners from Europe, Canada, USA, Russia and Australia confirmed their participation, totaling 10300 patients. Data from 4 partners were already received in the central data warehouse. Further databases are expected to accumulate quickly in the coming 9 months.

Conclusions: An international collaboration is successfully being set up to provide updated insights into the prognosis of patients with metastatic germ cell cancer who receive modern first line chemotherapy. An update of the project and preliminary results will be provided at the meeting.

No conflict of interest.

2198 POSTER
Phase II California Cancer Consortium trial of gemcitabine-eribulin combination (GE) in cisplatin ineligible patients (pts) with metastatic urothelial carcinoma (mUC): tolerability and toxicity report (NCI-9653; 1UM1CA186717-01, NO1-CM-2011-00038)

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Background: Cisplatin-based regimens are the mainstay of treatment (tx) for mUC. Unfortunately, pts with mUC are often elderly and have comorbid conditions that preclude cisplatin-based tx. This CTEP-sponsored trial seeks to assess the efficacy and tolerability of GE in this population. Here we report the safety and tolerability data from this ongoing trial.

Materials and Methods: A Simon 2 stage design was employed (7+14) to provide updated insights into the prognosis of patients with metastatic germ cell cancer who receive modern first line chemotherapy. An update of the project and preliminary results will be provided at the meeting.

No conflict of interest.

2199 POSTER
Effect of prior systemic therapy on clinical outcomes with cabozantinib vs everolimus in advanced renal cell carcinoma: Results from the phase 3 METEOR study

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Background: Determining the optimal sequence of systemic therapy for patients with advanced renal cell carcinoma (RCC) remains a clinical challenge. The Phase 3 METEOR trial (NCT01865747) evaluated cabozantinib (cabo), a tyrosine kinase inhibitor (TKI), vs everolimus (eve) in patients with RCC with prior treatment with >1 VEGFR TKIs. Overall survival (OS) was significantly prolonged with cabo vs eve (median of 21.4 mo vs 16.5 mo, HR 0.66, 95% CI 0.53–0.83, p = 0.0003; Choueiri Lancet Oncol 2016). Progression-free survival (PFS) and objective response rate (ORR) were also significantly improved with cabo vs eve. Clinical outcomes for patients by prior therapies are presented.

Materials and Methods: In METEOR, 658 patients were randomized 1:1 to receive cabo (60 mg qd) or eve (10 mg qd), with stratification by MSKCC risk groups and number of prior VEGFR TKIs. Clinical outcome measures included PFS (primary endpoint), ORR, OS, and safety.

Results: Demographics and baseline characteristics were similar for patients who received only sunitinib (suni; n = 267) or only pazopanib (pazoo; n = 171) as prior VEGFR TKI therapy and were balanced between arms. OS and PFS analyses by the number of prior VEGFR TKIs and type of prior therapy were consistent with those for the overall population. The OS HR for patients with only 1 prior TKI was 0.65 (95% CI 0.50–0.85) vs 0.73 (95% CI 0.48–1.10) for patients with ≥2 prior TKIs; PFS HRs were 0.52 (95% CI 0.41–0.66) and 0.51 (95% CI 0.35–0.74), respectively. Median OS was 21.4 mo with cabo vs 16.5 mo with eve (HR 0.66, 95% CI 0.47–0.93) for patients with suni as the only prior VEGFR TKI and 22.0 mo with cabo vs 17.5 mo with eve (HR 0.68, 95% CI 0.42–1.04) for patients with pazoo as the only prior VEGFR TKI. PFS HRs were 0.43 (95% CI 0.32–0.59) for patients with only prior suni and 0.67 (95% CI 0.45–0.99) for patients with only prior pazoo. The ORR per independent radiology review (IRC) with cabo was 16% for patients with only prior suni (vs 3.0% with eve) and 19% for only prior pazoo.
In patients with prior anti-PD-1/PD-L1 therapy (n = 32; primarily nivolumab), the HR for OS was 0.56 (95% CI 0.21–1.52), and the HR for PFS was 0.22 (95% CI 0.07–0.65), favoring cabo; ORR per IRC was 22% with cabo and 0% with eve. The most common adverse events recorded for patients with only prior suni, only prior pazo, and prior anti-PD-1/PD-L1 therapy were consistent with those for the overall study population.

Conclusions: PFS, OS, and ORR were consistently improved with cabo compared to eve in subgroups based on prior systemic therapy of only suni or only pazo as prior VEGFR TKI therapy and prior anti-PD-1/PD-L1 therapy. Cabo should be considered as a treatment option for previously-treated patients with RCC regardless of prior systemic therapy.

Conflict of interest: Ownership: A. Arroyo: Stock ownership in Exelixis; Pfizer; R.J. Motzer: Novartis, Eli Lilly, Pfizer; C. Knollmannsberger: Speakers’ Bureau, Pfizer, Novartis; H. Gurney: Astellas, Sanofi-Genzyme, BMS, Amgen; E. Grande: Pfizer, Novartis. Corporate-sponsored Research: E. Grande: Pfizer; R.J. Motzer: Research for clinical trial support to employer (MSKCC) Pfizer, Novartis, Genentech Roche; S. Pal: Pfizer, Bayer, BMS; H. Gurney: Pfizer; M. Gross Goupil: Novartis (GSK), Eli Lilly, BMS, Roche; D. George: Genentech, Inc., Genentech Roche, Janssen Oncology, Novartis, Pfizer, Viament Pharmaceuticals, Astellas Pharma, BMS, Millennium, Acerta Pharma, Bayer, GSK, Dendreon; T. Powles: Eli Lilly, Inc., Novartis, GSK, Genetech. Other Substantive Relationships: T.K. Choueiri: Consulting or Advisory role, Pfizer, GSK, Novartis, Merck, Bayer, E. Grande: Consulting or Advisory Role for Novartis, GSK, Pfizer, Bayer, Eli Lilly, Genentech, Roche, Janssen Oncology, Novartis, Pfizer, Viament Pharmaceuticals, Astellas Pharma, BMS, Millennium, Acerta Pharma, Bayer, GSK, Dendreon; T. Powles: Eli Lilly, Inc., Novartis, GSK, Genetech. No conflict of interest.

siRNA-mediated silencing of Snail-1 induces apoptosis and alters microRNA expression in human urinary bladder cancer cell line

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Background and Purpose: Snail-1 known as one of important Transcription factor is a mediator of survival and cell migration, and expression is raised in numerous cancer types. Snail-1 gene may show a role in recurrence of several cancers including bladder cancer by down-regulating E-cadherin, inducing an epithelial to mesenchymal transition and its related miRNA. The aim of this study was to investigate the effect of a specific Snail-1 siRNA on apoptosis and alter EMT related miRNA of EJ-138 (bladder cancer) cells.

Experimental approach: The cells were transfected with siRNAs using transfection reagent. The cytotoxic effects of Snail-1 siRNA, on bladder cancer cells were determined using MTT assay. Relative Snail-1 mRNA level were measured by QRT-PCR, respectively. Apoptosis was measured by TUNEL test based on labeling of DNA strand breaks. We also evaluated miR-29b, miR-21 and miR-203 expression by QRT-PCR to determine alteration in miRNA expression involved in EMT.

Key results: Snail-1 siRNA significantly reduced mRNA expression levels in a 48 hour after transfection at the concentration of 60 PM in bladder cancer cells. We also showed that the silencing of Snail-1 led to the induction of apoptosis and miR-21 and miR-29b depression have been shown in snail-1 suppressed group in EJ-138 cells in vitro.

Conclusions and Implication: These results propose that Snail-1 might play an important role in the progression of bladder cancer, and be a potential therapeutic target for trigger apoptosis and suppression EMT related miRNA in bladder cancer.

No conflict of interest.
Author index

Page numbers are followed by abstract numbers in parentheses; Lb, late breaking; Ba, best abstract; O, oral; Pd, poster discussion; Ps, poster spotlight; Po, poster. Abstract number in bold type indicates presenter.

A
Aalbers, A., S7 (Ba6BA)
Aapro, M., S167 (Pd1813)
Aaronson, N., S7 (O101)
Abad, M., S52 (Po438)
Abbas, A., S31 (Po224)
Abdallah, E., S105 (Po885)
Abdelaal, A., S63 (Po469)
Abdelaziz, M., S60 (Po461)
Abdelrahman, M., S180 (Po2052)
Abduljapparov, A., S50 (Po433)
Abesamis Tiambeng, M.L., S41 (Po255)
Abiko, S., S110 (Po902)
Abolmaali, N., S102 (O826)
Abotaleb, A., S116 (Po1023, Po1024)
Abou El-Kasem, F., S19 (Po188)
Abouelkhir, I., S19 (Po188)
Abramov, I., S127 (Po1206)
Adar, A., S34 (Po233), S77 (Po608), S111 (Po908), S112 (Po909), S118 (Po1031)
Acuña, L., S141 (Po1343, Po1344)
Adamchuk, H., S42 (Po256)
Adamsen, L., S166 (Po1812)
Adan, R., S146 (Po1406), S147 (Po1407)
Adedosu, O., S94 (Po708)
Adejumoh, F., S18 (Po185)
Adeleke, G., S94 (Po708)
Adolfsson, J., S188 (O2118)
Adriaansz, S., S124 (O1146)
Adusel-Poku, P., S163 (Po1801), S172 (Pd1928)
Aertgeerts, B., S166 (Pd1811, Po1810)
Aerts, H.J.W.L., S58 (Po456)
Afonso, E., S122 (Po1090)
Aflah, D.T., S187 (O2117)
Afzal, N., S76 (Po606)
Agarwal, S., S150 (Po1516)
Aggarwal, A., S187 (O2116)
Agrawal, D., S47 (Po324)
Agrawal, P., S111 (Po907)
Agrawal, R., S158 (Po1608)
Agrawal, S., S14 (Po171), S156 (Po1608)
Agrawal, S.K., S57 (Po455)
Aguilar, C., S139 (Po1336)
Agus, E., S60 (Po459A)
Agus, M., S60 (Po459A)
Ahmad, A., S147 (Po1408)
Ahmad Ansari, M., S22 (Po201)
Ahmed, B., S53 (Po442)
Ahmed, F., S13 (Po167)
Ahmed, G., S146 (Po1405)
Ahmed, H., S140 (Po1430)
Ahmed, M., S30 (Po221)
Ahmed, S.A., S145 (Po1403), S146 (Po1404, Po1405)
Aicher, B., S86 (Po636)
Aida, I., S59 (Po457A)
Akakpo, K., S148 (Po1461)
Akasu, T., S52 (Po440)
Akewanlop, C., S41 (Po255)
Akhtar, N., S12 (Po165, Po166), S106 (Po890), S117 (Po907)
Akkus Yildirim, B., S80 (Po615), S81 (Po616), S93 (Po705)
Akpo, E.I.H., S44 (Po262)
Akshija, I., S181 (Po2053)
Aктan, G., S16 (Ps177)
Aktas, S., S77 (Po608)
Al-Amar, A., S192 (Po2180A)
Al-Faer, A., S10 (Po158)
Al-Maghrabi, J., S192 (Po2180A)
Al-Sayyad, A., S192 (Po2180A)
Alabi, A., S18 (Po185)
Aladashvili, A., S73 (Po596)
Alaeddine, N., S88 (Po608)
Alagoo Joao, A., S122 (Po1090)
Alarilla, M.V., S165 (Po1809)
Alba, E., S1 (Lb2LBA)
Albini, A., S59 (Po457A)
Albrand, G., S114 (O967)
Alcazar, J.A., S52 (Po438)
Aldaz, M., S148 (Po1461)
Aleman, B.M.P., S29 (Pd216)
Alexander, S., S40 (Po251)
Alfaya, L., S128 (Pd1207)
Ali, A., S189 (Po2173)
Allat, Z., S132 (Po1270), S133 (Po1271)
Alimhemeti, I., S162 (Po1794)
Aliste, L., S51 (Po437)
Ailitto, A.R., S193 (Po2186)
Alkebro, I., S165 (Ps1806)
Akharafaf, B., S134 (Po1322, Po1323), S137 (Po1332)
Alleaume, G., S6 (Ba5BA), S171 (O1876)
Allen, M., S14 (Po170)
Alloisio, M., S179 (Po2047)
Almalki, M., S135 (Po1225)
Almeida, I., S74 (Po599)
Almeida, T., S26 (Po211)
Almonte, A., S16 (Ps177)
Aloi, M.B., S87 (Po638)
Aqelthami, H., S78 (Po609A)
Altaj, W., S106 (Po887)
Altini, M., S114 (O968)
Alves, V., S105 (Po885)
Alyami, M., S65 (Po476)
Alzain, B., S103 (Po877)
Amadori, D., S114 (O968)
Amin, K., S31 (Po224)
Amira, G., S36 (Po237), S90 (Po699)
Amira, S., S76 (Po606A)
Amjad, A., S104 (Po884)
Ammedondia, I., S28 (Po215)
Amr Abdelwahab, M., S145 (Po1403)
Anand, A., S23 (Po204), S113 (Po915)
Anderegg, M.C.J., S85 (Po833)
Andersen, C., S166 (Po1812)
Andersen, K.K., S174 (Pd1935)
Ando, T., S39 (Po246)
Andrade, E.I.G., S54 (Po447)
Andreas, M., S4 (Ba1BA)
Andreas, S., S4 (Ba1BA)
Andrew, S., S127 (Po1206)
Andrew, H., S61 (Po463)
Anduaga, M.F., S52 (Po438)
Angelov, K., S15 (Po174)
Angoso, M., S52 (Po438)
Ansalonli, L., S92 (Po703A)
Ansari, M.A., S23 (Po202), S163 (Po1799)
Antonowicz, S., S3 (Lb6LBA)
Antoun, S., S88 (Po693)
Antwi, W., S172 (Pd1928)
Aparicio, D., S122 (Po1090)
Aparicio, T., S114 (O967)
Apicella, G., S161 (Pd1793)
Apostolidis, K., S121 (Po1088)
Appleman, L., S196 (Pd2196)
Araujo, B., S123 (O1142), S128 (Ps1208)
Araujo, V.E., S54 (Po447)
Arce, A., S78 (Po610), S154 (Po1624), S182 (Po2056), S183 (Po2057), S193 (Po2186)
Ambizzio, A., S185 (Po2061)
Anguelo Rodriguez, C., S27 (Po212A)
Arikan, N., S103 (Po880)
Arroyo, A., S197 (Po2199)
Aruga, T., S20 (Po189, Po192), S33 (Po230), S44 (Po264), S157 (Po1682)
Ascierto, P., S128 (Po1207)
Ashraf, M.S., S145 (Po1403A)
Asian, M., S80 (Po612A)
Astarzad, I., S143 (Po1396, S144 (Po1399, Po1400), S146 (Po1406), S147 (Po1407)
Atakhanova, N., S74 (Po600)
Atallah, S., S88 (Po683)
Alef, D., S20 (Po191)
Attijouhi, H., S133 (Po1271)
Auer, M., S24 (Po207), S39 (Po249)
Aula, H., S13 (Po168)
Ault, P., S71 (O540), S123 (O1144), S126 (Po1201), S177 (O1992)
Aran, A., S86 (Po836)
Awad, A., S132 (Po1268)
Ayoobi, H.A., S137 (Po1331A)
Aytaç Arslan, S., S29 (Po216A)
Aytulu, T., S62 (Po468)
Azarova, V., S96 (Po713)
Azpeitia, A., S146 (Po1406)
Baradaran, B., S125 (Po1200)
Baranovsky, S., S96 (Po713)
Barbieri, A., S73 (Po597)
Barkhof, F., S46 (Po322)
Barrientos, R., S27 (Po213A)
Barve, A., S40 (Po253), S41 (Po254, Po255)
Barzi, A., S157 (Po1681)
Bashnagel, A., S107 (Po891)
Bassani, B., S59 (Po457A)
Basso, G., S99 (Po768)
Basso, S.M.M., S11 (Po160), S17 (Po180), S62 (Po466), S74 (Po601), S179 (Po2049)
Bastholt, L., S128 (Po1207), S139 (Po1337)
Basu, S., S67 (Po480)
Batar, B., S148 (Po1461)
Bauer, S., S155 (Po1628)
Bauer, T.M., S148 (Po1460)
Baum, R., S151 (Po1518)
Baumann, M., S102 (O826)
Baumhoer, D., S152 (O1568)
Baur, E., S8 (O102)
Biaconi, P., S138 (Po1332A)
Bilgi Doğru, E., S78 (Po610A), S125 (Po1200A)
Bilgin, E., S138 (Po1332A)
Bilgin, E., S138 (Po1332A)
Bitticher, N., S151 (Po1518)
Bjelic-Radisic, V., S30 (Po217)
Bjordal, E., S133 (Po1273)
Blackwood-Chirchir, A., S136 (Po1331)
Blalzey, B., S134 (Po1322, Po1323)
Bleiker, E., S34 (Po231)
Bissors, J., S5 (Ba3BA)
Boscia, L., S32 (Po256)
Blanchard, P., S101 (O962)
Blanco Sanchez, G., S48 (Po330)
Blank, C., S122 (O1141), S124 (O1146), S128 (Po1207, Ps1208), S159 (O1734)
Blay, J.Y., S153 (O1572), S155 (Po1628)
Bois, R., S96 (Po683)
Boi, K., S175 (Po1940)
Boku, N., S77 (Po607A)
Boland, J., S8 (O102)
Bont, H., S7 (BabBA, Ba7BA), S69 (Po485)
Booth, C., S191 (Po2176)
Cordero, F., S62 (Po465)
Cope, S., S136 (Po1330, Po1331)
Crepaldi, A., S179 (Po2047)
Crundwell, M., S186 (O2115)
Cristaudo, A., S28 (Po214)
Cui, Y., S39 (Po248), S68 (Po1267)
Cseh, A., S183 (Po2059)
Cudennec, T., S114 (O2115)
Cui, Y., S39 (Po248), S68 (Po483), S182 (Po2054A)
Cuicchi, D., S193 (Po2189)
Cudennec, T., S114 (O2115)
Cui, Y., S39 (Po248), S68 (Po483), S182 (Po2054A)
Cuicchi, D., S193 (Po2189)
Culine, S., S2 (Lb3LBA)
Cuni, X., S194 (Po2189)
Cymbaluk-Ploska, A., S174 (Po1934)

D
D’Adamio, D., S155 (Po1628)
Dağgölü, N., S78 (Po610A)
Daher, A., S53 (Po443)
Dahl, A.A., S172 (O1877)
Dake, V.A., S17 (Po181)
Dallol, A., S192 (Po2180A)
Damiani, A., S59 (Po458)
Dandachi, N., S39 (Po249)
Danesi, R., S68 (Po482)
Danson, S., S169 (Po1823)
Dartot, D.C., S132 (Po1269)
Darushah, M., S10 (Po158)
Dastani, H., S135 (Po1329)
Datar, R.H., S39 (Po249)
Dattar, N.R., S89 (Po694)
Daud, A., S123 (O142)
Davessar, J.L., S103 (Po880)
Dawas, K.I., S85 (Po630)
Dayama, K., S156 (Po1680)
De Becker, D., S53 (Po443)
De Bock, T., S36 (Po236A)
De Carvalho Castilgas, G., S149 (Po1463)
De Decker, L., S114 (O967)
De Filippis, L., S180 (Po2052A)
De Francesco, I., S82 (Po618A)
De Geus-Oei, L.F., S153 (O1571)
De Giorgi, U., S114 (O968), S190 (Po2175)
De Grève, J., S176 (O1991)
De Hingh, I., S7 (Ba6BA), S69 (Po486)
De Hingh, L.H.T., S72 (O541)
De Iaco, P., S92 (Po703)
De Ingunza Barón, L., S109 (Po897)
De Jong, J., S115 (O969)
De Koekkoek-Doll, P., S195 (Po2194)
De Lisi, D., S190 (Po2175)
De Lorenzo, F., S121 (Po1088)
De Noo, M., S55 (Po446)
De Oliveira Silva de Queiroz, A.P., S144 (Po1402)
De Paz, B., S115 (O970)
De Rooy, J., S153 (O1571)
De Schutter, H., S177 (O1993)
De Silva, C., S74 (Po599)
De Steur, W.O., S7 (Ba7BA)
De Valeriola, D., S132 (Po1268)
De Vita, F., S87 (Po636)
De Wijerslooth, E., S83 (Po623)
De Witt, J., S127 (Po1291)
De Witt, W., S2 (Lb3LBA)
De Witt Hamer, P., S46 (Po322)
Dean, M., S197 (Po2199)
Deantonio, L., S60 (Po459), S161 (Po1793)
Dearden, A., S124 (Po1198)
Decadt, I., S131 (Po1264), S132 (Po1267)
Dees, E.C., S36 (Po243)
Degl’Esposti, C., S183 (Po2057)
Deidda, S., S60 (Po459A)
Dejong, C., S49 (O380)
Dekker, A., S59 (Po458), S139 (Po1335)
Del Ben, F., S150 (Po1465)
Del Bene, G., S180 (Po2052A)
Del Carmen, S., S52 (Po438)
Del Conto, A., S74 (Po601), S179 (Po2049)
Delannoy, M., S153 (O1572)
Delatte, P., S84 (Po628)
Delshaj, D., S28 (Po214), S92 (Po704)
Dellafiore, F., S119 (Po1083)
Dell’Italia, P., S44 (Po446)
Denariyakoon, S., S35 (Po235A)
Deo, S.V.S., S22 (Po200), S42 (Po258), S43 (Po259), S57 (Po455), S106 (Po888)
Deodato, F., S28 (Po215), S92 (Po703), S154 (Po1624), S182 (Po2056), S193 (Po2186)
Dereix, S., S79 (Po611A)
Deshayes, E., S66 (Po478A)
Despande, A., S83 (Po624), S110 (Po903)
Desideri, I., S8 (O102), S19 (Po187), S107 (Po893), S154 (Po1625), S192 (Po2184)
Desjardins, M., S52 (Po441)
Desolneux, G., S52 (Po441)
Detiti, B., S192 (Po2184)
Dev, K., S65 (Po477), S125 (Po1199)
Dewaele, E., S165 (Po1808)
Dharmaraj, A., S157 (Po1683)
Dharsis, S., S120 (Po1086)
Di Brina, L., S19 (Po187)
Di Cataldo, V., S109 (Po901)
Di Cuonzo, D., S152 (O1569)
Di Desidero, T., S68 (Po482)
Di Genesio Pagliuca, M., S161 (Po1793)
Di Gennaro, L., S17 (Po180)
Di Lorenzo, G., S190 (Po2175)
Di Lullo, L., S28 (Po215)
Di Marco, M., S87 (Po638)
Di Paolo, A., S68 (Po482)
Diab, K., S36 (Po237), S90 (Po699)
Diab, S., S16 (Po177)
Diakun, D., S191 (Po2178)
Dias, R., S41 (Po254)
Dias, W., S122 (Po1090)
Diaz de Tudanca, B.G., S174 (Po1936)
Diaz Díaz, V., S109 (Po897)
Diaz Gomez, L., S58 (Po456A)
Diaz Gómez, L., S109 (Po897)
Dicato, M., S58 (Po457)
Dickgubner, N.J., S176 (O1991)
Dieperink, K.B., S139 (O1337)
Dieperink, K.B., S168 (Po1820), S174 (Po1935)
Dierckx de Castrofelé, B., S166 (Po1811, Po1810)
Dijkstra, S., S159 (O1736)
Dikken, J.L., S7 (Ba7BA)
Dikov, T., S15 (Po174)
Dinapoli, N., S59 (Po458)
Dino, M.J., S165 (Po1809)
Dinapoli, N., S59 (Po458)
Dinapoli, N., S59 (Po458)
Dinkic, S., S173 (Po1931)
Djuraev, F., S74 (Po600)
Djuraev, M., S85 (Po629)
Dooa, S., S76 (Po606A)
Dodd, N., S184 (Ps2060)
Dodov, R., S15 (Po174)
Doebele, R.C., S148 (Po1460)
Doğan, H., S62 (Po648)
Doi, H., S108 (Po895)
Doi, K., S159 (Po187)
Doi, K., S159 (Po187)
Ebbinghaus, S., S122 (O1141), S123 (O1142), S128 (Po1208)
Eberhardt, W.E.E., S136 (Po1331)
Eberl, A., S132 (Pd1269)
Echebarria, A., S146 (Po1406), S147 (Po1407)
Echeverria, C., S160 (O1738)
Edris, A., S103 (Po877)
Edwards, L., S171 (O1874)
Egamberdiev, D., S85 (Po629)
Ehrnrooth, E., S176 (O1991), S185 (Po2061)
Eicher, M., S160 (O1737)
Eichler, C., S40 (Po252)
Eissa, S., S147 (Po1409)
Ekborn, A., S128 (Pd1207)
El-Bahrawy, M., S89 (Po695)
El Gammal, M., S21 (Po196), S22 (Po197)
El Hadad, A., S146 (Po1405)
El Hawi, M., S20 (Po191)
El Hemaly, A., S146 (Po1404)
El Husseiny, K., S63 (Po469)
El-Kholy, E.A., S145 (Po1403)
El Nadi, E., S146 (Po1405)
El Nakali, I., S53 (Pd442, Po443)
El-Shaarawi, M., S10 (Po158)
Elbastawisy, A., S80 (Po612A)
Ebellaghy, M., S146 (Po1404)
Elder, K., S23 (Pd205)
Elhadad, A.M., S147 (Po1409)
Elias, F., S117 (Po1026)
Elkhateeb, N., S146 (Po1404)
Elershaw, J., S131 (Pd1265)
Elmashar, A., S145 (Po1403)
Elshof, L., S15 (Pd173)
Elshair, Y., S36 (Po236A)
Eman, M., S76 (Pd606A)
Emanuelle, V., S179 (Po2047)
Emirani, A., S180 (Pd2052A)
Emiliani, A., S86 (Pd628)
Engelen, L., S159 (O1735)
Epurescu, D., S40 (Po251)
Erdkamp, F., S1 (Lb2LBA)
Erdogan, M.A., S43 (Po258)
Ergasheva, Z., S87 (Po688)
Ergün Soytürk, C., S62 (Po468)
Ermani, M., S179 (Po2049)
Escudier, B., S187 (O2117), S196 (Pd2196), S197 (Po2199)
Eskandari, E., S137 (Po1331A)
Espenschied, C., S25 (Po208)
Espenschied, C.R., S149 (Po1462)
Espina, J.A., S51 (Po437)
Essers, M., S102 (O625)
Esteban, C., S52 (Po438)
Esteves, S., S189 (Po2172)
Etiennette-Sellourn, N., S48 (Po328)
Evelen, C., S79 (Pd611A)
Favret, A.M., S1 (Lb2LBA)
Fayard, C., S156 (Po1829)
Febraro, A., S87 (Po638)
Febraro, A., S87 (Po638)
Fedewa, S., S157 (Pd1681)
Federand, C., S8 (O103)
Federand, C., S8 (O103)
Feifel, J., S185 (Po2061)
Fellali, Y., S28 (Po214), S78 (Po610)
Ferdinando, C., S87 (Po689), S88 (Pd628)
Ferrero, A., S87 (Po689), S88 (Pd628)
Fernandez-Bernal, M., S147 (Po1407)
Fernandez-Teruel, C., S134 (Po1324)
Fernando, A., S104 (Po883)
Fernando, T., S99 (Po768)
Ferradore, C., S87 (Po689), S88 (Pd628)
Ferrioli, M., S92 (Po703), S182 (Po2056)
Fermiñán, E., S52 (Po438)
Fernandez, A., S175 (Pd1937)
Fernandez, A., S175 (Pd1937)
Ferrell, S., S163 (Po1800)
Farrugia, H., S23 (Pd205)
Fatigante, L.R., S28 (Po214)
Faut, M., S127 (Po1205A)
Favret, A.M., S1 (Lb2LBA)
Fayard, C., S156 (Po1829)
Febraro, A., S87 (Po638)
Fedewa, S., S157 (Pd1681)
Fedyanin, M., S96 (Po713)
Feit, K., S178 (O1994)
Feliugia, J., S182 (Po2180)
Felipe, E., S185 (Po2061)
Felli, J., S155 (Po1627)
Feng, R., S81 (Po617)
Feng, Y., S75 (Po603)
Fenton, D., S157 (Po1829)
Fennelly, D., S44 (Pd263)
Ferguson, B., S148 (Po1461)
Ferioi, M., S92 (Po703), S182 (Po2056)
Ferradore, C., S87 (Po689), S88 (Pd628)
Fischeder, C., S87 (Po689), S88 (Pd628)
Fischeder, C., S87 (Po689), S88 (Pd628)
Fizhbach, C., S134 (Po1324)
Fischer, G.O., S81 (Po618)
Fitzpatrick, P., S8 (O103)
Flamen, P., S53 (Po443), S84 (Pd628)
Flamini, V., S66 (Po483)
Flanagan, F., S8 (O103)
Flesch, H., S113 (Po914)
Flonta, T., S28 (Po214A)
Florindir, F., S121 (Po1088)
Flucke, U., S152 (O1570), S153 (O1571)
Fotlin, L., S87 (Po638)
Fonck, M., S52 (Po441)
Fong, L., S2 (Lb3LBA)
Fontana, A., S28 (Po214)
Formean, M., S104 (Po881)
Forni, F., S78 (Po610)
Forster, M., S134 (Po1324)
Fortpied, C., S101 (O823)
Fortunato, F., S60 (Po459A)
Fossa, S.D., S142 (Po1930)
Fossa, S.D., S142 (Po1930)
Fossey-Diaz, V., S114 (O967)
Foukakis, T., S3 (Lb5LBA)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
Fournier, F., S40 (Po251)
M

Ma, C., S76 (Po605A), S93 (Po705A, Po705B), S183 (Po2057A)
Ma, K.H., S47 (Po327)
Ma, L., S95 (Po710)
Maartense, E., S9 (O199)
Maas, M., S49 (O380), S54 (Po446)
Macacu, A., S177 (O1992)
Macchia, G., S28 (Po215), S78 (Po610), S92 (Po703), S154 (Po1624), S193 (Po2186)
Machado, C., S26 (Po211)
Machida, Y., S178 (O1995)
Macias Lozano, M.J., S109 (Po897)
Maciel de Souza Vianna, L., S149 (Po1983)
Mackeen, M., S170 (Po1825)
Mackillop, W., S191 (Po2176)
Madu, M., S124 (O1146), S126 (Po1203, Po1204), S127 (Po1205A, Ps1205)
Maes, E., S44 (Po262)
Maeshima, Y., S33 (Po228)
Maftouh, M., S86 (Po636)
Magdy, N., S89 (Po695)
Magon, A., S119 (Po1083)
Maguire, M., S131 (Po1265)
Mahajan, A., S83 (Po624), S110 (Po903)
Mahaseth, R., S168 (Po1818)
Mah–M A., S153 (O1752)
Mahjoubi, F., S137 (Po1331A)
Mahler, C., S4 (Ba1BA)
Mahon, G., S56 (Po457)
Mai, Y., S2 (Lb3LBA)
Maingon, P., S153 (O1752)
Mainwaring, P.N., S187 (O2117)
Maisey, T., S61 (Po463)
Majumdar, A., S70 (Po488)
Maki, R., S1 (Po1628)
Makris, C., S136 (Po1330, Po1331)
Maldonando, C., S92 (Po703A)
Malangone-Monaco, E., S191 (Po2178)
Malek, A., S91 (Po702)
Malhotra, B.D., S138 (Po1334)
Malki, A.A., S104 (Po882)
Malki, P.S., S183 (Po2056A)
Malinowski, M., S65 (Po475)
Mall, H., S124 (O1146)
Maloney, F., S131 (Po1265)
Maloney, L., S95 (Po710)
Maltese, M., S44 (Po263)
Maramarosulova, D., S87 (Po688), S94 (Po706)
Mammillapalli, G., S41 (Po255)
Manchon-Walsh, P., S51 (Po437)
Mancuso, A., S121 (Po1087)
Mandeville, H., S171 (O1874)
Manfredi, B., S28 (Po214), S92 (Po704)
Mangoni, M., S8 (O102), S19 (Po187), S192 (Po2184)
Manhas, J., S57 (Po455)
Manikandan, L., S12 (Po165)
Manikhas, A., S41 (Po255)
Manikhas, G., S96 (Po713)
Mann, B., S23 (Po205)
Manna, A., S160 (Po1789), S161 (Po1790)
Manna, G., S180 (Po2052A)
Manoukian, S., S11 (Po162)
Manten-Horst, E., S159 (O1735), S171 (O1875)
Mantini, G., S193 (Po1886)
Marafioti, L., S163 (Po1801A)
Marang-van de Mheen, P., S67 (Po480A)
Marazza, F., S28 (Po215)
Marchal, C., S153 (O1572)
Marcu, L., S28 (Po214A)
Marinaho, R., S122 (Po1090)
Marion, D., S126 (Po1203)
Martiotti, V., S25 (Po208A), S186 (Po2065)
Markar, S., S3 (Lb6LBA)
Marriott Music, M., S31 (Po223)
Marruzzo, L., S8 (O102)
Marsh, L., S171 (O1874)
Marsoner, K., S73 (O544)
Martelli, O., S183 (Po2057)
Marten, A., S176 (O1991), S184 (Ps2060)
Martillotta, A., S163 (Po1801A)
Martin, C., S165 (Po1806A)
Martin, J., S194 (Po2188)
Martin, R., S70 (Po489)
Martin-Guerrero, I., S143 (O1398), S144 (Po1399, Po1400), S147 (Po1407)
Martinez Bautista, M.J., S48 (Po330)
Martinez-Marin, V., S155 (Po1627)
Maruzzo, M., S190 (Po2175)
Marzo, K., S179 (Po2047)
Masat, S., S130 (Po1261), S133 (Po1272)
Mascarenhas, F., S26 (Po211)
Masci, I., S182 (Po2056)
Masciocchi, C., S59 (Po458)
Masi, L., S109 (Po901)
Masini, C., S114 (O968)
Maskell, D., S40 (Po251)
Mason, M., S187 (O2116)
Mason, S., S131 (Po1265)
Masood, M., S89 (Po695)
Massa, I., S114 (O968)
Massari, F., S190 (Po2175)
Massenzo, A., S163 (Po1801A)
Massiahna, D., S86 (Po636)
Masucci, G., S122 (O1141)
Mathieu, M.C., S36 (Po237A)
Mathoulin Pellissier, S., S114 (O967)
Mathur, S., S22 (Po200)
Matias-Pérez, A., S174 (Po1936)
Matoba, M., S178 (O1995)
Matorin, O., S111 (Po905, Po906)
Matos Rodrigues de Brito, L., S149 (Po1463)
Mátrai, Z., S1 (Lb1BA)
Matsuda, K., S110 (Po902)
Matsui, T., S178 (O1995)
Mattano, L., S42 (Po256)
Matteucci, F., S28 (Po214)
Mattucci, G.C., S78 (Po610), S154 (Po1624)
May, A., S9 (O105)
Mazoumi, C., S36 (Po237A)
Mazurek, M., S51 (Ps435)
Mazzotti, V., S28 (Po214)
McClulloch, T.M., S107 (Po891)
McGlinchey, T., S131 (Po1265)
McKenna, M., S186 (Po2065)
McNeil, C., S122 (O1141)
McNeill, I., S95 (Po710)
McPhee, A., S189 (Po2173)
Meacci, F., S8 (O102)
Mealing, S., S99 (Ps769)
Meatini, I., S8 (O102), S19 (Po187), S154 (Po1625), S192 (Po2184)
Meddah, B., S132 (Po1270), S133 (Po1271)
Meershoek-Klein Kranenburg, E., S9 (O104)
Meershoek-Klein Kranenburg, E., S7 (Ba7BA)
Meheus, L., S121 (Po1089)
Mehrotra, M., S23 (Po204)
Mehta, A., S135 (Po1327)
Meier, K., S132 (Po2189)
Meijer, G., S55 (Ps448)
Meijerink, W., S7 (Ba6BA)
Author index

Nuzzo, M., S193 (Po2186)
Nyakas, M., S128 (Pd1207)

O
Oades, G., S189 (Po2173)
Oaknin, A., S95 (Po710)
O'Boyle, G., S194 (Po2188)
O'Brien, M., S14 (Po170)
O'Byrne, K., S175 (O1991), S184 (Pd2060)
O'Day, S.J., S122 (O1141)
O'Doherty, A., S8 (O103)
Offerens, B.V., S9 (O106)
Ogale, S., S191 (Pd2178)
Oguz Soydinc, H., S138 (Po1332A)
Oh, S., S108 (Po896)
Ohiisson-Nevo, E., S165 (Ps1806)
Oji, B., S45 (Po316)
Okines, A., S14 (Pd170)
Olarte, M., S56 (Po452)
Oldenberg, H., S7 (O101)
Oldenmenger, W., S4 (Lb7LBA)
Olen, T., S196 (Pd2196)
Olling, K., S169 (Po1821)
Olmetto, E., S19 (O102)
Olsson-Bagge, R., S126 (Pd1202)
Olukiran, G., S18 (Po185)
Orfao, A., S52 (Po438)
Orlando, F., S26 (Po214), S92 (Po704)
Orlandi, P., S68 (Po482)
Orlov, S., S96 (Po713)
Oriz-Calahorra, J., S147 (Po1407)
Orzalesi, L., S8 (O102)
Oswieckia, K., S193 (Po2187)
Ottlund, U., S4 (Lb7LBA)
O'Sullivan, B., S101 (O823)
Oswald, D., S149 (Po1464)
Otaka, Y., S164 (Po1804)
Ottesen, M.K., S168 (Po1817)
Oudard, S., S196 (Pd2196)
Oude Ophuis, C., S127 (Po1204A, Po1205A)
Ougogue, K., S132 (Po1270), S133 (Po1271)
Overgaard, J., S9 (O106), S101 (O823), S102 (O824)
Owen, S., S75 (Po603), S87 (Po639), S90 (Po696)
Oyen, W., S153 (O1571)
Oza, A., S96 (O101)
Ozbagriaciik, M., S34 (Po233), S111 (Po908)

P
Paiar, F., S28 (Po214), S92 (Po704)
Paillaud, E., S114 (O967)
Pal, S., S150 (Po1516), S187 (O2117), S197 (Pp2186, Po2199)
Paladino, J., S131 (Pd1265)
Palanichamy, J.K., S99 (Po768)
Palascak, M., S186 (Po2065)
Palottta, S., S8 (O102)
Palombarini, M., S182 (Po2056)
Pamouklijan, F., S114 (O967)
Panaro, F., S66 (Po478A)
Panchal, R., S25 (Po208A)
Panni, V., S182 (Po2056)
Panos Smith, L., S25 (Po208), S149 (Po1462)
Panov, V., S189 (Po2171)
Pantano, F., S190 (Po2175)
Pantsulaiia, I., S73 (Po596)
Pantziarik, M., S121 (Pd1089)
Panwar, V., S46 (Po320)
Pappot, H., S139 (Po1337), S175 (Pd1940)
Pardini, B., S62 (Po465)
Pare, A., S156 (Po1629)
Parikh, R., S197 (Po2198)
Parizot Moraes, M., S144 (Po1402)
Park, J.Y., S92 (Po702A), S96 (Po714), S97 (Po720)
Park, K., S176 (O1991), S184 (Ps2060)
Park, S.H., S197 (Po2199)
Parmar, M.K., S101 (O823)
Parra, J., S41 (Po255)
Parrondo, R., S25 (Po208A), S186 (Po2065)
Parthasarad, C., S46 (Po318)
Parton, M., S14 (Po170)
Parveen, S., S35 (Po236)
Parvin, J., S148 (Po1461)
Paryani, J., S12 (Po165, Po166)
Passanisi, P., S11 (Po162)
Pasqualetti, F., S28 (Po214)
Passard, A., S87 (Ps638)
Passcher, E., S101 (O822)
Passot, G., S65 (Po476)
Patel, K., S25 (Po208A)
Patel, M., S83 (Po624), S107 (Po892), S110 (Po903)
Pathak, M., S42 (Po258), S43 (Po259)
Pathiraja, K., S38 (Po243)
Pathy, S., S183 (Po2056A)
Patiraki, E., S4 (Lb7LBA)
Patricio, A., S192 (Po2180)
Paudyal, T., S149 (Po1462)
Pauly, M., S58 (Po457)
Pauwels, K., S115 (O971)
Pavesi, L., S140 (Po1338, Po1339)
Pawar, S., S12 (Po165, Po166)
Pawar, S., S106 (Po890), S112 (Po912)
Paz-Ares, L., S176 (O1991), S184 (Pd2060)

Pe, M., S138 (Ps1333)
Peacock, J., S69 (Po487)
Pecic, V., S63 (Po470)
Pecorari, S., S180 (Pd2052A)
Peep, D., S124 (O1146)
Peeters, N., S58 (Ps456)
Peissel, B., S11 (Po162)
Peilech, S., S192 (Po2180)
Peley, G., S1 (Lb1LBA)
Peltola, K., S187 (O2117)
Penza, A., S147 (Pd1407)
Pencheva, D., S15 (Po174)
Pennella, E., S40 (Po253), S41 (Po254, Po255), S42 (Po256)
Penrod, J.R., S135 (O1329), S136 (Ps1330, Po1331)
Perakis, S., S24 (Po207)
Peretti-Watel, P., S6 (Ba5BA), S171 (O1876)
Perez Ochoa, A., S27 (Po212A)
Perez-Romasanta, L.A., S174 (Po1936)
Perini, R., S2 (Lb3LBA)
Perna, M., S154 (Po1625)
Perrin, R., S102 (O826)
Perrone, A.M., S92 (Po703)
Perrone, F., S92 (Po704)
Pertschy, B., S57 (Po455A)
Perveen, K., S47 (Po325)
Peters, G., S86 (Po363)
Peters, S., S160 (O1737)
Petersen, G., S175 (Pd1940)
Petit, B., S106 (Po889)
Petit, C., S101 (O823)
Petrella, T.M., S122 (O1141)
Petric-Mise, B., S88 (Po691)
Petrov, L., S63 (Po471), S64 (Po472, Po473, Po474)
Petrova, A., S27 (Po213)
Petrylak, D., S2 (Lb3LBA)
Pfeiffer, P., S69 (Po485)
Phelps, C., S96 (Po713)
Picentini, G., S140 (Ps1338, Po1339)
Piccart, M., S132 (Ps1268)
Piccirillo, M., S188 (Po2170)
Pienkowski, A., S154 (O1573)
Piergi, J.Y., S170 (Po1824)
Pieri, M., S28 (Po215)
Pigazzi, M., S99 (Po768)
Pignon, J.P., S101 (O823)
Pil, K., S167 (Po1814)
Pikkel, J., S197 (Po2199)
Pikin, O., S111 (Po905)
Pilar-Oribe, J., S147 (Po1407)
Pimi, C., S79 (Po611A)
Pinto, R., S137 (Po1332)
Pinho Carneiro, F., S149 (Po1463)
Piro, F., S163 (Po1801A)
Piruska, A., S150 (Po1465)
Piselli, P., S176 (Po1817)
Pitraf, F., S119 (Po1083)
Pizot, C., S79 (O102)
Pisella, J.T., S78 (Po609A)
Plummer, C.J., S9 (O2117)
Poccard, M., S79 (Po111A)
Author index

Thornton Snider, J., S135 (Po1329)
Thrift-Perry, M., S120 (Po1086)
Thulka, S., S22 (Po200)
Thywissen, T., S49 (O380)
Tian, Y., S149 (Po1462)
Tiessen, R., S41 (Po254)
Tigue, R., S175 (Ps1937)
Tilanus-Linthorst, M.M.A., S2 (Lb4LBA)
Tilgen Yasassever, C., S78 (Po610A), S125 (Po1200A), S138 (Po1332A)
Tillier, C., S195 (Po2192)
Timmerman, P., S127 (Ps1205)
Tinker, A.V., S95 (Po710)
Tinkler-Hundal, E., S61 (Po463)
Tiran, V., S39 (Po249)
Tilov, S., S91 (Po702)
Tjurlind, S., S96 (Po713)
Tobias, J., S101 (O823)
Todorov, G., S15 (Po174)
Tolan, K.H., S34 (Po233), S121 (Po909), S118 (Po1031)
Tolanyan, S., S16 (Ps177)
Tolento, G., S28 (Po215)
Tollenaar, R., S67 (Po480A)
Tostrup, L., S139 (Po1337)
Tomberger, A., S73 (O544)
Tomczak, P., S196 (Po2196)
Tomey, O., S117 (Po1027), S118 (Po1028)
Tonami, H., S178 (O1995)
Tong, D., S124 (Po1197)
Tonini, G., S190 (Po2175)
Tonison, J., S81 (Po618)
Topal, C., S77 (Po608)
Topal, H., S83 (Po623)
Topulli, J., S8 (O102)
Torinali, M., S190 (Po2175)
Torrens, C., S4 (Lb7LBA)
Torun, N., S80 (Po615)
Towers, R., S175 (Ps1937)
Tozzoli, R., S11 (Po160), S74 (Po601), S179 (Po2049)
Tran, T., S99 (Po768)
Trebeschi, S., S58 (Po456)
Tremlett, J., S186 (O2115)
Trennepohl, J., S144 (Po1402)
Triap, A., S7 (Ba7BA)
Tripaci, I., S156 (Po1679)
Tripathy, D., S17 (Po181)
Troitskaya, I., S63 (Po471), S64 (Po472)
Trombetta, L., S192 (Po2184)
Trompeitto, M., S62 (Po465)
Troost, E.G., S102 (O826)
Trotli, A., S101 (O823)
Truc, G., S153 (O1572)
Tsai, C.M., S183 (Po2059)
Tsai, M.S., S86 (Po634)
Tsaur, G., S143 (Po1397)
Tseng, C.H., S77 (Po608A)
Tseng, Y.Y., S46 (Po321)
Tsitsi, T., S143 (Po1396)
Tsuburaya, A., S72 (O542)
Tsyganova, I., S127 (Po1206)
Tunn, P.U., S152 (O1568)
Tuponogov, S., S143 (Po1397)
Turetta, G., S150 (Po1465)
Turgut Coşan, D., S18 (Po183)
Turgut Coşan, D., S19 (Po186)
Turkaj, A., S154 (Po1625)
Turner, N., S14 (Po170)
Turli, L., S60 (Po459)
Tuvin, I., S189 (Po2171)

U
Ubaii, P., S11 (Po160), S17 (Po180), S62 (Po466), S74 (Po601), S179 (Po2049)
Udayasankar, S., S37 (Po242)
Udvarhelyi, N., S1 (Lb1LBA)
Ueda, Y., S178 (O1995)
Uesaka, K., S77 (Po607A)
Ulhlmann, L., S4 (Ba1BA)
Ullah, M., S79 (Po611A)
Ulmasov, F., S85 (Po629)
Ulz, P., S24 (Po207)
Umerez, M., S143 (Po1398)
Unal, E., S34 (Po233), S77 (Po608), S111 (Po908), S112 (Po909), S118 (Po1031)
Undamatia, R., S25 (Po208A)
Unterrieder, K., S30 (Po217)
Uramoto, H., S178 (O1995)
Uranitsch, S., S57 (Po455A)
Urbic, D., S141 (Po1343, Po1344)
Ursino, S., S28 (Po214)
Ushimado, K., S39 (Po246)
Usmanij, E., S153 (O1571)
Usuda, K., S178 (O1995)
Utsumi, T., S39 (Po246)
Van den Heuvel, M., S159 (O1734)
Van den Does de Willebois, E., S36 (Po236A)
Van der Elst, E., S166 (Po1811)
Van der Geest, L.G.M., S72 (O541), S86 (Po637)
Van der Graaf, W., S152 (O1570), S153 (O1571), S159 (O1735), S171 (O1875)
Van der Hage, J., S126 (Po1203, Po1204), S127 (Po1205)
Van der Harst, E., S67 (Po480A)
Van der Hiel, B., S124 (O1146), S126 (Po1204), S127 (Po1205)
Van der Kaaij, R.T., S75 (Po604)
Van der Linden, Y., S159 (O1736)
Van der Meij, S., S7 (O101)
Van der Meulen, J., S187 (O2116)
Van der Poel, H., S195 (Po2192, Po2194)
Van der Roest, R., S195 (Po2192)
Van der Sande, M., S54 (Po446)
Van der Stok, E.P., S66 (Po479A)
Van der Valk, M., S55 (Po450)
Van der Velden, A.M.T., S5 (Ba2BA)
Van Dieren, J., S159 (O1734)
Van Dieren, J.M., S75 (Po604)
Van Dulken, E., S7 (O101)
Van Dulin, S., S86 (O2114)
Van Echteld, C., S151 (O1518)
Van Eijk, C.H.J., S72 (O541)
Van Eijndhoven, E., S135 (Po1329), S136 (Po1330, Po1331)
Van Erp, A., S152 (O1570)
Van Gils, C., S9 (O105)
Van Groenenstein, W., S7 (Ba6BA)
Van Grieken, N.C.T., S7 (Ba7BA)
Van Griethuysen, J., S54 (Po446)
Van Griethuysen, J.J.M., S58 (Po456)
Van Groningen, J., S67 (Po480A)
Van Harten, W., S34 (Po231), S101 (O822), S118 (Po1030), S129 (Po1259), S130 (Po1263)
Van Heeswijk, M., S54 (Po446)
Van Hemelrijck, M., S188 (O2118)
Van Krieken, A., S86 (Po636)
Van Laarhoven, C.J.H.M., S72 (O541)
Van Laarhoven, H.W.M., S85 (Po633), S86 (Po637)
Van Lanckveld, J., S7 (O101)
Van Leerdam, M., S159 (O1734)
Van Leeuwen, B., S127 (Po1205A)
Van Leeuwen, F., S15 (Po173), S195 (Po2192)
Van Leeuwen, F.E., S29 (Po216)
Van Leeuwen-Stok, E., S9 (O104)
Van Maaren, M.C., S2 (Lb7LBA)
Van Marcke, C., S106 (Po889)
Van Meerbeek, J.P., S177 (O1993)
Van Noordens, S., S89 (Po695)
Van Oijen, M., S53 (Po444), S68 (Po484)
Van Oijen, M.G.H., S85 (Po633)
Van Riel, C., S153 (O1571)
Van Rooijen, J.M., S5 (Ba2BA)
Van Sandick, J.W., S7 (Ba7BA), S75 (Po604)
Van Soest, J., S59 (Po458)
Van Thieli, L., S135 (Po1328)
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yonemori, K.</td>
<td>S94</td>
<td>Po709</td>
</tr>
<tr>
<td>Yong, Y.</td>
<td>S76</td>
<td>Po605A</td>
</tr>
<tr>
<td>Yoshida, H.</td>
<td>S94</td>
<td>Po709</td>
</tr>
<tr>
<td>Yoshimoto, Y.</td>
<td>S33</td>
<td>Po228</td>
</tr>
<tr>
<td>Youkstetter, J.</td>
<td>S196</td>
<td>Po2196</td>
</tr>
<tr>
<td>Younes, A.</td>
<td>S146</td>
<td>Po1405</td>
</tr>
<tr>
<td>Young-Afat, D.</td>
<td>S9</td>
<td>O105</td>
</tr>
<tr>
<td>Youssef, M.</td>
<td>S30</td>
<td>Po221</td>
</tr>
<tr>
<td>Youssef, O.</td>
<td>S30</td>
<td>Po221</td>
</tr>
<tr>
<td>Youssef, M.</td>
<td>S36</td>
<td>Po237</td>
</tr>
<tr>
<td>Yu, M.</td>
<td>S107</td>
<td>Po891</td>
</tr>
<tr>
<td>Yu, X.</td>
<td>S112</td>
<td>Po913</td>
</tr>
<tr>
<td>Yuan, J.</td>
<td>S41</td>
<td>Po255</td>
</tr>
<tr>
<td>Yuan, Y.</td>
<td>S135</td>
<td>Po1329</td>
</tr>
<tr>
<td>Yucel, M.</td>
<td>S34</td>
<td>Po233</td>
</tr>
<tr>
<td>Yue, J.</td>
<td>S81</td>
<td>Po617</td>
</tr>
<tr>
<td>Yukihide, S.</td>
<td>S129</td>
<td>Po1260</td>
</tr>
<tr>
<td>Yukekdağ, S.</td>
<td>S34</td>
<td>Po233</td>
</tr>
<tr>
<td></td>
<td>S118</td>
<td>Po1031</td>
</tr>
<tr>
<td>Yunokawa, M.</td>
<td>S94</td>
<td>Po709</td>
</tr>
<tr>
<td>Yusuf, A.F.</td>
<td>S149</td>
<td>Po1462</td>
</tr>
<tr>
<td>Yusuf, D.</td>
<td>S51</td>
<td>Ps435</td>
</tr>
<tr>
<td></td>
<td>S67</td>
<td>Po481</td>
</tr>
<tr>
<td>Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zabkiewicz, C.</td>
<td>S17</td>
<td>Po182</td>
</tr>
<tr>
<td>Zacchia, A.</td>
<td>S44</td>
<td>Po263</td>
</tr>
<tr>
<td>Zacharoulis, S.</td>
<td>S171</td>
<td>O1874</td>
</tr>
<tr>
<td>Zackrisson, B.</td>
<td>S101</td>
<td>O823</td>
</tr>
<tr>
<td>Zaghoul, M.</td>
<td>S146</td>
<td>Po1404, Po1405</td>
</tr>
<tr>
<td>Zagonel, V.</td>
<td>S87</td>
<td>Po638</td>
</tr>
<tr>
<td>Zaidi, S.S.A.</td>
<td>S10</td>
<td>Po157</td>
</tr>
<tr>
<td></td>
<td>S50</td>
<td>Po434</td>
</tr>
<tr>
<td></td>
<td>S87</td>
<td>Po689</td>
</tr>
<tr>
<td></td>
<td>S88</td>
<td>Po690</td>
</tr>
<tr>
<td>Zaky, I.</td>
<td>S145</td>
<td>Po1403</td>
</tr>
<tr>
<td>Zalotok, S.</td>
<td>S12</td>
<td>Po164</td>
</tr>
<tr>
<td>Zamagni, A.</td>
<td>S182</td>
<td>Po2056</td>
</tr>
<tr>
<td>Zamagni, C.</td>
<td>S28</td>
<td>Po215</td>
</tr>
<tr>
<td>Zanellato, S.</td>
<td>S59</td>
<td>Po457A</td>
</tr>
<tr>
<td>Zaniboni, A.</td>
<td>S87</td>
<td>Po638</td>
</tr>
<tr>
<td>Zarrati, S.</td>
<td>S11</td>
<td>Po161</td>
</tr>
<tr>
<td>Zatari, S.</td>
<td>S135</td>
<td>Po1325</td>
</tr>
<tr>
<td>Zaoutashvili, Z.</td>
<td>S42</td>
<td>Po256</td>
</tr>
<tr>
<td>Zaychikov, A.</td>
<td>S143</td>
<td>Po1397</td>
</tr>
<tr>
<td>Zebrack, B.</td>
<td>S139</td>
<td>Po1336</td>
</tr>
<tr>
<td>Zeevat, F.</td>
<td>S15</td>
<td>Po175</td>
</tr>
<tr>
<td>Zekri, A.R.</td>
<td>S76</td>
<td>Po606A</td>
</tr>
<tr>
<td>Zekry, W.</td>
<td>S145</td>
<td>Po1403</td>
</tr>
<tr>
<td>Zemankova, P.</td>
<td>S25</td>
<td>Po208</td>
</tr>
<tr>
<td>Zewdu, F.</td>
<td>S161</td>
<td>Po1792</td>
</tr>
<tr>
<td>Zhai, G.</td>
<td>S56</td>
<td>Po51</td>
</tr>
<tr>
<td>Zhang, H.</td>
<td>S80</td>
<td>Po614</td>
</tr>
<tr>
<td>Zhang, L.</td>
<td>S176</td>
<td>O1991</td>
</tr>
<tr>
<td>Zhang, Q.</td>
<td>S101</td>
<td>O823</td>
</tr>
<tr>
<td>Zhang, Z.</td>
<td>S68</td>
<td>Po483</td>
</tr>
<tr>
<td>Zhao, J.</td>
<td>S56</td>
<td>Po453</td>
</tr>
<tr>
<td>Zhao, Q.</td>
<td>S81</td>
<td>Po617</td>
</tr>
<tr>
<td>Zheng, F.</td>
<td>S68</td>
<td>Po483</td>
</tr>
<tr>
<td>Zhi, X.</td>
<td>S182</td>
<td>Po2054A</td>
</tr>
<tr>
<td>Zhou, H.</td>
<td>S128</td>
<td>Ps1208</td>
</tr>
<tr>
<td>Zhu, K.</td>
<td>S81</td>
<td>Po617</td>
</tr>
<tr>
<td>Zhu, Y.</td>
<td>S56</td>
<td>Po451, Po453</td>
</tr>
<tr>
<td>Zidan, M.</td>
<td>S140</td>
<td>Po1340</td>
</tr>
<tr>
<td>Zineb, A.</td>
<td>S169</td>
<td>Po1822</td>
</tr>
<tr>
<td>Zips, D.</td>
<td>S81</td>
<td>Po618</td>
</tr>
<tr>
<td>Zohdiaghdam, R.</td>
<td>S21</td>
<td>Po194, Po195</td>
</tr>
<tr>
<td>Zompatori, M.</td>
<td>S182</td>
<td>Po2056</td>
</tr>
<tr>
<td>Zöphel, K.</td>
<td>S102</td>
<td>O826</td>
</tr>
<tr>
<td>Zorcolo, L.</td>
<td>S60</td>
<td>Po459A</td>
</tr>
<tr>
<td>Zoumadakis, C.</td>
<td>S181</td>
<td>Po2054</td>
</tr>
<tr>
<td>Zuberi, M.</td>
<td>S98</td>
<td>Po766</td>
</tr>
<tr>
<td>Szabad, G.</td>
<td>S99</td>
<td>Po767</td>
</tr>
<tr>
<td>Zucali, P.</td>
<td>S179</td>
<td>Po2047</td>
</tr>
<tr>
<td>Zucali, P.A.</td>
<td>S181</td>
<td>Po2054</td>
</tr>
<tr>
<td>Zwisler, A.D.</td>
<td>S139</td>
<td>Po1337</td>
</tr>
</tbody>
</table>