**COMPARISON OF NUTRITIONAL ASSESSMENT WITH A NEW DEFINITION OF CACHEXIA IN DETERMINING OUTCOMES OF ADVANCED CANCER PATIENTS**

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**Background:** An international consensus statement providing a definition and diagnostic criteria for cancer cachexia was recently published. This study aimed to compare the relative prognostic utility of this definition with nutritional status as defined by the Patient-Generated Subjective Global Assessment (PG-SGA) tool.

**Methods:** A prospective cohort study was conducted in a tertiary hospital where chemotherapy naive patients with life expectancy ≥ 3 months were recruited by medical oncologists and a research dietitian. Kaplan-Meier survival analyses were used to determine the median survival of patients with advanced cancer in the cohort study, and a subset of patients who met the criteria for cancer cachexia as defined in the international consensus (Fearon 2011). The log rank chi-square test was used to evaluate the strength of predictors of overall survival (OS). A P value of <0.05 was considered significant.

**Results:** The following table demonstrates the patient baseline characteristics of the two cohorts.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cachexia (Met ≥1 criteria)</th>
<th>Malnourished (PG-SGA B/C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>80% (n= 62/78)</td>
<td>58% (n= 66/114)</td>
</tr>
<tr>
<td>Age, years, mean</td>
<td>61 (SD 8.7)</td>
<td>63 (SD 9.7)</td>
</tr>
<tr>
<td>Male, % (n)</td>
<td>63% (39)</td>
<td>57% (44)</td>
</tr>
<tr>
<td>% of weight loss in 6 months preceding, mean</td>
<td>11.1 (SD 5.5)</td>
<td>9.5 (SD 6.4)</td>
</tr>
<tr>
<td>Estimated OS, mths, median (95% CI) Log rank test (Mantel-Cox)</td>
<td>11.4 (5.5 – 17.3) 2.24</td>
<td>8.4 (4.06 – 12.69) 8.07</td>
</tr>
</tbody>
</table>

Sixty eight percent of the advanced cancer patients (53 of the 78) were both malnourished and met ≥1 of the proposed diagnostic criteria for cachexia at baseline. The log rank test from the Kaplan-Meier survival analysis demonstrated that nutritional status as defined by PG-SGA tool was a stronger overall predictor of OS than the recently defined criteria.

**Conclusions:** The concept of using the PG-SGA tool to identify potential patients with cachexia for future trials deserves further investigation given that malnutrition, as determined using this tool, had a better overall predictive value of cancer patients’ survival than the proposed diagnostic criteria for cachexia.

**Disclosure:** All authors have declared no conflicts of interest.

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**G-CSF AS SECONDARY PROPHYLAXIS OF CHEMOTHERAPY-INDUCED NEUTROPENIA IN PATIENTS WITH SOLID TUMORS: RESULTS OF A PROSPECTIVE, OBSERVATIONAL STUDY**

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**Background:** There are little available data on secondary prophylaxis of chemotherapy-induced neutropenia. We designed this multicentre, prospective and observational study to identify predictive factors of occurrence of neutropenic events (NE) subsequent to a previous episode, in patients with solid tumors (primary objective). Secondary objectives were to determine the incidence of NE, describe prophylactic strategy: cycle delay, dose reduction, G-CSF prescription, and its impact on the recurrence of NE.

**Results:** 625 patients included, 548 (87.7%) evaluable. 378 (69%) female, mean (SD) age (years) 61.7 (12.3), WHO PS 0-1 88.3%, breast: 40%, colorectal: 15.7%, lung: 11.9%. Metastatic disease: 53.3%. During cycle A, 88 patients (16.1%) experienced FN, 42 (7.7%) neutropenic fever and 418 (76.3%) neutropenia (any grade w/o fever). 44.5% had cycle delay, 22.3% dose reduction and 466 (85%) received G-CSF use (HR:0.32 (0.24; 0.43; p < 0.001) was an independent predictor of (CT), and F experienced since the last cycle was collected (patient’s subjective scale PSS: 0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = 3 + long-term condition). HB levels were also assessed at least once before each CT using the scale for Hb: 0 = 12, 1:[12-10], 2:[10-9], 3:[9-8], 4 = <8. Scores linear (mean) and non-linear (polynomial) were calculated using for F: grades from start to end CT and for anemia: mean grade per cycle. OS was calculated from CT initiation to death or censured at last contact.

**Results:** 1279 pts entered the program, 662 (equivalent to 4327 CT cycles) had at least 1 assessment of (fatigue + Hb). Excluded pts (617) due to lacking HB results did not differ from the 662 (log-Rank = 0.98). Median age = 64.9y, sex-ratio = 1.1, more frequent localization: lung (23%), breast (21%), prostate (13%), ovary (10%). 229 and 433 pts had respectively at least 1 or 2 HB results at each cycle. There were 5376 episodes of fatigue in total (PSS > 0), 694 pts experienced at least 1 episode. 516, 232, 101 and 35 pts experienced at least 1 anemia episode on scale 1, 2, 3 and 4 respectively. Median linear F score = 1.08 [0-3], non-linear = 1.57 [0-200]. Median linear anemia score = 0.78 [0-1.5], non-linear = 0.78 [0-1.6]. OS was 24.8m IC95% [21.6-30.4]. Linear scores were normally distributed and non-linear were discarded since much skewed. As expected, anemia and fatigue were cycle delay correlated (ANOWA, p < 0.0001). Linear F score (LFS) was good predictor of OS (L: HR = 2.5, IC95% [2.0-3.1], p < 0.0001). Patients with LFS > 2 (N = 72) had an increased death risk of 4.65 (IC95% [3.15-6.88]) with respect to LFS ≤ 1 (N = 247). HB mean and linear anemia score were good predictors for OS; respectively HR = 1.45 IC95% [1.31, 1.61] and HR = 1.86 IC95% [1.57, 2.19]).

**Conclusion:** A linear score of anemia and fatigue PSS were simple and efficient predictors of overall survival. They could be monitored to help clinicians in fatigue and anemia management.

**Disclosure:** S. Oudard: honoraria; Sanofi, Roche, Bayer. All other authors have declared no conflicts of interest.

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**FATIGUE (F) AND ANEMIA SCORES FOR OVERALL SURVIVAL (OS) PROGNOSIS**

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**Background:** F is an adverse reaction related both to disease and treatment in cancer patients (pts). Incidence of F episodes and anemia could be expressed using scores which association with OS could be useful for treatment management.

**Methods:** Pts included in the PROCHE program between 2008 and 2011 at the HEGP hospital (Paris, France). Pts were contacted before each chemotherapy
lower recurrence rate of NE. Pegfilgrastim seemed to offer the highest protection (HR: 0.23 (0.16; 0.32; p < 0.001).

Conclusion: Prophylactic strategy with G-CSF has significant efficacy in reducing the incidence of NE, and should be considered as the best option in the secondary prophylaxis setting.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Lipogfilgrastim (n = 101)</th>
<th>Pegfilgrastim (n = 101)</th>
<th>LS Mean Difference (95% CI), p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth of ANC nadir</td>
<td>7.0 (0.0 to 12.0)</td>
<td>9.0 (0.0 to 21.0)</td>
<td>1.00 (0.0001)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.8 (3.3)</td>
<td>7.4 (3.6)</td>
<td>1.00 (0.0001)</td>
</tr>
<tr>
<td>Time to ANC recovery (days)</td>
<td>7.0 (0.0 to 12.0)</td>
<td>9.0 (0.0 to 21.0)</td>
<td>1.00 (0.0001)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>5.8 (3.3)</td>
<td>7.4 (3.6)</td>
<td>1.00 (0.0001)</td>
</tr>
<tr>
<td>Mean (SD)</td>
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</tr>
</tbody>
</table>

Conclusions: Patients who received lipogfilgrastim had significantly faster time to ANC recovery than those who received pegfilgrastim.

ROLE OF TEMPORARY OVARIAN SUPPRESSION OBTAINED WITH GnRH ANALOG IN REDUCING PREMATUR E OVARIAN FAILURE (POF) INDUCED BY CHEMOTHERAPY IN PREMENOPAUSAL CANCER PATIENTS: A META-ANALYSIS OF RANDOMIZED STUDIES

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Background: Premenopausal cancer patients treated with chemotherapy (CT) are at risk of POF. The role of GnRHs in the prevention of CT-induced POF is still controversial. We performed a pooled analysis of randomized studies that evaluated the role of GnRHs as strategy to prevent POF.

Methods: studies were retrieved by searching the PubMed database and the proceedings of major conferences. Odds ratio (OR) and 95% CIs for CT induced POF were extracted from each trial and averaged to obtain pooled estimates using an inverse-variance model.

Results: we included in the meta-analysis 7 randomized trials involving 745 premenopausal women randomly assigned to receive chemotherapy or chemotherapy + GnRHs: five trials were carried out in breast cancer patients and two trials in patients with lymphoma. The pooled OR estimate for CT induced POF was 0.46 (95% CI, 0.3-0.72).

Conclusion: temporary ovarian suppression obtained with the use of GnRH analogues reduces the incidence of chemotherapy induced POF in premenopausal cancer patients.

Disclosure: All authors have declared no conflicts of interest.

EVALUATION OF THE QUALITY OF LIFE AND ECONOMIC BURDEN WITH GRANULOCYTE-COLONY STIMULATING FACTOR IN CHINESE BREAST CANCER PATIENTS RECEIVING DOCETAXEL, EPIRubicin AND CYCLOPHOSPHamIDE

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Background: Docetaxel, Epirubicin, cyclophosphamide (TEC) has been accepted as the standard care in the treatment of Chinese patients with breast cancer. However, little is known about the impact of primary prophylactic granulocyte-colony stimulating factor (G-CSF) on the quality of life (QOL) and economic burden in these patients.

Patients and methods: This was a randomized control study to compare G-CSF as primary prophylactic or not while breast cancer patients receiving TEC chemotherapy. Primary prophylactic G-CSF (PPG) was: filgrastim 3mcg/kg/day on day 3-8 (n = 53 patients); G-CSF for treatment was: filgrastim 5mcg/kg/day on the occasion that grade 3-4 neutropenia, febrile neutropenia, and delayed recovery of absolute neutrophil count on day 21 till the neutrophil recovery (n = 54 patients). A total of 107 patients from a single centre in China were included in the trial.

Side-effects, costs and the scores of the EORTC QLQ-C30 questionnaires were compared in the two groups.

Results: The addition of PPG to TEC significantly reduced the incidence of neutropenic fever (15.32% vs 6.94%, P = 0.0482), grade 3-4 neutropenia (52.3% vs 12.2%, P = 0.0011) and anaemia, thrombosis, anorexia, myalgia and dysuria. Patient’s QOL decreased during chemotherapy, more in TEC without PPG than with PPG, but returned to baseline afterwards. The addition of PPG significantly reduced the percentage of patients with clinically relevant Global Health Status deterioration at the end of treatment (60% versus 47%, P = 0.0331). The average cost of each cycle was quite approaching in the two groups (CNY 16432.01 in TEC with PPG vs CNY 16059.24 in TEC without PPG, P = 0.05), but the cost of G-CSF was increased at the end of chemotherapy without PPG.

Conclusions: The addition of PPG significantly reduces the incidence of neutropenic fever as well as that of some TEC-induced haematological and extra-haematological side-effects. The QOL is elevated during chemotherapy by using PPG, particularly in the end of treatment. Economically speaking, primary prophylactic G-CSF is cost-effective in Chinese breast cancer patients receiving TEC chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

COST-EFFECTIVENESS OF PRIMARY PEGIFLGRASTIM PROPHYLAXIS IN BREAST CANCER PATIENTS AT RISK OF FEBRILE NEUTROPEenia


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Purpose: Guidelines advise primary G-CSF prophylaxis during chemotherapy if risk of febrile neutropenia (FN) is more than 20%, but this comes with considerable costs. We investigated the incremental costs and effects between two treatment strategies of primary pegilgrastim prophylaxis.

Methods: Our economic analysis, using a health care perspective, was based on a randomized study in breast cancer patients with increased risk of FN comparing primary G-CSF prophylaxis throughout all chemotherapy cycles (G-CSF 1-6 cycles arm) with prophylaxis during the first two cycles only (G-CSF 1-2 cycles arm).

Primary outcome was the cost-effectiveness expressed as costs per patient with episodes of FN prevented.

Results: The incidence of FN increased from 10% (8 out of 84 patients) in the G-CSF 1-6 cycles arm to 36% (30 out of 83 patients) in the G-CSF 1-2 cycles arm, whereas the mean total costs decreased from € 20,658 (95%CI € 20,049 to € 21,247) to € 17,168 (95%CI € 16,239 to € 18,029) per patient, respectively. Chemotherapy and G-CSF largely determined total costs: 83% in the G-CSF 1-6 cycles versus 78% in the G-CSF 1-2 cycles arm. As expected, FN-related costs were higher in the G-CSF 1-2 cycles arm. The incremental cost-effectiveness ratio for the G-CSF 1-6 cycles compared to the G-CSF 1-2 cycles arm was € 13,112 per patient with episode of FN prevented.

Conclusion: We conclude that G-CSF prophylaxis throughout all chemotherapy cycles is more effective, but more costly, compared to prophylaxis limited to the first two cycles. Whether G-CSF prophylaxis throughout all chemotherapy cycles is considered cost-effective depends on the willingness to pay per patient with episode of FN prevented.

Disclosure: All authors have declared no conflicts of interest.

TRENDS IN G-CSF USE IN GERIATRIC ONCOLOGY: 2011 AFSOS SOFOG SURVEY

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Background: Age is a risk factor for chemo-induced febrile neutropenia (FN). According international guidelines, it should be considered when discussing G-CSF use for regimens with FN risk between 10% and 20%. Prophylactic G-CSF remains controversial for regimens with a lower risk.

Patients and methods: A survey was undertaken in France to describe current treatment practices in patients aged 70 years and older with gynecologic cancer. Individual data from 715 chemotherapeutic patients were collected (breast 74%, ovary 21%, uterus 5%, adjuvant 30%).

Results: According 101 practitioners, important factors to be considered for GCSF use are previous FN/neutropenic events (96%), bone radiotherapy (92%) or chemotherapy (86%), comorbidities (91%), performance status (PS) ≥ 2 (87%), recent septic event (92%); anemia (54%). In routine practice, GCSF was prescribed in 51% of the cases, ie 41% and 9% as primary and secondary prevention respectively and 0.4% in curative setting. Prophylactic GCSF prescription rates for regimens with FN risk ≥ 20%, 10-20% and <10% were 90%, 59% and 36%, respectively. Covariates associated with an increased GCSF use were adjuvant setting (Hazard Ratio [HR] = 1.6, p = 0.007), 3 or 4-weekly
regimens (HR = 2.5, p < 0.001). Physicians performing geriatric assessments were more prone to prescribe GCSF (HR = 1.5, p = 0.015), notably those involved in a comprehensive geriatric assessment network (HR = 1.5, p = 0.007). However, proven risk factors for FN were rarely considered: PS ≥2 (HR = 0.7, p = 0.05), comorbidities (HR = 1.3, p = 0.2), anemia < 12 g/dL (HR = 1.0, p = 0.8), malnutrition (albumin < 35 g/L, HR = 0.7, p = 0.03). In metastatic disease, previous FN (HR = 2.6, p < 0.001), or chemotherapy (HR = 1.9, p < 0.001) were significantly associated with higher rates of prophylactic G-CSF, but not previous irradiation (HR = 1.1, p = 0.8); a limited number of daily G-CSF injections were given in most cases (mean: 49.6±4%).

Conclusion: Our study suggests a trend to overtreatment in some cases, in comparison to international guidelines, and insufficient use of validated risk factors in risk assessment making.


Table 1. All patients presents other risk factors on CT regimens with 10-20% FN risk. Bioskimer filgrastim therapy by tumour type and CT toxicity. Table 2 filgrastim was initiated as primary prophylaxis in 70% of patients, at 24-72 hours CT toxicity:

- Dominantly solid tumours (79%), FN risk based on chemotherapy (CT) regimen
- In this mainly female (62%) and older (61.6 ± 11.9 years) cohort with Results:

- Across 12 European countries.
- This analysis describes treatment initiation with biosimilar filgrastim in the
- Introduction: MONITOR G-CSF is a prospective observational study of practice patterns and outcomes for prophylaxis of chemotherapy-induced febrile neutropenia (FN) with biosimilar filgrastim (Zarzio®, Sandoz Biopharmaceuticals).
- Methods: This analysis describes treatment initiation with biosimilar filgrastim in the 788 patients enrolled to date (target 1500) in the MONITOR G-CSF study relative to the 2010 EORTC G-CSF guidelines. Patients were enrolled at 134 centres (199 open) across 12 European countries.
- Results: In this mainly female (62%) and older (61.6 ± 11.9 years) cohort with predominantly solid tumours (79%), FN risk based on chemotherapy (CT) regimen was <10% in 18, 10-20% in 43% and >20% in 39% of patients. All patients with <10% FN risk had ≥1, 95% had ≥2 and 74% had ≥3 other risk factors. Biosimilar filgrastim was initiated as primary prophylaxis in 70% of patients, at 24-72 hours (51%) or days 5-8 (30%) after CT and typically (45%) for 5 days. Table 1 summarizes biosimilar filgrastim therapy by tumour type and CT toxicity. Table 2 presents other risk factors on CT regimens with 10-20% FN risk.

Table 1. All patients

<table>
<thead>
<tr>
<th>Tumour type:</th>
<th>Prophylaxis (%)</th>
<th>Initiation (%)</th>
<th>Duration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>70</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>Haematology</td>
<td>70</td>
<td>30</td>
<td>24</td>
</tr>
<tr>
<td>CT toxicity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 20%</td>
<td>76</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td>10-20%</td>
<td>74</td>
<td>26</td>
<td>49</td>
</tr>
<tr>
<td>&lt; 10%</td>
<td>56</td>
<td>44</td>
<td>54</td>
</tr>
</tbody>
</table>

Table 2. FN risk 10-20%

<table>
<thead>
<tr>
<th>Patient-related risk factors</th>
<th>Prophylaxis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td>79</td>
</tr>
<tr>
<td>Advanced disease (Stage IV)</td>
<td>74</td>
</tr>
<tr>
<td>History of prior FN</td>
<td>29</td>
</tr>
<tr>
<td>No prophylactic precautions</td>
<td>73</td>
</tr>
<tr>
<td>Poor performance (ECOG ≥2)</td>
<td>83</td>
</tr>
<tr>
<td>Female</td>
<td>76</td>
</tr>
<tr>
<td>HB &lt;&lt;12 g/dl</td>
<td>70</td>
</tr>
<tr>
<td>Liver, renal or CV disease</td>
<td>72</td>
</tr>
<tr>
<td>One or more risks</td>
<td>74</td>
</tr>
</tbody>
</table>

Conclusions: Variability exists in biosimilar filgrastim initiation by tumour type (day of initiation), CT toxicity and patient-related risk. About a quarter of patients with FN risk >20% or 10-20% in combination with other risk factors did not receive primary prophylaxis as recommended. The trend to initiate filgrastim in regimens with <10% risk may indicate of changing practice trends to optimise patient well-being and minimise FN risk needs to be further evaluated. The relationship between EORTC guideline congruence and clinical outcomes will be evaluated in future analyses.

neutropenia in patients with cancer. These consisted of two large multicentre observational studies plus three small single-centre studies conducted across 12 European countries. All studies were conducted in Europe and reflected real-life clinical use of biosimilar G-CSF. Patients receiving biosimilar G-CSF for interventional treatment were excluded from this analysis.

Results: Data from 1302 patients treated with biosimilar G-CSF were available for analysis. The most frequent types of cancer were breast cancer (n = 541; 42%), lung cancer (n = 212; 16%), and lymphoma/leukaemia (n = 201; 15%). Thirty-six percent of patients had a febrile neutropenia risk of >20% while 39.6% had a risk of 10–20% based on chemotherapy regimen. A further 12.1% of patients received biosimilar G-CSF despite a febrile neutropenia risk of <10% (12.4% data unknown or missing). Overall, 2.2% of patients experienced an episode of febrile neutropenia (2.0% of patients with breast cancer) and 8.5% had severe (grade 4) neutropenia (ANC ≤500 neutrophils/µL) (9.4% with breast cancer). Any disturbances to chemotherapy regimens are currently being analysed.

Conclusions: Biosimilar G-CSF appears to be effective for the prevention of chemotherapy-induced neutropenia. Occurrence of severe or febrile neutropenia was similar to that observed in studies of the originator G-CSF in clinical practice. The increased affordability of biosimilar G-CSF may encourage physicians to more closely adhere to clinical guideline recommendations, including increased use of G-CSF use as primary prophylaxis.

**1561P** PREDICTIVE DIAGNOSTICS FOR RESPONSE TO THERAPY OF CHEMOTHERAPY ASSOCIATED ANAEMIA WITH DARBEPOETIN ALFA +/- INTRAVENOUS IRON IN CANCER PATIENTS: PFAD-3 A MULTICENTRE COHORT STUDY IN OUTPATIENTS


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Introduction: Seven randomized studies have demonstrated a benefit of combining erythropoiesis stimulating agents (ESA) with intravenous iron (iv Fe) in the treatment of chemotherapy-associated anemia in cancer patients (pts). Because, so far there is no proven recommendation for the best pretherapeutic diagnostics to select optimal therapy (ESA, iron or both), we conducted a multicenter cohort study.

Methods: Cancer pts were included and eligible for response if they had a symptomatic anemia (hemoglobin (Hb) <11g/dl) received a chemotherapy, gave written informed consent, and had a pretherapeutic diagnostics of anemia: Ferritin (F), transferrin saturation (TSAT), endogenous erythropoietin (eEPO) and soluble transferrin-receptor (sTfR) on day 1 and 14. All pts were treated with Darboepoetin alfa (DA, 500 µg, q3w) with or without iv-III-hydroxy-succinyl (200mg in 250ml NaCl 0.9% q3w). The use of iv Fe based on the recommendations of the NCCN guidelines at the discretion of the oncologists. Pts with an absolute iron deficiency (F = <30mg/ml, TSAT ≤ 15%) were excluded.

Results: Between 03/07 - 08/10 in 9 outpatient clinics 331 pts received DA on day 0. Mean age was 66.3 years, 58% were women. 202 pts (61%) received at least one dose iv Fe additionally to DA on day 0. Baseline Hb was 9.53±g/dl (SD 0.78) and increased in average 1.23±g/dl (SD 1.34) and 1.53±g/dl (SD 1.49) til weeks 6 and 9, respectively. Transfusion rate in weeks 3-9 was 15.1%. Associations of relevant criteria with response are shown in the table.

Conclusion: The results confirm the increase of Hb within the first 3 weeks as strong predictor for response to DA in week 6. Pts with Hb-increase ≥0.6 g/dl have a 6-fold higher chance of being responders than those without. Ferritin is a stronger predictor

**1562P** A PROSPECTIVE DATA STUDY OF THE MANAGEMENT OF CHEMOTHERAPY-INDUCED ANAEMIA WITH DARBEPOETIN ALFA – THE APRIORI STUDY

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Background: Darboepoetin alfa (DA, Aranesp®) is an erythropoiesis-stimulating agent (ESA) used to treat chemotherapy (CT) induced anaemia (CIA). In 2008 EORTC guidelines changed to recommend starting ESA treatment at haemoglobin (Hb) 9 - 11 g/dL and stopping ESA if Hb was > 13 g/dL. In February 2008, the SmPC for DA was revised to recommend treatment start at Hb ≤ 10 g/dL and Hb be maintained in the 10 - 12 g/dL range. APRIORI was a prospective, noninterventional, observational, longitudinal, multicentre study collecting data from patients (pts) in Central and Eastern Europe with CIA receiving DA and CT. The aims were to evaluate the compliance with international guidelines and EU label for use of DA in treating CIA, to assess effectiveness of DA, and describe DA dosing characteristics.

Methods: This study collected clinical data of cancer pts over 4 consecutive years (11/2006 - 12/2010), at 120 centers in Poland, Czech Republic, Slovakia, Slovenia, Hungary, and Russia. Pts were enrolled before the label change (BLC) as well as after the label change (ALC). The data were collected at enrolment and at follow-up visits during CT until the first follow-up visit after the end of CT.

Results: Out of 6408 pts enrolled (mean (sd) age of 59.9 (+12.57) years, 44.4% male), 929/1648 (56.4%) pts enrolled Hb had BLC had Hb in the target 9 - 11 g/dL range, while 4284/7060 (90.0%) pts enrolled Hb had BLC had Hb in the target range of ≤ 10 g/dL. Total 666 (40.4%) pts had Hb < 9 g/dL and 53 (3.2%) pts had Hb > 11 g/dL. BLC, while 476 (10.0%) pts had Hb > 10 g/dL. ALC, 38 (35.8%) pts had any DA dosing withhold while exceeding the 13 g/dL. Hb concentration limit, at any time during the study and ALC, 55 (7.8%) pts had the doses reduced while exceeding the 12 g/dL Hb concentration limit, at any time during the study. DA effectively increased Hb concentrations; mean Hb after achieving the target anaemia Hb level BLC 11.94 g/dL vs. 11.29 g/dL ALC. Only 4.9% of pts required RBC transfusion after 5 weeks of DA initiation. Out of 9 ADRs no serious and no fatal ADRs was reported during the study. Mortality was 4.9% (305 pts).

Conclusion: Based on these data, the patients are being treated in accordance with the current European SmPC for darboepoetin alfa. This study was sponsored by Amgen GmbH CEE Headquarters.

7.4% myeloma. Of those patients with solid tumours, 30.1% of patients had a stage III and 21.6% had a stage IV tumour. Almost all patients received the biosimilar epoetin zeta (Retacrit®, Hospira UK Ltd., median dose 30,000 IU/week). Mean baseline Hb level across all patients was 9.6 g/dL, with 35.6% of patients having moderate anaemia (Hb 8.9-9.5 g/dL). Following treatment, Hb response was achieved in 81.6% and 86.5% of patients at 3 and 6 months, respectively. The overall mean change in Hb level was 1.5 ± 1.6 g/dL at 3 months and 1.72 ± 1.6 g/dL at 6 months. Transfusion rates were 9.4% and 5.8%, while the rate of thromboembolic events was 2.4% and 1.5%, at 3 and 6 months respectively. In conclusion, Retacrit was effective and well tolerated in the management of CIA in patients with solid tumours, lymphoma and myeloma.

Disclosures: M. Michallet: I received honoraria from Hospira for advisory boards and consulting. P. Soubeyran: I received honoraria from Hospira for advisory boards and consulting. H. Allbrand: Employed by Hospira. E. Luporsi: I received honoraria from Hospira for advisory boards and consulting.

Methods: A total of 72 patients between 38 and 76 years old with chemotherapy-related anaemia (Hb <10 g/dL; serum ferritin ≥100 ng/ml or transferrin saturation ≥15%) receiving chemotherapy and epoetin alfa (40,000 U/week) to 8 weeks plus oral 1 IU/kg daily for 8 weeks. Primary endpoint of the study was Hb response (increase in Hb level ≥ 2 g/dL from baseline), red blood cell transfusion and the safety profile of LI. Quality of life (QOL) with FACT-An questionnaire was also evaluated.

Results: 72 patients were evaluable for efficacy and safety. The percentage of patients with hematopoietic responses was high (only 4 patients showed no response to therapy). From baseline to study end, a mean increase in Hb levels of 2.2 g/dL was noted. The best response was obtained in the group of patients with hematoglobin levels between 9.10 g/dL. None of the patients required red blood cell transfusion and supplemented administration of oral LI was well tolerated in all patients. Improvement in QOL parameters was observed in all patients.

Conclusions: Our results suggest that for cancer patients with chemotherapy-related anaemia receiving supplemented epoetin alfa, daily subcutaneous injection of LI is safe and produces a significant increase in Hb and improved QOL. The increase of Hb is similar to those observed with the use of IV iron supplementation in several studies. Taking into consideration physician’s convenience and patient’s compliance, this regimen offers an optimal alternative to IV iron supplementation.

Disclosures: All authors have declared no conflicts of interest.
Methods: A prospective multicentre observational study conducted in Germany enrolling 1,066 patients (pts) with non-myeloid malignancies, symptomatic chemotherapy-induced anaemia and planned treatment with DA. The primary endpoint was a haemoglobin (Hb) level of 10–12 g/dL at week (wk) 6, or earlier, at the end of treatment. Red blood cell (RBC) transfusion needs and quality of life (QoL) were also assessed.

Results: In total, 984 pts met the protocol criteria and were included into the analysis. Cancer types included breast (n = 260; 26%), lung (n = 118; 12%), ovarian (n = 103; 10%), colorectal (n = 95; 10%) and other (n = 408; 41%). Median Hb levels rose from 9.6 g/dL at baseline (BL) to 10.8 g/dL at wk6. 519 pts (53%) reached the primary endpoint over 3.7 wks (median; IQR 0.1–7.1) of DA treatment. Median time to Hb level ≥10 g/dL was 14 days (IQR 8–21 days). RBC transfusion was required by 32% of pts from wk6 to wk16; 16% of pts required RBC transfusion in the first 3 wks from DA initiation. QoL improved (measured using FACT-G questionnaires and the Linear Analog Scale Assessment); however, a clinically important difference was only found using FACT-F. Of 30 reported adverse drug reactions, the investigators classified 12 as DA related. Of these, 1 was fatal.

Conclusion: Overall, DA use was in line with the current label and guidelines; most pts started DA at Hb levels of ≤10 g/dL and were treated to the Hb target level of 10–12 g/DL. DA seems to be effective in enhancing Hb response and improving QoL. Study sponsor: Amgen Europe GmbH. Editorial support: archived medical communication ag.

Median (IQR) or n (%). Information available for 984, 5880e, 726, 978r or 980° pts. *Primary endpoint or rise of 2 g/dL from BL.

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1568P THE USE OF BIOLOGICAL EPOETINS IN THE MANAGEMENT OF CHEMOTHERAPY-INDUCED ANAEMIA (CIA) IN PATIENTS WITH BREAST CANCER: A SUBANALYSIS OF THE ORHEO STUDY

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ORHEO (place of bioSimilars in the therapeutic management of anaemia secondary to chemotherapy in Haematology and Oncology) is being conducted in France to assess the efficacy and safety of biosimilar epoetins for the treatment of CIA in the clinical setting. A total of 2310 patients with solid tumours, myelodysplasia and lymphoma were included in the study. In the subanalysis, we assess the use of biosimilar epoetins in patients with lung cancer. A total of 421 patients >18 years with CIA (haemoglobin [Hb] <11 g/dL) associated with lung cancer and eligible for treatment with biosimilar epoetin were included in this analysis. Patient characteristics were recorded at baseline along with anaemia-related information such as observed and target Hb (as chosen by the treating clinician), brand and dose of epoetin biosimilar prescribed, and details of any other parallel treatments. Patients were followed-up at 3 and 6 months. Analyses included achievement of target Hb and Hb response (defined as Hb reaching ≥10 g/dL, an increase in Hb levels of at least 1 g/dL since inclusion visit, or reaching target Hb set by doctor at start of study, without any blood transfusions in the 3 weeks prior to measurement). Adverse events were also recorded. Of the patients included in this study, 33.5% had a stage III tumour and 30.8% a stage IV tumour, while metastases were identified in 71.5% of patients. At baseline, average Hb levels were 9.5 g/dL, with 36.8% of patients classified as having moderate anaemia. All patients received epoetin zeta (Retacrit®, Hospira UK Ltd.) Response to treatment with biosimilar epoetin was achieved in 76.7% and 86.0% of patients after 3 and 6 months, respectively, while average Hb levels had increased by 1.3 and 1.8 g/dL at 3 and 6 months, respectively. At 6 months, the transfusion rate was 0.7%, the rate of significantly clinically adverse events was 9.5%, while the rate of thrombotic events was 0.8%. Retacrit was effective and well tolerated in the treatment of CIA in patients with breast cancer.

Disclosure: M. Michallet: I have received honoraria from Hospira for advisory boards and consulting. E. Luporsi: I have received honoraria from Hospira for advisory boards and consulting. P. Soubeynan: I have received honoraria from Hospira for advisory boards and consulting. H. Albrand: Employed by Hospira.

1570P CHEMOTHERAPY-INDUCED THROMBOCYTOPENIA AND CLINICAL BLEEDING IN PATIENTS WITH GYNECOLOGIC MALIGNANCY

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Objectives: Chemotherapy-induced thrombocytopenia seemed to be a relevant problem in clinical practice. In this study, we investigated chemotherapy-induced thrombocytopenia recently performed in patients with gynecologic malignancy.

Methods: Between January 2009 and December 2011, we examined our reported chemotherapy-induced thrombocytopenia using the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. We analyzed the incidence and clinical features of chemotherapy-induced thrombocytopenia (≥grade3; platelet count <50,000/mL in patients with gynecologic malignancy.

Results: During this period we administered over 1614 infusions (29 regimens) to 249 patients with gynecologic malignancy. Median age was 60 years (24–84). Thrombocytopenia occurred in 43 (14.8%) patients over 56 (3.5%) chemotherapy cycles. Clinical bleeding occurred in 13 (4.5%) patients over 14 (0.9%) cycles. Major bleeding occurred in 7 (1.3%) cycles (gastrointestinal bleeding: 4; genitai bleeding: 2, anovular bleeding: 1; intracranial bleeding: 2; cardiac bleeding: 1).
bladder bleeding; 1). Platelet transfusions were administered for 8 cycles. No life-threatening bleeding occurred in any patient. Thrombocytopenia was associated with more than five previous chemotherapy cycle (p = 0.03), previous radiotherapy (p = 0.0001), disseminated disease (p = 0.006), distant metastatic disease (p = 0.02) and poor performance status (p = 0.0001). Classical bleeding was associated with previous radiotherapy (p = 0.003), distant metastatic disease (p = 0.03) and poor performance status (p = 0.02). Both classical bleeding were not related with age, bone marrow metastases or platinum-based regimens. Neutropenia was complicated with 35% of thrombocytopenia cycles and 43% of classical bleeding cycles.

Conclusions: By estimating risk factor of classical bleeding such as progression of disease and poor bone marrow reserve, safe management of chemotherapy-induced thrombocytopenia without unnecessary platelet transfusion may be possible in patients with gynecologic malignancy.

Disclosure: All authors have declared no conflicts of interest.

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PREVENTION OF DELAYED NAUSEA (DN): A POOLED ANALYSIS OF 562 WOMEN RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY (HEC) IN PROSPECTIVE CLINICAL TRIALS OF PALONOSETRON (PALO)

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Purpose: Chemotherapy-induced nausea occurs more frequently than vomiting, and women are particularly prone to experience DN instead of delayed vomiting. We conducted a pooled analysis to evaluate the efficacy of three regimens for preventing DN: 1-day regimen (n = 241): PalO plus dexamethasone 8 mg IV (Day 1); 3-day regimen (n = 209): PalO plus dexamethasone 8 mg (Day 1) and dexamethasone 8 mg PO (Days 2 and 3); triple regimen (n = 112): PalO plus dexamethasone 12 mg and aprepitant (Day 1) and dexamethasone 8 mg PO plus aprepitant (Days 2 and 3).

Methods: The analysis was based upon outcomes in 562 chemotherapeutic-naive women (mean age 52.7 years; 53% non-smokers; 93% treatable disease; 7% solid tumors (90% breast cancer) enrolled in two Phase III and two Phase II trials of HEC (AC-based: 91%; cisplatin: 9%). The pre-specified primary end point was the proportion of patients with no nausea during the delayed period (Days 2-5) after the first cycle of chemotherapy. The two primary comparisons were 3-day regimen vs. 1-day regimen, and triple regimen vs. 3-day regimen. Penalized multivariable logistic regressions were also performed adopting the Firth’s correction in order to adjust estimates for potential over-fitting, skewed data and multi-collinearity. Results were reported as adjusted odds ratios (OR) with two-sided probability values.

Results: The 3-day to 1-day regimen comparison was not statistically significant (DN, 46.4% vs. 44.4%, two-sided Fisher’s exact test, P = 0.777). The triple regimen to 3-day regimen comparison was significant (DN, 58.9% vs. 46.4%, P < 0.0001). For no nausea end point in the overall phase (Days 1-5) adjusted ORs (95% CI) were: 3-day regimen vs. 1-day regimen OR 1.19 (0.80 - 1.77), P = 0.398; triple regimen vs. 3-day regimen: OR 2.86 (1.44 - 5.83), P = 0.003.

Conclusions: This analysis suggests that PalO plus 1-day or 3-day dexamethasone have similar effects on DN. The addition of aprepitant to 3-day regimen improves the prevention of DN in women receiving HEC. Complete results accounting for risk factors (age and alcohol consumption) will also be presented.

Disclosure: All authors have declared no conflicts of interest.

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SAFETY AND EFFICACY OF ORAL PALONOSETRON IN PREVENTING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV) OVER MULTIPLE CYCLES OF MODERATELY EMETOGENIC CHEMOTHERAPY (MEC)

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Background: Palonosetron (PALO), a pharmacologically distinct 5-HT3 receptor antagonist (RA) offers superior CINV prevention compared with other 5-HT3 RAs when administered as a single IV dose. Oral PALO doses 0.25, 0.50, 0.75 mg were clinically comparable to the approved 0.25 mg IV dose in a pivotal phase 3 single-cycle trial, with 0.50 mg being the FDA/EMA approved dose. A dose of 0.75 mg was selected for the present study to best evaluate safety of oral PALO in multiple cycles of chemotherapy (CT).

Methods: In this multicenter, open-label study, patients received a single 0.75 mg dose of oral PALO (with [at investigator discretion] or without concomitant dexamethasone [DEX]) 60 min prior to MEC (up to a maximum of 4 consecutive cycles). The primary safety and efficacy assessments were adverse event (AE) reporting and the proportion of cycles showing patients complete response (CR: no emesis, no rescue medication) in the acute and delayed intervals.

Results: 217 patients (75% female; 61% white; 36% Hispanic; 66% CT-naive) received a total of 654 cycles of MEC (median 3 cycles). The median number of cycles was 3 with half of patients receiving 4 cycles. Concomitant DEX (8 mg Day 1) was administered in 483 cycles while PALO was given alone in 171 cycles. Generally, antiemetic efficacy was maintained across the CT cycles (Table) with higher CR rates when DEX was given concomitantly vs PALO alone (acute: 74% vs 61%; delayed: 63% vs 60% respectively, all cycles combined).

The majority of AEs were mild, with headache the most common related AE in 3.5% cycles PALO alone and 5.4% cycles PALO + DEX. In both the PALO alone and PALO + DEX groups, AEs decreased slightly from cycle 1 to 3 and remained about the same for cycle 4. There were few severe or serious AEs and the profile raised no safety concerns.

Conclusion: Oral PALO was well tolerated and effective in preventing CINV over multiple cycles in patients receiving MEC.

Disclosure: D. Voisin: Yes. Daniel Voisin is a Helsinn employee, S. Grunberg: Yes Steven Grunberg is an Helsinn HealthCare consultant.

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THE DOPAMINE D2/D3 RECEPTOR ANTAGONIST APD421 IN COMBINATION WITH ONDANSETRON EFFECTIVELY PREVENTS ACUTE CICPLATIN-INDUCED NAUSEA AND VOMITING (CINV)

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Conventional dopamine D2 antagonists are among the oldest antiemetics and are considered to be of only moderate efficacy in CINV. Central dopamine D2 receptors have recently been demonstrated to be involved in the emetic reflex arc, but so far no clinical data have been published for any agents acting at these receptors. In preliminary clinical data have been published for APD421, a potent D2 and D3-antagonist, showed some single-agent efficacy in clinical trials of palonosetron (PALO). By estimating risk factor of clinical bleeding such as progression of disease and poor bone marrow reserve, safe management of chemotherapy-induced thrombocytopenia without unnecessary platelet transfusion may be possible in patients with gynecologic malignancy.

Disclosure: All authors have declared no conflicts of interest.

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BIOEQUIVALENCE AND ABSOLUTE BIOAVAILABILITY OF A SINGLE ORAL DOSE OF TWO FORMULATIONS OF 0.75 MG PALONOSETRON IN HEALTHY VOLUNTEERS (HV)

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Background: Palonosetron HCl (PALO) is a potent 5-HT3 receptor antagonist (5HT3-RA) with a stronger receptor binding affinity and unique mechanism of action
compared to older 5HT3-RAs. The primary objectives were to investigate the bioequivalence of two PALO 0.75 mg formulation(s) (Frob) b2 and b3 and their absolute bioavailability when compared to b1. PALO 0.75 mg i.v. F (see table for: b1, b2 and b3). Secondary objective was to evaluate the safety profile of the three PALO Frob.

Methods: 36 male and female hv were randomized in this open-label, 3-treatment, cross-over study. 30 subjects received treatments b1, b2 and b3 in a 3-period randomized order (14-day interval set between periods). Treatments b2 and b3 were analyzed for bioequivalence by ANOVA CVs and defined bioequivalent if the 90% confidence limits (CL) for the AUCo∞, AUCo-t, and Cmax treatment ratios lie within 80% to 125% range CL Absolute Ratios. Absolute bioavailability of the oral Frob was calculated using the extent of exposure measure AUCo∞ and AUCo-t.

Results: The oral 0.75 mg Frob b1 and b2 showed bioequivalence in terms of rate and extent of absorption: The 90% CI for PALO AUCo∞, AUCo-t and Cmax treatment ratios lie within 95.87% to 106.47%, 96.47% to 107.76%, 99.67% to 103.59%, respectively. All CI limits were the 90% confidence interval set to 80% to 125% range CL Absolute Ratios. Absolute bioavailability of the oral Frob was calculated using the extent of exposure measure AUCo∞, AUCo-t and Cmax treatment ratios. The oral 0.75 mg Frob b1 and b2 showed bioequivalence in terms of rate and extent of absorption: The 90% CI for PALO AUCo∞, AUCo-t and Cmax treatment ratios lie within 80% to 125% range CL Absolute Ratios. Absolute bioavailability of the oral Frob was calculated using the extent of exposure measure AUCo∞ and AUCo-t.

Conclusions: The study has shown bioequivalence of two PALO 0.75 mg oral formulations. No significant changes were observed in the absolute bioavailability between the two oral formulations and the i.v. 0.75 mg. All tested formulations showed a good safety profile. All authors have declared no conflicts of interest.

ADME study of [14C]netupitant administered as an oral 300 mg suspension to healthy male subjects

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Background: Netupitant (NETU) is a highly selective neurokinin 1 receptor antagonist developed to provide protection from nausea and vomiting induced by emetogenic chemotherapy. The objectives of the study were to investigate the pharmacokinetic (PK) profile, the mass balance recovery, the excretion pathways and the metabolism of [14C]NETU in an open-label study in 6 healthy male subjects receiving a single-nominal-dose of 300 mg as oral suspension.

Methods: Plasma, urine and feces samples were collected up to 336h after dosing, plus two additional 24h excreta collections until 696h. Total radioactivity was measured by liquid scintillation counting (liquid samples) and after combustion in oxygen (non-liquid samples). PK parameters for NETU and its metabolites were analyzed by liquid chromatography-tandem mass spectrometry.

Results: [14C]NETU is rapidly absorbed with peak in plasma concentration ranging between 2h and 5.5h post dose. Elimination is mainly via the feces, with approximately 71% of the total radioactivity recovered at 696h. Urinary elimination accounts for less than 4% of total radioactivity. Cumulative percent of total radioactivity suggests that approximately half of the administered dose was recovered within 120h and, based on an extrapolation, elimination was completed by 486h. NETU undergoes extensive metabolism forming phase I and II metabolites. The main metabolites of NETU are M1 (N-demethylation NETU), M2 (NETU N-oxide) and M3 (monohydroxylated NETU) which, on average, account respectively for 29%, 14% and 33% of the NETU plasma exposure. Phase II metabolites observed include those formed through N-demethylation, mono and di-hydroxylation, N-oxidation, desaturation, N-formylation, oxidation and reduction to a keto group and oxidation to an acid. Phase II metabolites include those formed by glucuronidation and conjugation to a hexose group.

Conclusions: These data indicate that the hepatic/biliary route, rather than renal clearance is the major elimination route for drug-related entities. NETU undergoes extensive metabolism via phase I and II metabolic reactions with M1, M2 and M3 as the main circulating metabolites. NETU was well tolerated.

Disclosure: C. Giuliano: Helsinn employee, S. Calcagnile: Helsinn employee, All other authors have declared no conflicts of interest.

SAFETY AND PHARMACOKINETIC EVALUATION OF PALONOSETRON GIVEN ON DAY 1 AND 3 FOR PATIENTS WHO ARE TO RECEIVE A HIGH OR MODERATE RISK OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV)

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Purpose: To assess safety, pharmacokinetics and tolerability of repeated dosing of palonosetron in patients receiving chemotherapy categorized as having a high or moderate emetic risk.

Method: Nineteen patients undergoing high or moderate emetic risk for CINV were given palonosetron 0.75mg intravenously once daily for 30 min on day 1 and 3. Blood samples for the first 6 patients were obtained for pharmacokinetics analysis from day 1 through 5. To evaluate safety profiles, serial complete blood cell counts, blood chemistry tests and electrocardiograms were also performed.

Results: The pharmacokinetic studies of 6 patients showed mean Cmax values on day1 and 3 were 2.05 and 2.90ng/mL, respectively, with coefficients of variation (CV) of 30.9% and 34.2%. Mean AUC0-48hr values were 42.4 and 58.3 ng*h/mL on day1 and 3, with a CV of 21.2% and 23.2%, respectively. T1/2 of palonosetron was approximately 40 hours and was constant in day1 and 3. Accumulation of palonosetron on day3 was 1.42-fold for Cmax and 1.37-fold for AUC0-48hr.

Conclusions: Repeated dosing of palonosetron on day1 and 3 was safe and well tolerated in patients who received high to moderate emetic risk chemotherapy.

Disclosure: All authors have declared no conflicts of interest.
in the first 24 hours, about 20% of the administered dose. The prevention of early and late emesis was equivalent with both alternatives.

**Conclusions:** Palonosetron SC administration showed similar AUCO-24h to that of the IV route, with the same exposure to the drug, and good prevention in the prevention of early and late emesis, which can benefit the management of outpatient treatments.

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**Disclosure:** All authors have declared no conflicts of interest.

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**Background:** For prevention of emesis during anthracycline (A)/cyclophosphamide (CPA) therapy for breast cancer, use of aprepitant (AP) combined with serotonin receptor antagonist (5HT3) and dexamethasone (DEX) is recommended. AP, known to function as a CYP3A4 inhibitor, has been reported to interfere with metabolism of chemotherapeutic drugs. It has also been reported that AP does not influence the AUCs of 4-OH and DCE. Although, in the previous clinical reports for AC, the toxicities were not significant in patients who were given AP, compared to those without AP, we have experienced a case of severe hyponatremia probably related to AP. Thus, we investigated an impact of AP on Na metabolism during chemotherapy using CPA for breast cancer.

**Material and methods:** We investigated serum levels of Na in primary breast cancer patients who received CPA-combined therapy with the use of AP as anti-emesis, or not. They all received 600mg/m² of CPA combined with either of anthracycline or docetaxel. Their ages were to be less than 65 years, and their GFR’s were to be more than 60 ml/min/1.73m². Their prior electrolytes were to be within normal range. In the first cycle, we evaluated serum Na levels before the CPA start and that at 24 hours after. We defined serum Na level lower than 135 mEq/L as “hyponatremia” based on previous study. We enrolled 81 patients, in whom 52 were given AP and 29 were without AP, between December 2010 and April 2012.

**Results:** The background between the two groups, with AP and without AP, were comparable, in whom the median ages were 53.0 (33-64) and 53.2 (38-65), and the prior Na levels were 139.84 ± 1.89 mEq/L and 140.25 ± 1.82 mEq/L in the AP-group and non-AP group, respectively. The uses of 5HT3 and DEX were similar between the two groups. The incidence of CPA-induced hyponatremia was significantly higher in AP-group than in non-AP group (26.9% vs. 6.9%, P = 0.04). The average Na level at 24 hours after chemotherapy was 136.32 ± 3.73 mEq/L in AP-group, and 138.60 ± 2.92 mEq/L in non AP-group. Among 14 patients who developed hyponatremia in AP-group, they were resolved without any intervention in 13, and one needed Na replacement. The patient did not develop hyponatremia without AP in the third cycle.

**Conclusions:** According to our cohort study, AP cause hyponatremia more frequently in the CPA-combined chemotherapy.

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Novartis and unrestricted research grants from Amgen and Roche, D. Patrick: Research funding from Amgen Inc., D.H. Henry: Advisory board member, served on the speakers bureau, and received research funding from Amgen Inc., V. Hirsh: Advisory board member for Amgen Inc., A. Feng: Employed by and owns stock, Amgen Inc., Z. Cong: Employed by and owns stock/stock options in Amgen Inc., A. Braun: Employed by and owns stock/stock options in Amgen Inc., All other authors have declared no conflicts of interest.

**Material and methodology:** Interim analysis of an observational multicentre study, in which patients reporting moderate-severe pain, at 1st time in the oncology services, were treated following investigator criteria. We present results of the patients treated with strong opioids during 1 month (N = 298).

**Results:** Baseline characteristics: 65% male, mean ± SD age: 66 ± 13 years (27% ≥ 75 years old), ECOG 1: 54%; receiving chemotherapy 64% and radiotherapy 41%. Main localization of the primary tumour: lung (28%), colon/rectum (12%), head and neck (11%). Metastatic cancer: 79%: 67% of patients reported pain secondary to metastases. Comparison between patients treated with oxycodone/naloxone (n = 217) with those treated with other strong opioids (n = 81) showed a good pain control in both groups (NRS0-1.2 and 1.2 points respectively; p = 0.08). It was confirmed a significant improvement of bowel function (=0.01) in patients treated with oxycodone/naloxone versus those treated with other strong opioids, which worsened their bowel function.

**Conclusions:** Clinical practice confirms significant improvements in pain relief in cancer patients reporting moderate pain at the first time in the oncology services, and treated with strong opioids. But patients treated with oxycodone/naloxone improve their bowel function, unlike those treated with other strong opioids.

**Disclosure:** All authors have declared no conflicts of interest.

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**PAIN AND BOWEL FUNCTION EVOLUTION, IN CANCER PATIENTS TREATED WITH STRONG OPIOIDS AT THE FIRST TIME THAT THEY REPORT MODERATE-SEVERE PAIN. C2 STUDY**

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**Introduction and objectives:** Opioids remain the cornerstone of analgesic treatment for cancer patients, but gastrointestinal side effects have a great impact on their quality of life. The aim of this analysis was to evaluate the use of strong opioids in these patients, and if oxycodone/naloxone combination provides benefits in terms of analgesia, without compromising bowel function.

**Results:** In total, 298 patients were included. Patients in the oxycodone/naloxone group received analgesia, without compromising bowel function.

**Conclusions:** In patients treated with strong opioids, oxycodone/naloxone combination provides benefits in terms of analgesia, without compromising bowel function.

**Disclosure:** All authors have declared no conflicts of interest.

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**PAIN AN D BOWEL FUNCTION EVOLUTION, IN CANCER PATIENTS TREATED WITH STRONG OPIOIDS AT THE FIRST TIME THAT THEY REPORT MODERATE-SEVERE PAIN. C2 STUDY**

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**Material and methodology:** Interim analysis of an observational multicentre study, in which patients reporting moderate-severe pain, at 1st time in the oncology services, were treated following investigator criteria. We present results of the patients treated with strong opioids during 1 month (N = 298).

**Results:** Baseline characteristics: 65% male, mean ± SD age: 66 ± 13 years (27% ≥ 75 years old), ECOG 1: 54%; receiving chemotherapy 64% and radiotherapy 41%. Main localization of the primary tumour: lung (28%), colon/rectum (12%), head and neck (11%). Metastatic cancer: 79%: 67% of patients reported pain secondary to metastases. Comparison between patients treated with oxycodone/naloxone (n = 217) with those treated with other strong opioids (n = 81) showed a good pain control in both groups (NRS0-1.2 and 1.2 points respectively; p = 0.08). It was confirmed a significant improvement of bowel function (=0.01) in patients treated with oxycodone/naloxone versus those treated with other strong opioids, which worsened their bowel function.

**Conclusions:** Clinical practice confirms significant improvements in pain relief in cancer patients reporting moderate pain at the first time in the oncology services, and treated with strong opioids. But patients treated with oxycodone/naloxone improve their bowel function, unlike those treated with other strong opioids.

**Disclosure:** All authors have declared no conflicts of interest.
Objective: To explore patient and nurse satisfaction, compliance with practice guidelines, technical feasibility, and safety of home infusion of the bisphosphonate ZOL.

Methods: This was a prospective longitudinal 1-year survey of home ZOL therapy in patients with bone metastases secondary to a solid malignancy. Randomly selected physicians prescribed home ZOL therapy (4 mg Zometa®, 15-min IV infusion, every 3-4 weeks). Three questionnaires were administered at 3 time points: physician questionnaire, nurse satisfaction and feasibility questionnaire, and patient satisfaction questionnaire. The main end-points were patient and nurse satisfaction with home ZOL therapy.

Results: Of the 154 physicians who agreed to participate, 87 (56.5%) enrolled 818 patients for whom 788 case report forms were received of which 765 met inclusion criteria. Overall, 414 patients (97.5% community). Patient characteristics were: median age 68 yrs (30-95), male-female ratio 40:60; primary cancer: breast 55.2%, prostate 28.4%, lung 7.2%, other 9.4%; ECOG-PS 0 or 1: 78.6%. Overall, 90.9% of nurses were either highly satisfied or satisfied with how home ZOL therapy was run; 96.7% found the infusion either very easy or easy to perform; 97.5% felt that home therapy promoted a good relationship with patients, and 73% were either highly satisfied or satisfied with their home ZOL therapy. However, improved compliance with practice guidelines should be encouraged.

Background: Cancer cachexia, mainly characterized by muscular atrophy and subsequent cancer induced weight loss (CIWL), is attributed to about a third of cancer deaths. Despite worsening prognoses with the symptoms, clinical factors involved and the effect of CIWL to the overall status remain unexplained. We planned a prospective cohort study, Japan Nutrition and QOL survey in patients with advanced NSCLC study to investigate changes in CIWL in relation to grip, QOL, and clinical parameters to understand their effects on prognosis.

Methods: Untreated stage IV NSCLC patients with ECOG PS of 0-2 were registered. Their body weight (BW), grip, QOL, Karnofsky Performance Scale, biochemical assay, and survival were recorded every four weeks for one year from the start of cancer treatments. Patients were classified by BW loss ≥ 5% and cachexia diagnosis by BW loss, fatigue, anorexia, and abnormal assay results. Estimated survival curves were drawn by Kaplan-Meier method, and Log-rank test was applied. To evaluate the effect of cancer cachexia attribution to QOL, we performed principal component analysis, factor analysis, and analysis on time course data using generalized estimating equation (GEE).

Results: Out of 466 patients registered, 406 were evaluable and analyzed. Patient characteristics were: median age: 67 (33-87) years, male/female ratio: 280/126, median BW: 56.5kg, PS 0: 39.2%, and PS 1: 51.5%. The patients with BW loss of ≥ 5% (n = 219) reported more early deaths than those without (n = 166, p = 0.0001). Patients with cachexia (n = 169) reported more early deaths than those without (n = 216, p = 0.0001). All correlations between principal component scores estimated from the variables considered the signs of cancer cachexia (cancer cachexia attributions: more weight on anorexia, fatigue, BW and grip) and each factor scores of QOL domains estimated from QOL factor analyses were significant (p < 0.01). From the time course data analyses using GEE, cancer cachexia attributions of each visit are shown as useful variables for all QOL domains (p < 0.01).

Conclusion: Cancer cachexia decreased QOL and possibly affected prognoses. Cachexia prevents treatments and treatments based on the further elucidation of its pathology are needed.

Disclosure: All authors have declared no conflicts of interest.

QOL AND SURVIVAL SURVEY OF CANCER CACHEXIA IN ADVANCED NSCLC PATIENTS - JNUQ-LOC STUDY, TORG0912

Background: Malnutrition reduces tolerance to treatment, quality of life, and survival in numerous cancers, including metastatic colorectal cancer (mCRC). Previous...
studies have shown that chemotherapy toxicity may be linked to low muscle tissue (sarcopenia). Our study evaluated the effect of sarcopenia on chemotherapy toxicity among mCRC patients.

**Methods:** In this prospective, cross-sectional, multicenter study, demographic, oncological, and nutritional data were collected in all consecutive mCRC patients in three hospitals. Computed tomography (CT) images were analyzed using Slice-O-Matic software V4.3 (Tomovision) to evaluate cross-sectional areas (cm²) of muscle tissue (MT), visceral adipose tissue (VAT), and subcutaneous adipose tissue (SAT). The 3rd lumbar vertebra (L3) was chosen as a reference, since L3 and whole-body measurements are linearly related. Indexed on height, MT, VAT and SAT (cm²/m²) were described, after stratification on sex. Sarcopenia was defined as MT <55 cm²/m² for men (M) and <39 cm²/m² for women (W). Images were obtained within one month of clinical evaluation. Toxicities were evaluated according to the NCI-CTC, version 3.0, in the two months following clinical evaluation.

**Results:** 53 mCRC patients (72% M), participated in the study. According to body mass index (BMI) only 6.7% of F and 2.6% M were malnourished (BMI < 17 kg/m²), and 60% F and 42% M were of normal weight or overweight. These results are to be compared to the 38% F and 82% M of patients with sarcopenia. Grade 3-4 toxicities were observed in 28% of the cases, with neurotoxicity in 23%, diarrhea 15%, anemia 9.4%, leucopenia 9.4%, and nausea and vomiting 6%. In multivariate analysis including age, sex, BMI, sarcopenia, SAT and VAT, the only factor associated with grade 3-4 toxicity was sarcopenia (OR= 13.55 95% CI [1.08;169.31], p = 0.043).

**Conclusions:** In mCRC patients undergoing chemotherapy, sarcopenia was much more frequently observed (48%) than “visible” malnutrition (4%). Despite the small number of patients included in our study, we showed that sarcopenia was associated with severe chemotherapy toxicity.

**Disclosure:** M. Barrett: The study received financial support from Nutricia Advanced Medical Nutrition®, St. Ouen, France. All other authors have declared no conflicts of interest.

**1588P ANAMORELIN’S EFFECTS ON APPENDICULAR LEAN BODY MASS IN CANCER PATIENTS WITH CACHEXIA: RESULTS FROM A PHASE II RANDOMIZED, DOUBLE BLIND, MULTICENTER STUDY**

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**Background:** Cancer cachexia is associated with increased morbidity and poor survival, and is characterized by decreased muscle strength and overall lean body mass including in the extremities (appendicular LBM or aLBM). As most lean tissue in the extremities is striated muscle, aLBM is a good surrogate for muscle mass. Anamorelin is an investigational orally active ghrelin receptor agonist with orexigenic and anabolic activity. We present here a Phase II study post-hoc analysis on a subset of patients who were assessed for aLBM.

**Methods:** A Phase II trial enrolled patients with advanced cancer, performance status 0-1, and surgically resected or non-resectable tumors represented prevalent malignancy (>93%) with no difference in cancer types between treatment groups.

**Results:** Analysis of aLBM indicated that PL-treated patients lost aLBM in the arms during the whole 12 weeks, while in the legs was more stable. In ANA-treated patients, aLBM increased significantly in the arms and in the legs. At week 12, the percentage change from baseline of aLBM in arms + legs showed a statistically significant increase in ANA vs PL groups (5.8% and 1.5%, respectively; p < 0.05). HGS change from baseline also improved in ANA-treated patients vs PL although this difference was only significant at 8 weeks. No significant difference in QoL (ASAS score) was observed, but numerically ANA-treated patients were better than PL. ANA was well tolerated, and types and prevalence of AEs were similar between treatment arms.

**Conclusion:** Decreased LBM and HGS are poor prognostic factors in cancer cachexia patients. This study demonstrates that 50mg ANA treatment for 12 weeks significantly increased aLBM and HGS. Together with the orexigenic activity of ANA, these results support the use of ANA in treating cancer cachexia/anorexia and the evaluation of higher ANA doses.

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**1589P THE SUICIDE IDEATION OF STOMACH CANCER SURVIVORS AND ITS CORRELATES IN KOREA**

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**Purpose:** Although the suicide rate of cancer-survivors is higher compared to that of general population, there are few studies examined on the suicide related risk factors. We evaluated the suicide ideation and investigate its correlates among the survivors with stomach cancer, which is one of the most prevalent cancer in Korea.

**Method:** We requested 391 stage I-II stomach cancer survivors to participate. Our population was composed of patients who were diagnosed of cancer between year 2001 and 2002 and had been disease-free for at least 1 year. Our survey contained demographic characteristics as well as Quality of Life (QOL) assessments including European Organization for Research and Treatment of Cancer QLQ-C30 and its stomach module, McGill Quality of Life (MQOL), Brief Fatigue Inventory (BFI) and Question 9 of Beck Depression Inventory (BDI) regarding suicide ideation. We performed multi-variable logistic regression analysis for the all individuals except the 13 individuals who missed Question 9 of BDI.

**Results:** Of 378 stomach cancer survivors, 131 (34.65%) experienced suicide ideation and univariate analyses showed that monthly income, comorbidity and smoking in the demographic category were statistically significant. General health status, emotional functioning, fatigue, nausea, dyspepsia, appetite loss, constipation, diarrhea, financial problem, eating restriction, anxiety, dry mouth, trouble belching, hair loss, body image, existential well-being and social support in QOL category were statistically significant. The multi-variable logistic regression using the variables that were statistically significant in univariate analyses showed that diarrhea (adj. OR= 2.84, 95% CI:1.44-5.62), hair loss (aOR 2.77; 95%CI 1.04-7.36), poor existential well-being (aOR, 6.18; 95% CI 2.91-13.1), and poor usual fatigue (aOR 2.29; 95% CI 1.30-4.06) were statistically significant for suicide ideation.

**Conclusion:** Our study demonstrated that high prevalence of suicide ideation among stomach cancer survivors and survivors who had diarrhea, hair loss, fatigue poor existential well-being tend to have greater suicide ideation. It is critical to identify suicide ideation among cancer survivors, especially with diarrhea, hair loss, fatigue, and poor existential well-being.

**Disclosure:** All authors have declared no conflicts of interest.

**1590P PROSPECTIVE VALIDATION OF PATIENT NEUROTOXICITY QUESTIONNAIRE (PNQ) FOR ASSESSMENT OF OXALIPLATIN NEUROTOXICITY: CSP-HOR 16**


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**Background:** Oxaliplatin-containing regimens are the standard of care for colorectal cancers. Quality of life is impaired in patients with oxaliplatin neurotoxicity. Patient-reported outcomes are important for evaluating adverse effects that are difficult for physicians to assess objectively. We prospectively investigated the feasibility and validity of a patient-based scale, the Patient Neurotoxicity Questionnaire-Oxaliplatin (PNQ), for cumulative neurotoxicity of oxaliplatin.

**Methods:** We enrolled 121 oxaliplatin-naïve patients treated with FOLFOX4 or modified FOLFOX6 for colorectal cancer. Neurotoxicity was evaluated with PNQ, Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 and Functional Assessment of Cancer Therapy / Gynecologic Oncology Group-Neurotoxicity questionnaire (FACT/GOG-Ntx). Assessments were conducted at baseline, after q 2 treatment cycles and q 8 weeks after completion of chemotherapy. We evaluated compliance, correlation and concordance between PNQ, CTCAE and FACT/GOG-Ntx subscales, and test-retest reproducibility. The probability of experiencing neurotoxicity with cumulative oxaliplatin exposure was estimated by the Kaplan-Meier method.

**Results:** One hundred thirteen patients were evaluable. The median cumulative dose of oxaliplatin was 688±4 mg/m² (range 83.4-1655.0). Questionnaire completion rate was >90% for all assessments during treatment. CTCAE consistently resulted in

**Disclosure:** All authors have declared no conflicts of interest.
lower sensitivity and correlation compared to PNQ (weighted kappa coefficients of sensory and motor components were 0.50 and 0.38). Sensory and motor component grades of PNQ were significantly correlated with the FACT/GOG Ntx-subscale (r = 0.63 and 0.45). The test-retest reliability of PNQ sensory and motor components demonstrated Spearman correlation coefficients of 0.81 and 0.59. PNQ sensory grades increased similarly with CTCAE. PNQ motor grades were worse compared to CTCAE.

Conclusions: The PNQ has adequate feasibility and validity to prospectively assess oxaliplatin neurotoxicity. The PNQ is a convenient, accurate and reliable tool for oxaliplatin neurotoxicity.

Disclosure: All authors have declared no conflicts of interest.

PHASE II STUDY OF TOPICAL MENTHOL FOR CHEMOTHERAPY-INDUCED PERIPHERAL NEUROTOXICITY (CIPN)

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Background: Chemotherapy-induced Peripheral Neurotoxicity (CIPN) is a major dose-limiting toxicity of many commonly used chemotherapeutic agents that can limit successful disease control in cancer care. Although some agents have been available, a significant proportion of patients are left with long-term pain and disability which is difficult to treat. Transient Receptor Potential Melastatin-8 (TRPM-8) is distributed in peripheral nerves and has been shown to associate with cold hypersensitivity, noxious cold, sensory disturbance, and impaired thermoregulation. Menthol is a compound derived from mint leaves that functions as an agonist of TRPM-8. Preclinical and clinical works have shown the effect of topical menthol on CIPN. We conducted a phase II study to investigate the effects of menthol on CIPN.

Methods: 27 patients with CIPN caused by treatment with oxaliplatin (n = 22), paclitaxel (n = 3), capcitabine (n = 1), and irinotecan (n = 1) applied 1% topical menthol twice daily to affected skin areas. CIPN symptoms were assessed separately for the hands and feet using the Numerical Rating Scale (NRS) and modified Peripheral Neuropathy Scale (PNS) based on patient questionnaires at baseline, 4 and 8 weeks after treatment. Responders and good responders were defined as 10% and 30% reduction in NRS respectively.

Results: Three patients (11%) could not continue the study due to adverse events (skin swelling, desquamation and aggravation of Hand Foot Syndrome). Efficacy of topical menthol was evaluated in 24 patients. Eighteen patients (75%) showed over 10% decrease of NRS, and 12 patients (50%) showed over 30% decrease of NRS. Median scores of NRS of baseline, 4 and 8 weeks were 4.3, 4.1 and 3.6 in hands (p = n.s., paired t test); 5.4, 4.9 and 4.4 in feet respectively (p = 0.03, paired t test). In modified PNS that assessed the severity of neurological symptoms and functional disabilities caused by CIPN, a decrease of score was observed in 19 of 24 patients (79.2%).

Conclusions: Topical menthol was well tolerated and demonstrated significant therapeutic response for CIPN.

Disclosure: All authors have declared no conflicts of interest.

CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY: THE ROLE OF THE MODIFIED TOTAL NEUROPATHY SCORE.

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Background: Chemotherapy induced peripheral neuropathy (CIPN) is a common, potentially reversible side-effect of some chemotherapeutic agents. Common toxicity scales used in clinical practice are subjective, insensitive to change, and may underreport this phenomenon. The use of nerve conduction studies is invasive and impractical in routine practice. The modified total neuropathy score (mTNS) provides a comprehensive non-invasive measure of CIPN. CIPN is associated with decreased balance, function and quality of life (QoL). This association has to date been under-investigated.

Methods: All patients receiving neurotoxic chemotherapy regimes over a seven week period during July / August 2011 were identified using the hospital pharmacy database and once screened for inclusion/exclusion criteria, were invited to complete the mTNS, Berg Balance Scale (BBS), Timed Up and Go (TUG), and the FACT-G QoL questionnaire. mTNS scores were profiled and correlated with BBS, TUG and FACT-G using Spearmans correlation coefficient. All assessments were carried out under the supervision of a Senior Physiotherapist.

Results: A total of 29 patients undergoing a variety of neurotoxic chemotherapy regimes (taxanes n = 9, vinca-alkaloids n = 3, platinum n = 13, combination platinum/taxane regimens n = 4) were assessed. The patients mTNS scores ranged between 1 and 12 (median score = 5), indicating that all patients had some signs of neuropathy on mTNS, and 93% (n = 27) had scores indicative of CIPN. No significant correlations were found between mTNS and BERG (r = –0.289; p = 0.05), TUG (r = 0.136; p = 0.05), or FACT-G (r = 0.005; p = 0.05).

Conclusion: This study found a high prevalence of CIPN in patients treated with neurotoxic chemotherapy regimes as assessed by the mTNS. The mTNS provided a clinically applicable, sensitive screening tool for CIPN which could prove useful in clinical practice. mTNS did not correlate with BERG, TUG or FACT-G in this study, which may be due to relatively mild levels of CIPN and consequent subtle impairments which were not adequately captured by gross functional assessments.

Disclosure: All authors have declared no conflicts of interest.

INFLUENCE OF BASELINE OXIDATIVE STRESS LEVEL ON CHANGES IN LEFT VENTRICLE ECHOCARDIOGRAPHIC PARAMETERS IN PATIENTS WITH BREAST CANCER RECEIVING ANTHRACYCLINE CHEMOTHERAPY

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Background: Breast cancer (BC), like other malignancies, is associated with chronic increase of oxidative stress (OS). Anthracyclines (ANTS), potent inducers of OS, represent lifeline of BC. OS induction by ANTS is believed to be the key factor in ANTS-related left ventricle dysfunction and the subsequent development of heart failure, which are major complications of ANTS therapy. The aim of the present study is to establish the role of malignancy-related OS present before ANTS therapy in the development of changes in echocardiographic (ECHO) parameters after chemotherapy in patients with breast cancer.

Patients and methods: The study population consists of 99 adult female suffering from breast cancer (mean age 52.1 ± 12 years) receiving ANTS chemotherapy. Catalase (CAT) activity as a surrogate marker of OS level and ECHO examination were established at the baseline in all patients. Follow-up ECHO examinations were performed at the end of therapy and again one year after the start of therapy. The correlations between baseline CAT activities and changes in ECHO parameters were evaluated.

Results: Statistically significant correlation between baseline CAT activity and unfavorable change in end-diastolic left ventricle diameter (r = 0.24; p = 0.02) was observed soon after the ANTS therapy. Statistically significant correlation between baseline CAT activities and unfavorable change in end-diastolic left ventricle diameter (r = 0.38; p = 0.003) was found at one year following the start of ANTS therapy.

Conclusion: The results of our study suggest a possible correlation between baseline OS level and the future development of morphological cardiac changes after ANTS chemotherapy in patients with breast cancer. Whether pre-treatment levels of OS can predict ANTS induced left ventricle dysfunction and/or the development of heart failure will be shown by a further follow-up of the study population. The study was supported by the grant awarded by Ministry of Health, Czech republic, IGA MZ CR NS 9774 4.

Disclosure: All authors have declared no conflicts of interest.

PREVENTION STRATEGIES FOR CHEMOTHERAPY INDUCED HAND-FOOT SYNDROME: A META-ANALYSIS OF PROSPECTIVE RANDOMISED TRIALS

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Introduction: Hand-foot syndrome (HFS) is a distinctive adverse event relatively frequent to some chemotherapeutic agents as capetitabine, pegylated liposomal doxorubicin, docetaxel or sorafenib, and often recognized as a dose-limiting reaction. The prevention of HSF would be therefore crucial to avoid treatment interruptions, and many studies have been developed in the attempt to reach this purpose. The aim of this meta-analysis is to analyze the clinical efficacy of current prevention strategies.

Methods: A wide search through PubMed/MEDLINE was performed using the terms related to hand-foot syndrome, chemotherapy and random in all fields. ASCO and ESMO Meeting Abstracts from 2000 to 2011 were also scanned. Randomized trials comparing intervention versus observation or placebo were selected and had their data collected. The end-points evaluated were the dichotomic data for mild...
TOPICAL APPLICATION OF TJ-14 (HANGESHASHINTO) IN THE TREATMENT OF CHEMOTHERAPY-INDUCED ORAL MUCOSITIS: A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, PHASE II TRIAL

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Background and aims: Although chemotherapy-induced oral mucositis (COM) is a common side effect of many anticancer therapies, the optimal treatment for this condition is not well established. Recent studies showed that one of the traditional Japanese herbal medicines (Kampo) called TJ-14 (hangeshahinto) may be useful for COM via downregulating pro-inflammatory prostaglandins in the cyclooxygenase pathway (ASCO-G2101, AGA2012). The efficacy of TJ-14 for the prevention and/or treatment of COM was exploratively tested in a randomized, double-blind, placebo-controlled trial in colorectal cancer patients.

Methods: Ninety-three patients who developed COM during FOLFOX, FOLFIRI or XELOX treatment for advanced colorectal cancer were centrally randomized to receive either a topical application of TJ-14 or placebo. Patients were advised to apply 2.5 g of TJ-14 or placebo in 50 mL of tap water and rinse their oral cavity three times daily for 10 seconds with the solution before expectorating it. Patients followed this oral care throughout the treatment before the next course of chemotherapy began. The COM grade was evaluated using the Common Terminology Criteria for Adverse Events (CTCAE) version 4 and a self-administered Short Form-36 (SF-36) questionnaire before and after the 2-week treatment with the TJ-14 or placebo solution. The study endpoints included the incidence of worst grade COM, the healing time of COM.

Results: Amongst 195 potential articles, only six matched the inclusion criteria, while no significant difference in the incidence of grade 2 or higher COM was found between the two groups. The median healing time of COM was 5.5 days vs. 10.5 days (p = 0.018). No significant difference was observed between the two groups with regard to the incidence of grade 2 or higher adverse events.

Conclusions: Topical TJ-14 rinse appears to have a significant ability to treat grade 2 or higher COM and reduce the risk of developing grade 3 COM. Our results are encouraging and warrant further phase III trials.

Disclosure: All authors have declared no conflicts of interest.

REFERENCES

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Background: Panitumumab (Pmab) has been associated with a high incidence of skin toxicity. The STEPP study evaluated whether prophylactic treatment with a topical steroid and oral doxycycline during the first 6 weeks of Pmab-containing
therapy reduced incidence of grade 2 or higher skin toxicities compared to reactive treatment. Prophylactic treatment resulted in skin toxicity incidence of 29% compared with 62% in the reactive treatment arm.

**Purpose:** The aim of this study was to evaluate the efficacy of combination prophylactic therapy with topical adalapane and oral minocycline in patients receiving Pmb.

**Methods:** Patients with KRAS wild-type unresectable/curable colorectal cancer enrolled in a prospective phase II clinical trial of third-line Pmb plus irinotecan (GROVer 1) or Pmb monotherapy were included. Prophylactic therapy with topical adalapane, a third-generation topical retinoid used in the treatment of mild-to-moderate acne, and oral minocycline were started from one day prior to the first Pmb dose and continued for 6 weeks. Adalapane was administered once daily in the evening, along with oral minocycline 100 mg twice per day. Skin toxicity was evaluated according to NCI CTCAE, version 4. The primary endpoint was incidence of grade 2 or higher skin toxicities during the 6-week skin treatment period.

**Results:** Between January 2011 and December 2011, 48 patients were included in this study (27 men, 21 women, median age, 62.0 years; 43 CPT-11+Pmb, 5 Pmb alone). During the 6 weeks of prophylactic therapy, incidence of skin toxicities (rash, dry skin, and paronychia) was 83.3%. The incidence of skin toxicities of grade 2 or higher was 29.2%, similar to STEPP trial results (29%). The median adherence to topical adalapane was 90% (range, 0-100%), while minocycline was 100% (range, 17-100%). In the good adalapane adherence group (≥ median), the incidence of skin toxicity of grade 2 or higher was 20.8% compared to 37.5% in the poor adherence group (< median) (OR, 0.44; 95% CI, 0.1-1.6). The mean relative dose intensity for Pmb was 95%.

**Conclusion:** The incidence of skin toxicities during the 6 weeks of prophylactic therapy was similar to the STEPP trial. These results suggest that adalapane may be an effective prophylactic treatment option for management of Pmb-related skin toxicity.

**Disclosure:** All authors have declared no conflicts of interest.

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**ASSOCIATION OF CISPLATIN INDUCED NEPHROTOXICITY WITH CLINICAL CHARACTERISTICS AND TREATMENT METHODS IN PATIENTS WITH THORACIC MALIGNANCY**

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**Background:** Cisplatin contained regimen is one of the optimal treatment in patients with thoracic malignancy. Nephrotoxicity is a well-known side effect in cisplatin treatment. The purpose of this study was to evaluate risk factors of cisplatin induced nephrotoxicity.

**Methods:** We retrospectively reviewed 497 patients with thoracic malignancy who were treated with CDDP (≥60 mg/m²)-containing regimen as first-line chemotherapy from 2009 to 2011 at our institution. Renal function was evaluated by serum creatinine level (sCr). We evaluated association of the incidence of Grade 2 or more sCr elevation according to CTCAE version 4.0 during first-line chemotherapy with clinical characteristics (sex, age ≥70, PS ≥2), complication with diabetes mellitus (DM), anemia (<11g/dL), serum albumin level (<3.5g/dL), creatinine clearance (Ccr) (<50ml/min), co-administered non-steroidal anti-inflammatory agents (NSAIDs), and treatment methods (cisplatin dose ≥80mg/m²), concurrent topical radiotherapy, use of apprepitant, non-prescribing magnesium (Mg) before chemotherapy.

**Results:** Clinical characteristics of patients were; male/female: 386/111, median age: 64 (range: 28-79) years, PS 0-1.2/4: 483/14, median Ccr (using the Cockcroft-Gault formula): 82 ml/min. 47 (9%) patients had DM, and 127 (20%) patients had co-administered NSAIDs. 358 (72%) patients were treated with CDDP (≥80mg/m²) contained regimen, and 161 (32%) patients with Mg preloading regimen. 316 (64%) patients used apprepitant as antiepileptic drug. The median number of chemotherapy cycles was 4. 150 (30%) patients during all cycles had Grade 2 or more sCr elevation. In multivariate analysis, cisplatin induced nephrotoxicity significantly associated with co-administered NSAIDs (odds ratio (OR): 2.18, 95% confidence interval (CI): 0.30-0.70) and non-Mg preloading [OR: 3.82, 95% confidence interval (CI): 2.36-6.41].

**Conclusions:** The results of this study indicate that co-administered NSAIDs and non-Mg preloading are significant risk factors of cisplatin induced nephrotoxicity in patients with thoracic malignancy.

**Disclosure:** All authors have declared no conflicts of interest.
declined to relatively lower level of QOL and then steadily back to moderate QOL. The third type of QOL covered 39.6% of patients and represented "steadily moderate level of QOL." The factors significantly related to the first type of QOL trajectory were physical function, pain, uncertainty and self efficacy were related to the second type of QOL trajectory; and depression and uncertainty were related to the third type of QOL trajectory.

Conclusion: Based on the QOL trajectories and identified factors, the timely and tailored intervention could be developed, and tested its potential effectiveness in enhancing advanced lung cancers patients’ QOL during the most distressful first 6 months of having lung cancer. Acknowledge This study is supported by National Health Research Institute (NIRHI) in Taiwan.

Disclosure: All authors have declared no conflicts of interest.

1601P  PATIENT DIGNITY INVENTORY (PDI) QUESTIONNAIRE: THE VALIDATION STUDY IN ITALIAN PATIENTS WITH SOLID AND HAEMATOLOGICAL CANCERS ON ACTIVE ONCOLOGICAL TREATMENTS

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Background: In Oncology, little is known about the dignity – related distress and the issues that influence the sense of dignity for patients. We validated the Patient Dignity Inventory (PDI) questionnaire in Italian patients on oncological active treatments.

Methods: After the translation procedures, the PDI was administered to 266 patients along with other questionnaires to assess the psychometric properties of the Italian version of PDI. Factor structure was tested by both explorative and confirmatory factor analyses. Concurrent validity was tested through convergent and divergent validity with validated questionnaires inquiring about physical and psychological symptoms, and religiosity. The test/retest reliability was assessed through the concordance coefficient of Linn (two weeks interval, 80 patients).

Results: The explorative analysis suggested one factor only loading highly on all the 25 items (>0.45) and explaining 48% of variance; confirmatory analysis and Cronbach alpha (0.96) confirmed the adequacy of the one-factor model. In the 2 weeks test-retest study a concordance coefficient of 0.73 (95% C.I.:0.64; 0.83) was found. High correlations of problems with dignity were found with both physical and psychological symptoms, and religiosity. The test/retest reliability was assessed through the concordance coefficient of Linn (two weeks interval, 80 patients).

Conclusions: The Italian version of Herth Hope Index (HHI) is a valid and reliable assessment tool, useful to initiate conversation with someone who is troubled but finds it difficult to talk, in cancer patients on active oncological treatment during the non advanced stage of the disease, with either solid and haematological cancers.

Disclosure: All authors have declared no conflicts of interest.

1602P  HOPE HERTH INDEX (HHI): A VALIDATION STUDY IN ITALIAN PATIENTS WITH SOLID AND HAEMATOLOGICAL MALIGNANCIES ON ACTIVE ONCOLOGICAL TREATMENTS

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Aims and background: Although Hope is a term widely used, the experience of hope in patients with chronic diseases or even life threatening is often disregarded due to the scarcity of assessment tools carefully crafted and validated. The aim of the study was to validate the Hope Herth Index (HHI) questionnaire in the Italian population of patients with solid or haematological cancers during oncological active treatment.

Methods: After the translation procedures, the psychometric properties of the Italian version of the Hope Herth Index (HHI) were evaluated in 266 patients with non-advanced cancer cared for in four different settings. Summative scores ranged from 12-48, with a higher score denoting greater hope. Confirmative factorial analysis to assess dimensionality was performed. The test/retest reliability was assessed by means of the Linn concordance coefficient (two weeks interval, 80 patients). Concurrent validity was assessed through the following questionnaires: Hospital Anxiety and Depression Scale (HADS), Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being (FACIT-Sp), Edmonton Symptom Assessment Scale (ESAS) and System Belief Inventory (SBI-15R).

Results: A total of 266 patients were enrolled. Confirmative Factor analysis did not confirm the original three factors solution, whereas a one factor solution did perform well. Cronbach alpha was 0.84. Test-retest reliability was 0.64 (95% C.I.: 0.51; 0.76). Large convergence was found with spiritual well being as measured by the FACIT-Sp (0.69) and with anxiety-depression as measured by the HADS (inverse correlation: -0.51). Physical symptoms and religiousness were only slightly correlated, as expected.

Conclusions: The Italian version of Herth Hope Index (HHI) is an established tool to assess in cancer patients on active oncological treatment during the non advanced stage of the disease, with either solid and haematological cancers.

Disclosure: All authors have declared no conflicts of interest.

1603P  SERUM PLASMA LEPTIN LEVELS AND LIFE EXPECTANCY IN CANCER PATIENTS WITH TERMINAL ILLNESS

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Introduction: Excess body fat (assessed by Body Mass Index, BMI) is an established risk factor in various cancers and high BMI is directly associated with elevated levels of leptin. Leptin, in addition to its metabolic and central nervous system functions, may also regulate appetite, can act as a mitogen and an angiogenic factor and it seems also associated with cancer cachexia and chronic inflammation. However, data on the association between leptin levels and cancer progression are contradictory and not definitive. The objective of the present prospective study was to investigate the relationship between leptin and life expectancy in advanced cancer patients, regardless of the primary tumor.

Methods: We assessed Palliative Prognostic (PaP)-Score in cancer patients from the Medical Oncology Unit at CampusBio-Medico Hospital in Rome. PaP-score ranked patients into three groups with a different 30-day survival probability (A = 82%; B = 52.7%; C = 9.6% respectively). We enrolled 20 patients for each PaP-Score subgroup. For each patient, leptin serum levels were measured by ELISA (Enzyme-Linked ImmunoSorbent Assay) using commercially available kit (R&D System). Statistical analysis was performed using Mann-Whitney U-test.

Results: The mean leptin serum concentration in PaP-Score C subgroup was significantly higher compared to PaP-Score A patients subgroup (P = 0.046) with an increase in mean leptin levels of 115%. No statistically significant difference was observed in mean leptin serum levels between PaP-Score B vs PaP-Score A patients (increase of 7%).

Conclusions: This study showed for the first time a correlation between leptin serum levels and life expectancy in end-stage cancer patients according to PaP-Score. Further studies in larger populations are warranted to clarify the weight of these preliminary results.

Disclosure: All authors have declared no conflicts of interest.

1604P  CASE-CONTROL PHASE II CLINICAL TRIAL TO ASSESS EFFICACY AND SAFETY, OF THE SAME ANTIINEOPLASTIC TREATMENT(S) IN ELDERLY “FIT” COMPARED TO ADULT PATIENTS WITH CANCER AT DIFFERENT SITES

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Background: We designed a case-control phase II open, prospective non-randomized trial in elderly “fit” (≥65 yo) cancer patients (pts) compared to well-matched adult (45-65 yo) cancer pts to assess whether the same standard antiineoplastic treatment could achieve comparable results in efficacy and safety. Planned sample size: 125 pts per arm. Endpoints: safety, QoL, FRS, ORR, dose intensity.

Patients and methods: Only elderly “fit” pts at MGA were included. Inclusion criteria for elderly: histological diagnosis of cancer with either advanced disease with measurable lesions or radically resected (adjuvant setting); life expectancy >3 mo.; adequate baseline functional parameters; written informed consent. Inclusion criteria for adults: the same as for elderly plus ECOG-PS 0-1.

Results: At September 2011, 254 pts were enrolled, 127 elderly and 127 adults, all evaluable for toxicity. Elderly pts clinical characteristics: M/F ratio 69/56; mean age 70.8 ± 4.5 y. Adult pts: M/F ratio 58/69; mean age 53 ± 5.4 y. Tumor sites: colorectal (23.5%), head and neck (16.4%), breast (14.1%), lung (11.7%), ovarian (9.3%); prostate (6.2%), NHL (4.7%), gastric (4.7%), liver (4.7%), uterus (3.9%), pancreas (0.8%); 92.1% of pts were stage IV, 5.9% stage III and 2.0% stage II. In the elderly no
grade 4 toxicity were observed, hemoglobin and non hematological grade 3 toxicities were observed in 12.2% and 13.8% of pts, respectively. In the adults, grade 4 hematological and non hematological toxicity were observed in 3.8% and 1.9% of pts, respectively. grade 3 hematological toxicity in 22.2% and non hematological toxicities in 21.3% of pts. The difference was statistically significant (p = 0.042) in favor of the elderly. At September 2011, 234 pts could be assessable for response: the ORR was 56.7% for elderly and 51.1% for adults. No differences were observed for quality of life and dose intensity between the two groups. PFS was 10.6 mo. (3.12- mo) for elderly and 9.05 mo. (3-12) for adults.

Conclusion: The promising results of this single Institution study warrant to be confirmed by a larger clinical trial.

Disclosure: All authors have declared no conflicts of interest.

1600P  PARENTAL CANCER: REVIEWING THE CONCERNS OF BREAST CANCER PATIENTS WITH CHILDREN

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Background: In recent years, it is estimated that 24% of cancer patients have a child under 18 years of age. Affected parents may experience heightened distress related to the worries about their illness as well as their inability to perform parenting activities. Many parents also struggle with what and how to tell their children about their own or their loved one’s illness and future. Since 2008, St. Luke’s International Hospital (Tokyo, Japan) started a service called “Child Support”, for these patients to discuss their concerns, providing them with appropriate suggestions and useful resources.

Objective: The objective of this research is to review and organize the concerns breast cancer patients with children have, and to review the types of support provided by the professionals.

Method: Medical charts of breast cancer patients with aged children, who were offered to a child support service between the period of April 2010 and November 2011, were reviewed (n = 172).

Result: 75% of the child support sessions started from the direct offering by the Child Life Specialist (CLS). Nurses were slightly more active in referring the patients to the service. 70% of the patients’ concerns were topics that directly related to their children. The two most common concerns were “confrontation to the children about parent’s illness” (30%), and “how the illness will impact the child” (40%). While less than 10% showed absolutely no concern, others showed concerns in topics related to one’s own life and disease (10%), family related matters (10%)

Discussion: When post-traumatic stress levels of 126 breast cancer patients and 56 of their children were measured, 51% of the mothers scored above the cut-off score of 25 with the use of IES-R (Impact of Event Scale – Revised) and 52% of the children were shown to have moderate to severe post-traumatic stress syndrome symptoms. These findings clearly indicate the need for professional intervention within this patient and family population. While we have identified some of the major concerns of these affected parents, currently in Japan, there is not enough support system for this specific population. Knowing what these patient populations worry about, and knowing how to give appropriate support may be a gateway to our nation’s providing a better support system for these patient population.

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FAMILY PHYSICIANS (FP) ARE RARELY INVOLVED IN MANAGING ACUTE ONSET SYMPTOMS DURING CANCER TREATMENT

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Objective: The emergency oncology department (EOD) manages the acute onset symptoms (AOS) of cancer patients being treated at our institution. About 80% of them visited the EOD without referring to their FP. The aim of our study is to analyse if these specialised consultations are justified.

Methods: This is a prospective study. Cancer patients (n = 112) who visited the EOD for AOS were questioned about the reasons for not referring to their GP. The second part is to evaluate if the AOS require a specialised advice. This assessment has been conducted by a junior FP (JFP) and a senior physician (SP) specialised in supportive care. Patients who couldn’t answer the questions were excluded.

Results: Prior to admission to the EOD, 37.5% had a consultation with their FP and 57% of them visited the EOD despite their FP’s advice. The GP was judged not qualified to manage AOS by 35% of the patients. Colorectal, breast, lung, and prostate cancer were identified in 16%, 14%, 12%, 12%, of visits. The main complaints were fever (21%), pain (16%), dyspnoea (14%), gastrointestinal issues (13%) and fatigue (13%). These AOS required an urgent assessment in 75% for JFP and 71% of the cases for SP. This assessment had to be conducted by a trained physician in supportive care in 73% of the cases for JFP and 85% for SP.

Conclusions: Our study shows that an assessment was required by a well trained physician in supportive care for more than ¾ of the acute onset symptoms.

Disclosure: All authors have declared no conflicts of interest.

1608P  BRONCHOSCOPIC INTERVENTION FOR AIRWAY STENOSIS CAUSED BY THYROID TUMOR

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Background: Although, bronchoscopic intervention has become a widespread way to palliate respiratory symptoms due to airway stenosis due to thyroid tumor. The aim of this study was to evaluate the efficacy and safety of bronchoscopic intervention in patients with tracheobronchial stenosis due to thyroid tumor. We retrospectively investigated patients who underwent bronchoscopic treatment using rigid and flexible bronchoscopes under general anesthesia from July 2006 to December 2011 at Nagoya Medical Center.

Results: During the study period, we performed 428 bronchoscopic interventional procedures for 312 patients. Of the 312 patients, nineteen (7 male, 12 female; median age 77 years [range 52-89]) had airway stenosis due to thyroid tumor (benign in 4, malignant in 15). Fifteen patients underwent stenting (silicone stent placement in 7, self expandable metallic stent placement in 1, expandable metallic stent placement followed by expandable metallic stent placement in 1), and the remaining 4 patients underwent bronchoscopic airway reanastomosis using argon plasma coagulation, electrocauterity or rigid bronchoscopic coring without stenting. Respiratory symptoms improved immediately after the procedure in 15 of 19 patients. The amount of supplemental oxygen could be tapered in all 6 patients who needed supplemental oxygen before the procedure. In patients requiring oxygen therapy, oxygen requirements decreased from 1 to 0 immediately after the procedure. In patients requiring respiratory support, respiratory symptoms improved immediately after the procedure in 15 of 19 patients. The amount of supplemental oxygen could be tapered in all 6 patients who needed supplemental oxygen before the procedure.

Conclusions: Bronchoscopic intervention is an effective and safe treatment for patients with airway stenosis due to thyroid tumor.

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Background: In cancer chemotherapy, patients have various side effects. In general, if patients’ quality of life is negatively affected (e.g., toxicity of grade 3 or higher), the treatment will be discontinued. On the other hand, if symptoms are mild or moderate (e.g., toxicity of grade 2 or lower), the treatment will be continued with supportive therapy. Patients with mild or moderate side effects must tolerate such adverse effects for a prolonged period. Therefore, to continue chemotherapy safely, it is very important to understand the extent of symptoms and to provide suitable supportive care as required. We conducted a survey of outpatient cancer chemotherapy.

Methods: We retrospectively investigated the characteristics of side effects and the reasons for discontinuation or delay of chemotherapy during July 2009 and March 2011 at Nagoya Daichi Red Cross Hospital in Japan.

Result: Data on 924 patients (8221 cases) were analyzed. The following data are presented in the order of grade 2 and grade 3 or higher. Nonhematologic toxicities were constipation (32.0, 0.7%), fatigue (21.3, 2.7%), anorexia (17.0, 0.6%), neuropathy (15.3, 1.4%), nausea (14.6, 0.8%), pain (13.7, 1.0%), vomiting (7.5, 0.6%), diarrhea (6.6, 0.3%), dysgeusia (6.0, 0.2%), oral mucositis (4.1, 0.1%), and nail changes (3.6, 0.1%). Hematologic toxicities were neutropenia (16.3, 1.9%), thrombocytopenia (4.1, 2.1%), and anemia (26.1, 7.0%). Nonhematologic toxicities Grade 2 or lower had a high average incidence of 44.6%. Chemotherapy was discontinued in 1341 patients (16.3%). The reasons for discontinuation or delay were laboratory abnormalities (35.4%), chief complaints of patients (34.0%), and others (30.1%).

Conclusion: In patients with grade 3 or higher toxicity, appropriate care was provided, including dose reduction or discontinuation of treatment. In patients with grade 2 or lower toxicity, treatment tended to be continued. Our results showed that a large proportion of patients tolerate mild or moderate side effects that do not lead to discontinuation or delay of treatment. It is necessary to evaluate the extent of symptoms and to provide supportive care.

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established. Medication performance was assessed during the treatment period using a 5-point scale (0 = poor to 4 = excellent). Responses at 30 min. and at 60 min. post dose were “good” to “excellent” for 79.3% (124/1576 BTP) and 82.4% (1574/1668 BTP) respectively. Patients’ quality of life and functional status (modified Brief Pain Inventory short version 7 item subscale (BPI-7S)) improved after treatment with BTP [BPI-7S global score [mean (SD)] decreased from 39.7 (15.85) before to 31.6 (16.8) after treatment. The ease of use of BTP was rated “very easy/convenient” and “easy/convenient” for 82.5% (174/211) of patients. Safety data do not indicate concerns with use of BTP and were as expected for cancer patients with opioid treatments. These results demonstrate that BTP was safe and efficacious in a real-world clinical practice setting with a large number of cancer patients experiencing BTP.


Conclusions: MTAs display frequent and varied OAEs that sometimes clearly lack precision in their descriptions. These OAEs can be severe and are not well captured by the NCI CTCAE. Finally, these OAEs are not well reported in the publications of the pivotal clinical trials. Efficient collaboration between clinical trial conductors and ophthalmologists should help defining and handling the OAEs occurring in patients treated with MTAs.

Disclosure: All authors have declared no conflicts of interest.

ONCOLOGICAL EMERGENCIES

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Background: The Acute Oncology Service (AOS) has been recommended in the UK since 2008, when the National Chemotherapy Advisory Group (NCAG), and the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) reported the results of safety and quality in systemic therapy for cancer patients. The National Patient Safety Agency (NPSA) recommended that cancer related emergencies be dealt in a systematic approach. This abstract refers to the data from patients with known or undiagnosed cancer, admitted in Musgrove Park Hospital (MPPH) and referred to the AOS.

Materials and method: We collected the data of patients admitted to MPPH because of cancer or treatment-induced complications or diagnosed cancer. Patients were referred via the inpatient referral system and were registered daily in a purpose built database. We recorded patients’ demographics, diagnosis, metastatic sites, treatment type, reason of admission and length of in-hospital stay (LOS).

Results: From June 2010 to April 2012, 846 patients were admitted with oncological complications. 48% had multiple metastatic sites, 18% had primary diagnosis of breast cancer, 19% urological, 16% lung, 24% upper and lower GI cancers and 5% of unknown primary. Only 1% of patients were referred from A&E department, 28% from medical assessment unit and 71% from the medical wards. 29% of patients were admitted during their chemotherapy period, 8% during their radiotherapy treatment, whereas for 38%, the type of treatment was not reported. The reasons of admission were: Dyspnoea 14%, Neutropenic sepsis 8%, CNS related 9%, metastatic spinal cord compression 6%, pain 12%, miscellaneous/unknown 51%. Admission was attributed to cancer and/or treatment in 73% of patients and it was unclear/unknown in 23%. The number of referrals has increased from 50 for the first 2 months to 97, the last 2 months. The LOS ranged from 0-102 days and the median remained stable at 10 days.

Conclusion: The majority of cancer patients with complications are admitted in medical wards. This real time audit will be used to re-define the appropriate AOS model. Further education, communication, recourses and training are mandatory to reduce the patients’ LOS and develop a cost-efficient service.

Disclosure: All authors have declared no conflicts of interest.

OCULAR ADVERSE EFFECTS (OAES) OF MOLECULARLY TARGETED AGENTS (MTAS) APPROVED IN ONCOLOGY: A SYSTEMATIC REVIEW

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Background: MTAs display different toxicity profiles than conventional cytotoxic agents, with primarily non-hematological toxicity. This study aimed to describe the OAEs reported with the use of MTAs approved in oncology.

Methods: EMEA and FDA product information files (PIFs) were reviewed including all MTAs approved in oncology as of January 1st, 2012. Incidence, severity and types of OAEs were recorded. OAEs reported in these files were compared to the ones reported for 62.5% of the MTAs, and included conjunctivitis, periorbital edema, blepharitis, keratitis, periorbital edema, amblyopia, conjunctival hemorrhage, eye hemorrhage, eye infection, eye edema and eyelid infection. Serious OAES (Grade ≥3 or with a warning in the PIFs) were reported for 62.5% of the MTAs, and included conjunctivitis, periorbital edema, keratitis, eyelid edema, blepharitis, papilledema, uveitis, cataract, iritis, episcleritis, scleritis, corneal perforation, and retinal vein occlusion. All these serious OAEs were uncommon with a frequency ranging from 0.1% to 1%. Intriguingly, OAES were reported in the publications of the corresponding pivotal trials for only 5 out of the 14 MTAs for which OAES were reported in the PIFs.

Conclusions: MTAs display frequent and varied OAEs that sometimes clearly lack precision in their descriptions. These OAES can be severe and are not well captured by the NCI CTCAE. Finally, these OAES are not well reported in the publications of the pivotal clinical trials. Efficient collaboration between clinical trial conductors and ophthalmologists should help defining and handling the OAES occurring in patients treated with MTAs.

Disclosure: All authors have declared no conflicts of interest.

THE IMPACT OF ANEMIA IN ADVANCED SOLID TUMORS TREATED WITH SORAFENIB (SO) AND SUNITINIB (SU): A POOLED ANALYSIS OF 6 TRIALS

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Introduction: Anemia is a frequent and serious complication experienced by many cancer patients, especially those receiving chemotherapy. Targeted therapies are associated with a significant risk of anemia too but this data is often underreported in clinical trials. We described in a published meta-analysis of 24,310 patients affected by solid tumours, that the addition of targeted therapies to standard treatment increased by 7% the risk of all grades anemia (p = 0.09). Now we perform a pooled analysis to evaluate the risk of anemia in patients treated with Su and So in single agent therapy.

Materials and methods: We searched PubMed for published, randomized, controlled, Phase II and III trials (RCTs), and we have performed a pooled-analysis to calculate the incidence of anemia associated with so and Su. Relative risk (RR) with 95% confidence interval has been calculated to quantify the burden of anemia in these patients.

Results: Six studies have been selected, for a total of 2802 patients analysed. Four trials included Su and 2 So. Comparison arms were: Axitinib in 1 trial, Bevacizumab/ INF or Bevacizumab/Tensirolimus in 1 trial, placebo in 3 trials and no therapy in 1 trial The overall incidence of anemia was 44% in experimental vs 34% in control arms (incidence difference 9.8%; p = 0.0001). The RR was 1.19 (p = 0.02). The risk is significant only for low grade anemia (G 1-2: incidence 42%) with RR = 1.19 (p < 0.0001). A meta-regression was performed to calculate the weight of median treatment duration on anemia risk and the results is significant (p = 0.00046).

Conclusions: The treatment with Sunitinib and Sorafenib increases by about 20% compared with control arms the risk of anemia, and it increases the longer is the duration of treatment. We think that this information is particular useful in kidney cancer patients which often are affected by anemia subsequent kidney surgery. Because of the potential deleterious effects of anemia on patients’ quality of life, performance score, and therapeutic outcomes, the treatment of anemia is an important component in the overall care of cancer patients.

Disclosure: All authors have declared no conflicts of interest.

LOW MOLECULAR WEIGHT HEPARIN (LMWH) RESISTANCE IN CANCER PATIENTS

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Introduction: Cancer patients have an increased risk of developing venous thrombo-embolism (VTE). Treatment of VTE involves the administration of heparin, low molecular weight heparin (LMWH) or coumarin derivatives. Heparin resistance is a situation in which the administration of heparin does not result in an increase of the activated partial thromboplastin time (APTT) and blood anticoagulation. While heparin resistance is a known entity, LMWH resistance is not well documented, and anti factor Xa activity is not tested routinely in cancer patients treated with LMWH. Here, we report the pharmacokinetics of LMWH in cancer patients suffering from VTE and receiving treatment at standard dosages of 1 mg/kg twice daily.

Patients/methods: Patients suffering from malignancy and VTE, and treated with the LMWH, enoxaparin at standard dose of 1mg/kg q12 h were enrolled. Ambulatory
patients were admitted to the oncology day care unit for 8 hours in order to facilitate repeated blood testing. Blood samples were obtained before the injection of LMWH and 1, 2, 3, 4, 6, and 8 hours after LMWH subcutaneous administration, and tested for anti Xa activity as a surrogate marker of bioavailable LMWH levels. The trial was approved by the ethics committee of Shaare Zedek Medical Center. ClinicalTrials.gov Identifier: NCT00716989. Study funding: Israel Cancer Association.

**Results:** Eleven patients were enrolled; one was excluded from analysis due to complete remission at time of VTE diagnosis. Peak anti Xa activity was achieved after 2, 3, 4, 6, and 8 hours in 2, 3, 2, and 1 patient respectively. 60% of the patients (n = 6) did not reach the therapeutic anti Xa activity target (0.6 - 1.0 IU/ml) at 4 hours after subcutaneous administration of LMWH. Average anti Xa activity at 4 hours was 0.62 ± 0.29 IU/ml as opposed to 1.1 IU/ml in historical controls of non-oncology patients.

**Conclusions:** Our results show that a substantial number of cancer patients suffering from VTE and treated with standard dose enoxaparin do not reach therapeutic target anti Xa activity. If confirmed in a larger study, our results suggest that cancer patients suffering from VTE should be tested for anti Xa activity and LMWH dose should be titrated accordingly in order to achieve effective anticoagulation.

**Disclosure:** All authors have declared no conflicts of interest.

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**EDMONTON SYMPTOM ASSESSMENT SCALE (ESAS) FOR ROUTINE SYMPTOM ASSESSMENT OF NON-ADVANCED PATIENTS WITH SOLID OR HAEMATOLOGICAL MALIGNANCIES ON ONCOLOGICAL THERAPIES**

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The Edmonton Symptom Assessment Scale (ESAS) was developed for use in daily symptom assessment of palliative care patients. We used the ESAS validated version in Italian Language to assess the presence and intensity of symptoms (not at all = 0; mild 1-4, not controlled ≥5) in 108 patients with solid and 86 with haematologic malignancies and no metastases, on active oncological treatments (156 patients) or during follow-up. In haematologic group, dyspnoea was ≥5 in 12% of the patients in respect to 3% of solid tumour group (chi2 test, p = 0.002). Not controlled fatigue, drowsiness and dyspnoea were significantly more frequent in patients on cure (p = 0.043; p = 0.026; p = 0.010 respectively). The intensity of all the symptoms was higher in patients with a KPS of 70-90 in respect to those with KPS > 90, and in patients above the clinical HADS cutoff respectively). The intensity of all the symptoms was higher in patients with a KPS of 70-90 in respect to those with KPS > 90, and in patients above the clinical HADS cutoff respectively). The intensity of all the symptoms was higher in patients with a KPS of 70-90 in respect to those with KPS > 90, and in patients above the clinical HADS cutoff respectively).

**Disclosure:** All authors have declared no conflicts of interest.

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**CILASTATIN ATTENUATES CISPLATIN-INDUCED NEPHROTOXICITY WITHOUT COMPROMISING ANTITUMORAL ACTIVITY**

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**Introduction:** Cisplatin (CDDP) is a very effective and common treatment in solid malignancies used mostly in breast, ovarian, bladder, esophageal, gastric head and neck cancer and germ cell tumors. One of the most important side effects of CDDP is the nephrotoxicity, especially with CDDP doses higher than 60 mg/m2, affecting as much as 30% of the patients. Nephrotoxicity is a limiting side effect on treatment with CDDP, preventing patients with limited kidney function of receiving the drug and stopping treatment once kidney function has worsened. Cilastatin (Cls) is a specific inhibitor of renal dehydropeptidase I (DHP-I) which prevents hydrolysis of impenem and its accumulation in the proximal tubule. In this work we hypothesized that Cls acts as a nephroprotector against CDDP-induced damage without compromising antitumor activity.

**Methods:** Primary cultures of proximal tubular cells (PTCs) and cell lines of different malignancies (colon, breast, ovarian, bladder) were cultured with different concentrations of CDDP (1, 10 and 30 µM) in the presence or absence of Cls. Cell viability was assessed with MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Raft staining was measured with toxine B and 1620

**WEIGHT LOSS DESPITE ORAL GLUTAMINE SUPPLEMENTATION PREDICTS POOR PROGNOSIS IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH CONCURRENT CHEMORADIOThERAPY**

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**Background:** In this retrospective study, we investigated potential impact of weight change according to oral glutamine supplementation (GLT) on survival in patients with stage IIIb non-small cell lung cancer (NSCLC) treated with concurrent chemoradiotherapy.

**Results:** Netu inhibited the CYP3A4-dependent metabolism of the two isoform selective probe-substrates midazolam and testosterone with estimated IC50 (±S.E.) values of 5.9 ± 1 and 1.7 ± 0.2 µM respectively. For the hydroxylisation of diclofenac, catalyzed by CYP2C9, IC50 (±S.E.) of 18.0 ± 6 and 22.6 ± 3 µM were calculated in two different experiments, utilizing both the free base, and the Netu hydrochloride as inhibitors. Netu showed no significant inhibition potential for CYP1A2, 2C19 and 2D6 (IC50 > 100 µM).

**Conclusions:** Significant metabolic drug-drug interactions in human are not anticipated for compounds metabolized mainly by CYP1A2, 2C19 and 2D6 and are very unlikely for CYP2C9 metabolized drugs based on the expected human plasma concentration of Netu in the low umolar range. However, metabolic drug-drug interactions are possible for co-medicated drugs metabolized mainly by CYP3A4, based on the high in vitro affinity of Netu for this isozyme, as tested with testosterone and midazolam (app Ki = 1.1 to 2.2 µM) and for the inhibition potential of the metabolites M1 and M2 similar to the parent compound. The in vivo CYP3A4 interaction has been studied in appropriate designed clinical interaction studies.

Materials and methods: Of the 142 patient evaluated retrospectively, 84 received GLT (GLT+), and 58 refused GLT intake (GLT-) and analyzed as control group. GLT was given at a daily dose of 30 g in powder form mixed with fruit juices. All patients received thoracic radiotherapy (TRT) to a total dose of 60-66 Gy (2Gy/Fx) concurrently with 2 cycles of cisplatin-based chemotherapy.

Results: During CRT, 76 (53.5) cases lost weight while remaining cases retained or gained weight. Weight loss in GLT- group (74.1%) was more frequent than GLT+ group (39.3%) (p < 0.001). Although not statistically significant, GLT+ cases had superior overall survival than GLT- ones (21.8 vs 19.8 m; p = 0.068). Cases that retained or gained weight during CRT had longer overall survival than those with weight loss (25.6 vs. 15.4 months, p < 0.001). Comparative survival analyzes according to weight change with respect to GLT supplementation (Table 1) revealed cases in GLT+ group that retained or gained weight had the best outcome compared to the others. Bonferroni correction of two groups that retained of gained weight (p must be <0.0084) revealed the preservation of statistical significance for the survival advantage in GLT+ group (21.7 m vs. not reached yet; p = 0.0041).

Conclusion: Results of this study demonstrated that GLT supplementation during CRT could prevent weight loss, yielding a better survival outcome in locally advanced NSCLC. Moreover, weight loss indicates poor prognosis irrespective of CRT could prevent weight loss, yielding a better survival outcome in locally advanced NSCLC. Moreover, weight loss indicates poor prognosis irrespective of GLT use, and no long term survivors in GLT- group with weight loss suggests GLT resistance as a potentially poor prognostic factor, which warrants to be verified by further studies with larger cohorts.

Disclosure: All authors have declared no conflicts of interest.

FERTILITY PRESERVATION IN YOUNG EARLY BREAST CANCER: STRATEGIES AND PATIENT PREFERENCES

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Background: In Italy, approximately 1800 women younger than 39 years of age are diagnosed with breast cancer (BC) every year. Chemotherapy (CT)-induced loss of fertility is a major concern for these patients. Different strategies are available to attempt to preserve ovarian function and they should be considered as early as possible during treatment planning. We evaluated feasibility and patient preferences of two different strategies: oocyte cryopreservation (OC) and temporary ovarian suppression with the administration of LHRH analogue (LHRHa) during CT.

Materials and methods: From March 2010 to April 2012 28 BC patients younger than 41 years (median age: 38 [range 33-41]) candidates for CT, referred to our institution. They were offered the possibility to reduce the gonadotoxic effects of such treatments by two different strategies. The oncologist proposed both the administration of LHRHa before and during CT, and a reproductive counselling performed by the gynecologist, where OC was discussed.

Results: The majority of patients (25 [89.3%]) accepted to undergo a treatment with LHRHa, started at least 1 week before CT. Nineteen patients (67.9%) refused the reproductive counseling; the reasons for refusal were: previous pregnancies (13 patients [46.4%]) and no desire for children (6 patients [21.4%]). Out of 9 patients (32.1%) that accepted the reproductive counselling, only 3 (10.7%) accepted to undergo OC. The reasons for refusal were: fear of delaying cancer treatment (2 patients [7.1%]), fear of the ovarian stimulation required (1 patients [3.6]), not eligible for comorbidities (1 patients [3.6]), low successful rate of the technique (1 patients [3.6]) and unknown in 1 cases (3.6%). The 3 patients underwent a controlled ovarian stimulation with the use of daily injections of recombinant FSH: median length of stimulation was 9 days (range, 8 to 9 days); peak estradiol levels ranged from 280 to 521 pg/ml. An average of 13.3 ± 5.7 oocytes was retrieved, and 8.3 ± 3.1 oocytes cryopreserved per patient.

Conclusions: This analysis suggests that the majority of patients (89%) accept the administration of LHRHa during CT and approximately 11% of patients undergoes OC.

Disclosure: All authors have declared no conflicts of interest.

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Table: 1620 Survival results according to glutamine supplementation (GLT) and weight loss (WL)

<table>
<thead>
<tr>
<th></th>
<th>GLT+ and KK+</th>
<th>GLT- and KK+</th>
<th>GLT+ and KK+</th>
<th>GLT- and KK-</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS Months (%) (95%CI)</td>
<td>15.7 (11.8-19.6)</td>
<td>21.7 (12.1-31.3)</td>
<td>13.5 (9.8-17.2)</td>
<td>Not reached yet</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-year OS</td>
<td>65.1</td>
<td>93.3</td>
<td>60.6</td>
<td>98.0</td>
<td></td>
</tr>
<tr>
<td>2-year OS</td>
<td>12.1</td>
<td>44.9</td>
<td>3.8</td>
<td>58.3</td>
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</table>
Dicarbamin 100 mg/day on day 5 before chemotherapy administration. Treatment with Dicarbamin continued for all treatment period. 34 patients of control group (202 cycles of chemotherapy) were not given any prophylaxis of neutropenia. Neutropenia was evaluated with Common Toxicity Criteria, Version 3.0.

**Results:** Median age was 48 (29 – 55), Grade 4 neutropenia was reported in 6 (14.2%) patients treated with Dicarbamin and in 11 (32.3%) patients treated without Dicarbamin. The beneficial effect of Dicarbamin was also demonstrated by a quick recovery of granulocyte levels in controls. In 15 (35.7%) patients treated with Dicarbamin granulocytes levels were normal all period of chemotherapy. The dose intensity of chemotherapy was more in group with Dicarbamin prophylaxis. The toxicity of Dicarbamin was not observed.

**Conclusions:** Dicarbamin is an active agent for prophylaxis of neutropenia without specific toxicity.

**Disclosure:** All authors have declared no conflicts of interest.

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**Method:** We conducted a retrospective analysis of lung cancer pts treated with cytotoxic chemotherapy with ChT in a routine clinical practice at University Clinic Golnik (2009-2011), to recommendations. A routine use of ppG-CSF in clinical practice seems to be intermediate FN (iFN) risk ChT schemas and primary prophylaxis with granulocyte colony-stimulating factors (ppG-CSF) should be used in a majority of pts according to recommendations. A routine use of ppG-CSF in clinical practice seems to be variable. Therefore, we conducted a retrospective analysis of lung cancer pts treated with ChT in a routine clinical practice at University Clinic Golnik (2009-2011), estimating the rate and severity of neutropenia, the rate of FN and treatment strategies.

**Patients and methods:** A typical collective of 190 pts with advanced lung cancer (SCLC 29% and NSCLC 71%) treated with ChT alone were included. Most of pts received platinum based ChT (cisplatin 64.7%, carboplatin 20.0%), only 15.3% received other ChT schemas. For most of the pts it was first line ChT (86.8%). Majority of the pts received 6 cycles of ChT (46.3%), 53.7% of pts received 2-6 cycles. Only one patient received >12 ChT. Secondary prophylactic G-CSF was used in 14/190 (7.4%) of pts, 8 of them received G-CSF after the episode of FN, and 6 of them due to higher grade neutropenia without FN. All pts withFN received standard antibiotic treatment, while secondary prophylaxis with G-CSF has not been initiated in 8 pts due to the dose reduction in following cycles and death in one case. No patient suffered from recurrent FN episode.

**Conclusion:** Despite a negligible use of ppG-CSF in our collective of pts a very low rate of FN (8.4%) was observed. Due to retrospective nature of the analysis we certainly might have missed some cases of FN, less likely there were some major occupations due to missed FN. Based on this retrospective analysis we cannot neglect the use of ppG-CSF in lung cancer patients receiving IFN risk ChT, though, the actual proportion of patients needing ppG-CSF is questionable.

**Disclosure:** All authors have declared no conflicts of interest.

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**Background:** Febrile neutropenia (FN) is a serious complication of chemotherapy (ChT). Lung cancer patients are fragile with much comorbidity mostly receiving intermediate FN (iFN) risk ChT schemas and primary prophylaxis with granulocyte colony-stimulating factors (ppG-CSF) should be used in a majority of pts according to recommendations. A routine use of ppG-CSF in clinical practice seems to be variable. Therefore, we conducted a retrospective analysis of lung cancer pts treated with ChT in a routine clinical practice at University Clinic Golnik (2009-2011), estimating the rate and severity of neutropenia, the rate of FN and treatment strategies.

**Patients and methods:** A typical collective of 190 pts with advanced lung cancer (SCLC 29% and NSCLC 71%) treated with ChT alone were included. Most of pts received platinum based ChT (cisplatin 64.7%, carboplatin 20.0%), only 15.3% received other ChT schemas. For most of the pts it was first line ChT (86.8%). Majority of the pts received 6 cycles of ChT (46.3%), 53.7% of pts received 2-6 cycles. Only one patient received >12 ChT. Secondary prophylactic G-CSF was used in 14/190 (7.4%) of pts, 8 of them received G-CSF after the episode of FN, and 6 of them due to higher grade neutropenia without FN. All pts withFN received standard antibiotic treatment, while secondary prophylaxis with G-CSF has not been initiated in 8 pts due to the dose reduction in following cycles and death in one case. No patient suffered from recurrent FN episode.

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**Disclosure:** All authors have declared no conflicts of interest.

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**Background:** Nivestim™ is a European Union (EU)-licensed biosimilar filgrastim used in the treatment of chemotherapy-induced neutropenia and febrile neutropenia. Nivestim™ has similar pharmacokinetic and pharmacodynamic properties to its reference compound Neupogen®, and has demonstrated equivalent safety and efficacy (VErträglichkeit von NIvestim™ in clinical trials. However, the safety of biosimilars in general is closely scrutinised.

**Method:** Nivestim™ was treated with cytotoxic chemotherapy in real-world clinical-practice. The use of chlorhexidine as topical anti-septic may help prevent complications due to missed FN. Based on this retrospective analysis we cannot neglect the use of ppG-CSF in lung cancer patients receiving IFN risk ChT, though, the actual proportion of patients needing ppG-CSF is questionable.

**Disclosure:** All authors have declared no conflicts of interest.

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**Background:** Chlorhexidine can prevent surgical wound infection and BSI related to central venous catheters, but its effects on preventing BSI associated with Port-A use in cancer patients remain obscure.

**Methods:** Solid cancer patients who were implanted with a Port-A since December 2010 at our department for systemic anti-cancer therapies were prospectively followed for the occurrence of Port-A-associated BSI (PABSI), defined as BSI without other identifiable infection focus. All patients used chlorhexidine for Port-A topical care. The time to first PABSI in this cohort was compared with a previous cohort for whom iodine was used as topical anti-septic. Risk factors of PABSI were analyzed by Cox proportional hazards model.

**Results:** The baseline characteristics of the two cohorts were similar (table). The PABSI incidence was 0.740 and 1.051 per 1000 catheter-day for the chlorhexidine and iodine cohorts, respectively. The use of chlorhexidine can significantly delay the time to first Gram-positive cocci (GPC) PABSI (hazard ratio (HR) 0.41, 95% CI 0.20-0.84, p = 0.015). Other Independent predictors of increased GPC PABSI incidence included previous chemotherapy (HR = 13.65, 95% CI = 4.12-45.26), total parental nutrition (HR = 5.17, 95% CI = 2.51-10.63), chronic steroid use (HR = 7.02, 95% CI = 2.68-18.90), and postoperative antibiotics (HR = 2.06, 95% CI = 1.02-4.14). Chlorhexidine had no significant effects on preventing Gram-negative bacilli or fungal PABSI.

**Conclusion:** The use of chlorhexidine as topical anti-septic may help prevent GPC-related PABSI in cancer patients, (supported by grants NTUH 100-S1805).

**Disclosure:** All authors have declared no conflicts of interest.
Results:

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prespecified algorithm, which defined a patient as anemic based on 1) hemoglobin
primary endpoint was the point prevalence of anemia as determined using a
treatment. Data for all centers/consenting patients were included in the analyses. The
Methods:
This was a cross-sectional, observational survey. Centers had to prespecify
tumors being treated with chemotherapy (±radiotherapy) in a clinical practice setting.
Purpose:
The purpose of this study was to describe the prevalence of anaemia in treatment-naïve patients with solid tumours, the incidence of anaemia after four months of cancer treatment and anaemia management.

Methods: Multicenter, prospective and observational study that included newly diagnosed cancer patients. Data on anaemia parameters and its management were collected at baseline and after four months of cancer treatment. The primary outcome was the proportion of patients with anaemia defined as a haemoglobin (Hb) concentration <12 g/dL. Moreover, we studied the prevalence and incidence of iron-deficiency (ID) defined by a transferrin saturation <16%.

Results: The study included 295 patients (153 females), with a mean (±SD) age of 61.0 (±12.5) years and an ECOG performance status of 0-1 in 90.3% of the patients. The prevalence of anaemia at cancer diagnosis was 38.6% (49.4% for gastrointestinal [GI], 35.7% for lung and 27.3% for breast cancer patients). The severity of anaemia at baseline was moderate in 20.2% of patients. Prevalence of ID was 48.5% among those patients with available data and 51.9% in anaemic patients. A total of 106 patients (60.2%) without anaemia at baseline, developed anaemia over the four months of cancer treatment (39.5% for GI, 53.9% for lung and 75.3% for breast cancer patients). Baseline anaemia was treated only in 32.5% patients. At the four-month visit, 47.4% of anaemic patients at baseline and 67% of patients with new-onset anaemia had not received anaemia treatment.

Conclusions: The prevalence of anaemia and iron deficiency in treatment-naïve cancer patients is very high. While the prevalence of anaemia was higher among GI cancer patients at baseline, the incidence of anaemia during chemotherapy treatment was higher in breast cancer patients. Despite international recommendations, our study indicates an undertreatment of anaemia in cancer patients.

Disclosure: All authors have declared no conflicts of interest.

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Background: Anemia is a frequent complication in cancer patients. This
haematological abnormality may be related to cancer itself and/or induced by chemotherapy. The objective of the present study was to describe the prevalence of anaemia in treatment-naïve patients with solid tumours, the incidence of anaemia after four months of cancer treatment and anaemia management.

Methods: Multicenter, prospective and observational study that included newly diagnosed cancer patients. Data on anaemia parameters and its management were collected at baseline and after four months of cancer treatment. The primary outcome was the proportion of patients with anaemia defined as a haemoglobin (Hb) concentration <12 g/dL. Moreover, we studied the prevalence and incidence of iron-deficiency (ID) defined by a transferrin saturation <16%.

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Conclusions: The prevalence of anaemia and iron deficiency in treatment-naïve cancer patients is very high. While the prevalence of anaemia was higher among GI cancer patients at baseline, the incidence of anaemia during chemotherapy treatment was higher in breast cancer patients. Despite international recommendations, our study indicates an undertreatment of anaemia in cancer patients.

Disclosure: All authors have declared no conflicts of interest.

ANEMIA POINT PREVALENCE IN PATIENTS RECEIVING CHEMOTHERAPY IN 56 CENTERS IN ITALY AND AUSTRIA
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Purpose: To evaluate the point prevalence of anaemia in patients with non-mycobacterial tumors being treated with chemotherapy (single-agent therapy) in a clinical practice setting. Methods: This was a cross-sectional, observational survey. Centers had to prespecify a single day, during a 4-month enrollment window, to report specific data collected as part of normal clinical practice for patients attending in relation to chemotherapy treatment. Data for all centers/consenting patients were included in the analyses. The primary endpoint was the point prevalence of anaemia as determined using a prespecified algorithm, which defined a patient as anaemic based on 1) hemoglobin (Hb) ≤10 g/dL on/within 3 days prior to visit, 2) ongoing anaemia treatment at visit, or 3) physician diagnosis of anaemia together with ≥1 haematological symptom at visit. Results: For site visit, patient demographics, tumor type, systemic therapy, Hb levels, and consequences of anaemia, were secondary endpoints. Patients provided informed consent where required by local regulations.

Results: Between 18/11/2010-18/3/2011, data for 1412 patients were collected (Italy n = 656 [46.6%]; Austria n = 252 [20.2%]). Of these, 42% were men, median age 65 years and most (80%) had solid tumors (colorectal: 18%; breast: 18%; lung: 14%; prostate: 3%; other solid tumors: 28%). Overall, 57% of patients had received ≥3 chemotherapy cycles. The point prevalence of anaemia was 32% (95% CI: 29.4%, 34.2%); 14% of patients were deemed anaemic based on Hb levels ≤10 g/dL, 9% based on evidence of anaemia treatment and 8% based on physician assessed prevalence of anaemia with Hb ≤10 g/dL symptom. Overall, 82% of patients had Hb data; the median (SD) Hb level was 117 (1.7) g/dL. 32% of patients had anaemia symptoms, the most common were fatigue (28%), diarrhea (20%) and dizziness (8%). Few patients (4%) had had their current chemotherapy cycle delayed due to anaemia. On visit day or ≥28 days prior, 6% of patients had evidence of whole blood or red blood cell transfusion, 13% had evidence of erythropoiesis-stimulating agent use and 6% had evidence of iron use.

Conclusions: In this survey of one-third of patients with non-mycobacterial tumors undergoing chemotherapy were found to be anaemic on the prespecified study day.

Disclosure: L. Belton: Contract worker for Amgen Ltd, B. Pujol: Employed by Amgen EuropeAll other authors have declared no conflicts of interest.

ANEMIA IN LUNG CANCER AND MESOTHELIOMA PATIENTS TREATED WITH CHEMOTHERAPY IN A ROUTINE CLINICAL PRACTICE – AN INSTITUTIONAL EXPERIENCE
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Background: Anemia is common in patients with lung cancer. The aim of our analysis was to establish the rate and severity of anemia in a collective of advanced lung cancer and mesothelioma patients, treated with chemotherapy in a routine clinical practice. In addition, the impact of anemia and its treatment strategies on patient outcome have been evaluated.

Patients and methods: 146 patients treated for advanced lung cancer and/or mesothelioma at University Clinic Gočnik in 2009 who received at least 2 cycles of ChT have been included. Majority of patients received platinum based CRT (120/146, 89%). The decision for transfusion administration and ESA treatment was left to the attending physician. The registered products of epoetin alfa in the standard recommended weekly dosages were used. The response to treatment was evaluated according to the RECIST criteria. Progression free survival was estimated by Kaplan-Meier curves.
HEMODYALYSIS IN CERVICAL CANCER PATIENTS: CLINICAL ASPECTS AND OUTCOME IN 95 PATIENTS FROM THE BRAZILIAN NATIONAL CANCER INSTITUTE (INCA)

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Cervical Cancer is a serious issue in development and underdeveloped countries. It is the second most prevalent (18000 new cases expected for 2012) and the fourth deadliest cancer among women in Brazil. Most patients (pts) (68,3%) are diagnosed with advanced disease- increasing their risk of renal failure due to local progression and cisplatin-based chemotherapy. Benefits of hemodialysis in these patients are well described, however care in this population is often delayed or neglected. The aim of this study was to observe the clinical aspects, complications and outcomes of hemodialysis in cervical cancer patients.

Results: 95 pts were treated with HD at the INCA between 2007 and 2012, with a follow-up until March 2012. The mean age of the population was 56.30 years (45-76). Most patients (68,3%) were between 45-54 years of age. The main reasons for starting HD were uncontrolled renal failure and progression of the main disease. 45 pts (47,4%) received HD concomitantly to chemotherapy.

Conclusion: In our experience, HD was a safe treatment modality to be used in cervical cancer patients. Small sample size, a single center study and the difficulty to follow patients on HD long term are the main limitations of our study. We suggest to perform studies with larger sample size and longer follow-up to better define the role of HD in these patients.

Disclosure: All authors have declared no conflicts of interest.
INTENSIVE CARE AS A KEY PLAYER IN THE CHANGING PARADIGM OF MODERN CANCER CARE: A SINGLE INSTITUTION EXPERIENCE

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Background: Many metastatic cancers are now treated similar to other chronic diseases. Expanding treatment options, increasing age, co-morbid illness; and improving cancer-specific survival means that decisions regarding the timeliness & appropriateness of transfer to the Intensive Care Unit (ICU) are complex. We sought to examine the clinical, demographic & outcome characteristics of oncology haematology patients (pts) transferred to ICU at a large academic teaching hospital.

Methods: Data was extracted from a prospectively maintained database for all pts with documented malignancy admitted to ICU between September 2009 & December 2011. Clinicopathological variables examined included: cancer type; tumour stage; time from diagnosis; age; co-morbidities; and treatment history. The Sequential Organ Failure Assessment (SOFA), an ICU-specific scoring system, was reviewed for each patient (pt). We report 30 day & 6-month mortality.

Results: A total of 52 of an eligible 83 pts have been analysed in detail to date. The common cancer types were well represented: breast (11.5%), colorectal (11.5%), lung (11.5%) & acute leukaemia (19.2%). Mean age at time of ICU admission was 60 years (range 29-82). The number of prior lines of chemotherapy (CT) was 5 (range 0-5). Approximately 50% of pts had metastatic disease at time of ICU admission. The most frequent reasons for admission were sepsis (n = 16, 31%) & respiratory distress (n = 15, 29%). Use of mechanical ventilation, vasopressors & renal dialysis was 51.9%, 61.5% & 21.1% respectively. Four pts (7.7%) received CT in the ICU setting. ICU-specific mortality was 28.8% (n = 15). Thirty-day and 6-month mortality rates were 38.5% & 61.5% respectively. Data on the remaining 31 pts is currently being analysed and will be available for presentation at the meeting.

Conclusions: A significant proportion of pts admitted to ICU had advanced disease & had received multiple lines of CT previously. The ICU-specific mortality rate was lower than expected at 28.8% and may reflect stringent selection criteria. Pts transferred tend to have had long periods of disease remission/stabilisation or had a new diagnosis of malignancy with unknown CT sensitivity status. Analysis of pt selection at ward level is on-going and will identify other factors influencing ICU transfer decisions.

Disclosure: All authors have declared no conflicts of interest.

COMBINATION OF SERUM PROCALCITONIN AND C-REACTIVE PROTEIN LEVEL AS A DIAGNOSTIC MARKER OF DISCRIMINATING INFECTION FROM NEOPLASTIC FEVER IN FEBRILE LUNG CANCER PATIENTS

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Background: Neoplasic fever in lung cancer is assessed on clinical course only, and is difficult to discriminate from infection.

Objective: To evaluate the diagnostic role of procalcitonin (PCT) and C-reactive protein (CRP) in discriminating neoplasic fever and infection.

Methods: We reviewed the medical records of 112 consecutive febrile episodes of 52 patients (59 males, mean age 67.1 y/o), who were diagnosed as lung cancer from November 2009 to April 2012 at our Saiseikai Central Hospital in Tokyo, Japan. Based on clinical, laboratory, and bacteriological results, patients were classified as having neoplasic fever (NF, n = 53), suspected or definite bacterial infection (BI, n = 59). Values of white blood cell count (WBC), PCT, and CRP were measured on day 1 of onset of fever. Microbiological specimen and radiological imaging study were also performed to diagnose infectious diseases or other febrile conditions.

Results: The most common infection was pneumonia (38.4%). Mean WBC (12000 vs. 14800) were not statistically significant. Mean values of PCT were significantly higher in patients with BI compared with NF (0.14 vs. 3.95 mg/ml, p < 0.05). Mean values of CRP were also significantly higher in patients with BI compared with NF (8.6 vs. 15.2 mg/dl, p < 0.05). Combination of CRP level at the threshold value of 10.2 mg/dl and PCT level at the threshold value of 0.32 mg/dl were the most sensitive from ROC curve for discriminating infection to neoplasic fever.

Conclusion: Combination of PCT and CRP on the day of onset of fever is useful in discriminating neoplasic fever from infection in febrile lung cancer patients.

Disclosure: All authors have declared no conflicts of interest.

INCIDENCE OF THROMBOEMBOLIC EVENTS IN PATIENTS TREATED WITH CISPATIN-BASED CHEMOTHERAPY

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Introduction: Cancer patients on chemotherapy have higher risk in developing thromboembolic events (TEE), with great impact on morbidity and mortality. The aim of this study is to determine the incidence of venous and arterial TEE in patients treated with cisplatin-based chemotherapy. We also investigated the prognostic value of patients baseline and treatment characteristics in predicting TEE occurrence.

Methods: We performed a retrospective analysis of all patients with cancer treated with cisplatin-based chemotherapy between January 1, 2011, and April 10, 2012, with at least 4 weeks of follow-up after their last cisplatin dose. A TEE was considered cisplatin-associated if it occurred between the time of the first dose of cisplatin and 4 weeks after the last dose.

Results: Among 141 patients, 27 (19.1%) experienced a TEE. The TEE observed was 14 (8%) DVT, 14 (8%) PE, 12 (8%) combined DVT and PE, 8 (5.7%) arterial thrombosis, and 1 (0.7%) combined DVT and arterial thrombosis. The majority of TEEs were considered cisplatin-associated if it occurred between the time of the first dose of cisplatin and 4 weeks after the last dose.

Disclosure: All authors have declared no conflicts of interest.
important to carry out randomized studies to conclude the need for prophylaxis of TEE in these patients.

Disclosure: All authors have declared no conflicts of interest.

1640 ARE THERE FACTORS THAT PREDICT ACUTE CARE ADMISSION IN CANCER PATIENTS AGE ≥65 YEARS RECEIVING CHEMOTHERAPY? A RETROSPECTIVE ANALYSIS
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Background: There is growing evidence that older patients derive the same benefits from chemotherapy as younger patients, but often at the cost of increased toxicity. A retrospective analysis was done of cancer patients ≥65 years who received chemotherapy, with the aim of identifying patient or treatment factors associated with subsequent hospital admission.

Methods: Medical records and an electronic prescribing system (EPS) were used to identify all cancer patients ≥65 years who received chemotherapy at Northern Health. For each patient, age, treatment dose at onset, ECOG, presence of metastases, cardiac comorbidities, chronic kidney disease stage, liver function tests and reason for admission were documented. Univariate and multivariate logistic regression analysis was used to assess the association between a factor and subsequent hospitalisation. An Odds Ratio greater than or less than 1, and a P value <0.05 were considered statistically significant.

Results: Between June 2009 and October 2010, 102 patients ≥65 years received chemotherapy on the EPS, which assigns full dose chemotherapy unless reduced by the clinician. 35 patients had a dose reduction at the outset. 49 patients were admitted following at least one cycle of chemotherapy; 33 (67%) for a treatment admission. Surprisingly, a lack of dose reduction did not appear to increase risk of admission, indicating that high-risk patients were being effectively identified and that the EPS was being implemented appropriately in this population of older adults.

Conclusion: This inclusion of 102 older patients no factors were found that accurately predicted subsequent acute care admission. Surprisingly, a lack of dose reduction did not appear to increase risk of admission, indicating that high-risk patients were being effectively identified and that the EPS was being implemented appropriately in this population of older adults.

Disclosure: All authors have declared no conflicts of interest.

1641 EFFECT OF ZOLEDRONIC ACID USED CONCURRENTLY WITH RADIATION THERAPY ON GROWTH OF EPiphySEAL PLAQUE
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Background: Radiotherapy (RT) has an important and efficient role in the treatment of majority of childhood cancers. However, shape deformities and shortness may result from the delivery of RT in children with incomplete skeletal growth. Fractionation studies and trials using amphotISE and melatonin as radioprotectant have demonstrated significant reduction in such RT-induced deformities. In this study, impact of zoledronic acid (ZA), a commonly used drug in oncological practice, on prevention of RT-induced epiphyseal injury was investigated.

Materials and methods: Six week old male Sprague-Dawley rats were enrolled to one of the four groups (n = 7 for each): Group 1 was assigned as control group; Group 2 received fractionated RT alone; Group 3 received 20 µg/kg ZA injection alone; and Group 4 received 20 µg/kg ZA injection prior to fractionated RT. Fractionated RT in the irradiated groups was delivered to distal femur and proximal tibia in the left legs of each rats to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. Vitamin D3 supplementation administered prior to fractionated radiotherapy (RT) in reducing RT induced epiphyseal injury is investigated.

Results: RT resulted in a mean percent overall limb growth loss of 56.2 ± 6.7 and a mean percent overall limb discrepancy of 12.7 ± 1.3. Administration of 50000 IU/kg i.m. vitamin D3 injection alone and Group 4 received 50000 IU/kg i.m. vitamin D3 injection prior to fractionated RT. Fractionated RT in the irradiated groups was delivered to distal femur and proximal tibia in the left legs of each rats to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. Vitamin D3 injection in Group 3 was performed on the day before the RT. Bone growth was calculated according to the lengths of femur, tibia and total leg measured on the radiographs taken at the time and 6 weeks after the delivery of RT.

Results: RT resulted in a mean percent overall limb growth loss of 56.2 ± 6.7 and a mean percent overall limb discrepancy of 12.7 ± 1.3. Administration of 20 µg/kg ZA before RT reduced the mean percent overall limb growth loss and the mean percent overall limb discrepancy to 35.4 ± 6.8 and 9.2 ± 1.8, respectively. These values were significantly different compared with the groups receiving irradiation alone (P = 0.001 for each).

Conclusion: These results demonstrate the potential for ZA administered before fractionated RT to significantly reduce the RT-induced epiphyseal injury, with no additional toxicity.

Disclosure: All authors have declared no conflicts of interest.

1642 ROLE OF VITAMIN D3 IN PREVENTION OF RADIOTHERAPY-INDUCED EPPHYSEAL INJURY
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Background: Vitamin D is a growth factor improving bone mineralization, and regulating osteoblastic activity and longitudinal bone growth. In this study, impact of vitamin D supplementation administered prior to fractionated radiotherapy (RT) in reducing RT induced epiphyseal injury is investigated.

Materials and methods: Six week old male Sprague-Dawley rats were enrolled to one of the four groups: Group 1 was assigned as control group (n = 7); Group 2 received fractionated RT alone; Group 3 received 50000 IU/kg i.m. vitamin D3 injection alone; and Group 4 received 50000 IU/kg i.m. vitamin D3 injection prior to fractionated RT. Fractionated RT in the irradiated groups was delivered to distal femur and proximal tibia in the left legs of each rats to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. Vitamin D3 injection in Group 3 was performed on the day before the RT. Bone growth was calculated according to the lengths of femur, tibia and total leg measured on the radiographs taken at the time and 6 weeks after the delivery of RT.

Results: RT resulted in a mean percent overall limb growth loss of 56.2 ± 6.7 and a mean percent overall limb discrepancy of 12.7 ± 1.3. Administration of 50000 IU/kg i.m. vitamin D3 injection alone and Group 4 received 50000 IU/kg i.m. vitamin D3 injection prior to fractionated RT. Fractionated RT in the irradiated groups was delivered to distal femur and proximal tibia in the left legs of each rats to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. Vitamin D3 injection in Group 3 was performed on the day before the RT. Bone growth was calculated according to the lengths of femur, tibia and total leg measured on the radiographs taken at the time and 6 weeks after the delivery of RT.

Results: RT resulted in a mean percent overall limb growth loss of 56.2 ± 6.7 and a mean percent overall limb discrepancy of 12.7 ± 1.3. Administration of 50000 IU/kg i.m. vitamin D3 injection alone and Group 4 received 50000 IU/kg i.m. vitamin D3 injection prior to fractionated RT. Fractionated RT in the irradiated groups was delivered to distal femur and proximal tibia in the left legs of each rats to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. Vitamin D3 injection in Group 3 was performed on the day before the RT. Bone growth was calculated according to the lengths of femur, tibia and total leg measured on the radiographs taken at the time and 6 weeks after the delivery of RT.

Conclusions: These results demonstrate the potential for ZA administered before fractionated RT to significantly reduce the RT-induced epiphyseal injury.

Disclosure: All authors have declared no conflicts of interest.

1643 ANALYSIS OF THE ASSOCIATION BETWEEN THE NUMBER OF REGIMENS AND THE FREQUENCY OF SIDE EFFECTS IN OUTPATIENTS RECEIVING CANCER CHEMOTHERAPY. CAN PROGRESSION-FREE SURVIVAL BE THE PRIMARY END POINT?
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Background: In general, chemotherapy with more than one regimen is carried out sequentially. An increased number of regimens can lead to cumulative, potentially severe side effects. Recently, whether the primary endpoint of phase III clinical trials should be progression-free survival has been actively discussed. With the extension of progression-free survival, late side effects may develop. We investigated whether an increased number of chemotherapeutic regimens is associated with severe side effects.

Methods: We retrospectively investigated the incidence of major grade 2 or higher nonhematologic and hematologic toxicities in outpatients who received 1st line, 2nd line, and 3rd line or subsequent cancer chemotherapy between July 2009 and March 2011 at Nagoya Daichi Red Cross Hospital in Japan.

Results: A total of 924 patients (453 men and 471 women) were studied. The median age was 62 years (range: 2 to 89). The major diagnoses were lung cancer (20.3%), breast cancer (16.7%), lymphoma (12.3%), and colorectal cancer (11.6%). The following data are presented in the order of 1st line, 2nd line, and 3rd line or subsequent therapy. Nonhematologic toxicities were constipation (29, 21, 27%), fatigue (20, 14, 23%), anorexia (14, 13, 18%), neuropathy (13, 16, 18%), nausea (12, 9, 14%), pain (12, 11, 16%), vomiting (6, 11, 16%), diarrhea (5, 6, 11%), dysgeusia (5, 3, 6%), oral mucositis (3, 2, 8%), and nail trouble (2, 3, 6%). Hematologic toxicities were neutropenia (29, 31, 27%), anemia (29, 25, 35%), and thrombocytopenia (6, 0, 0%). Nonhematologic toxicity showed a significant trend to increase in patients who received 3rd line or subsequent therapy (p < 0.01).

Conclusion: The extension of progression-free survival can delay initiation of treatment and lead to the late occurrence of side effects. We consider...
progression-free survival very useful from the viewpoint of side effects, even in phase III clinical trials.

Disclosure: All authors have declared no conflicts of interest.

PROSPECTIVE EVALUATION OF THE EFFECT OF A MANUAL FOR DIABETIC PATIENTS WHO RECEIVE CANCER CHEMOTHERAPY

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Background: How to safely administer cancer chemotherapy to patients with diabetes mellitus is an important issue. Our institution is a general core hospital in Japan. In 2010, we surveyed the current status of diabetic patients given cancer chemotherapy. Adequate medical examinations were not performed. In 2011, we designed a manual for diabetic patients who receive cancer chemotherapy. We now report an improvement in medical examinations of diabetic patients who receive cancer chemotherapy since introducing our manual.

Methods: We decided that adequate medical examinations should include the following: adequate measurement of blood sugar levels; evaluation of the patient by a diabetologist; making standards for decreasing the dose of steroids given before cancer chemotherapy; and making standards for nutritional guidance. We compared the present status (as of March 2012) with that before the introducing our manual for diabetic patients receiving cancer chemotherapy.

Results: The proportion of diabetic patients increased from 12% to 19%. The rate of measuring blood sugar levels at the start of new regimens of chemotherapy increased from 69% to 72%. The rate of adequate continuous monitoring of blood sugar levels increased from 48% to 81%. The rate of evaluation by a diabetologist increased from 36% to 50%. The rate of decreased premedication with steroids increased from 55% to 66%. The rate of providing nutritional guidance was unchanged (23% to 24%).

Conclusions: The rates of adequate continuous monitoring of blood sugar levels, decreasing premedication with steroids, and evaluation by a diabetologist improved. The increase in the proportion of diabetic patients was attributed to adequate blood sugar examinations. However, the low rate of providing of nutritional guidance remains an unsolved problem.

Disclosure: All authors have declared no conflicts of interest.