supportive care

1544O COMPARISON OF NUTRITIONAL ASSESSMENT WITH A NEW DEFINITION OF CACHEXIA IN DETERMINING OUTCOMES OF ADVANCED CANCER PATIENTS

S. Clarke1, C. Tari2, J. Reid3, V. Phan4, J.K. Peat5 and P. Beale6
1Medical Oncology Department, Royal North Shore Hospital, Sydney, NSW, AUSTRALIA, 2Nurtition and Dietetics Department, Concord Hospital, Sydney, NSW, AUSTRALIA, 3Prince of Wales Hospital, Sydney, NSW, AUSTRALIA, 4Medical Oncology Department and Sydney Cancer Center, Concord Hospital, Sydney, NSW, AUSTRALIA, 5Consultant Biostatistician, Concord Hospital, Sydney, NSW, AUSTRALIA

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></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>67% (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)</td>
<td>11.4 (5.5 – 17.3) 2.24</td>
<td>8.4 (4.06 – 12.69) 8.07</td>
</tr>
<tr>
<td>Log rank test (Mantel-Cox)</td>
<td></td>
<td></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.

1545O FATIGUE (F) AND ANEMIA SCORES FOR OVERALL SURVIVAL (OS) PROGNOSIS

Y. Gomadha1, R.T. Elaidi1, F. Scottie1, V. Yano2, N. Pécuchet2, J. Gachet1, J. Medioni3, E. Fabre3 and S. Oudard3
1Oncology, Hospital G.Pompidou, Paris, FRANCE, 2Medical Oncology, Georges Pompidou Hospital, PARIS Cedex 15, FRANCE, 3Medical Oncology, Georges Pompidou Hospital and René Descartes University, Paris, FRANCE

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 (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 F grades from start to end CT and for anemia: mean grade per cycle. OS was calculated from CT initiation to death or censored 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 [0-200.7]. Median linear anemia score = 0.78 [0-1.5], non-linear = 0.78. 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 delayed (ANOVA, p = 0.0001). Linear F score (LFS) was good predictor of OS (LR: 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, 1.6] and HR = 1.66 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.

1547PD G-CSF AS SECONDARY PROPHYLAXIS OF CHEMOTHERAPY-INDUCED NEUTROPENIA IN PATIENTS WITH SOLID TUMORS: RESULTS OF A PROSPECTIVE, OBSERVATIONAL STUDY

G. Freyer1, N. Jouvenin2, G. Yazbek3, C.B. Villanueva4, A. Hussain5, A. Bethune5, M. Rotarski6, H. Simon7, V. Boulanger8 and M. Hummerlsberger9
1Medical Oncology, Centre Hospitalier Lyon Sud, Pierre- Bénite, FRANCE, 2Medical Oncology, Institut Jean Godinot, Reims, FRANCE, 3Medical Oncology, Centre Hospitalier Universitaire, Besançon, FRANCE, 4Medical Oncology, Centre Hospitalier Quimper, Quimper, FRANCE, 5Medical Oncology, Centre Hospitalier de Carcassonne, Carcassonne, FRANCE, 6Medical Oncology, Centre de Radiothérapie et Oncologie Médicale, Béziers, FRANCE

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.

Patients and methods: Patients ≥ 18 years were included if they experienced a NE during any previous cycle (reference cycle A), with no prior G-CSF administration. Neutropenic events were defined as any neutropenia grade 1-4, febrile or not, that impacts on the subsequent cycle (cycle delay and/or dose reduction and/or use of G-CSF). Patients were followed for a total of 5 cycles. Risk factors of febrile neutropenia (FN), and prophylactic strategies (with or without G-CSF) were included in univariate and multivariate analyses to assess their predictive value on 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 (85%) neutropenia (any grade w/o fever). 44.5% had cycle delay, 22.3% dose reduction and 466 (85%) received prophylactic G-CSF (pegfilgrastim 59.7%, lenograstim 27.3%, filgrastim 10.3% and bosuliminar 2.1%). Incidence of NE in subsequent cycles and prophylactic strategies are shown in the table below. In multivariate analysis, G-CSF use (HR:0.32 [0.24; 0.43] < p < 0.001) was an independent predictor of

© European Society for Medical Oncology 2012. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com

Downloaded from https://academic.oup.com/annonc/article-abstract/23/suppl_9/ix499/218718 on 31 May 2018
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>Cycle A</th>
<th>Cycle B</th>
<th>Cycle C</th>
<th>CycleD</th>
<th>Cycle E</th>
</tr>
</thead>
<tbody>
<tr>
<td>(no G-CSF)</td>
<td>N = 548</td>
<td>N = 548</td>
<td>N = 548</td>
<td>N = 442</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>88 (16.1%)</td>
<td>3 (0.5%)</td>
<td>4 (0.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenic fever</td>
<td>42 (7.7%)</td>
<td>2 (0.4%)</td>
<td>4 (0.7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Neutropenia w/o fever</td>
<td>418 (76.3%)</td>
<td>111 (20.3%)</td>
<td>93 (17.3%)</td>
<td>50 (11.3%)</td>
</tr>
<tr>
<td>Cycle delay</td>
<td>-</td>
<td>244 (44.5%)</td>
<td>44 (8.0%)</td>
<td>23 (5.2%)</td>
</tr>
<tr>
<td>Dose reduction</td>
<td>-</td>
<td>122 (22.3%)</td>
<td>27 (4.9%)</td>
<td>17 (3.8%)</td>
</tr>
<tr>
<td>Use of Prophylactic G-CSF</td>
<td>-</td>
<td>466 (85.0%)</td>
<td>413 (75.4%)</td>
<td>332 (75.0%)</td>
</tr>
</tbody>
</table>

Disclosure: G. Freyer: Consultant for Amgen. All other authors have declared no conflicts of interest.

1549PD ABSOLUTE NEUTROPHIL COUNTS IN A STUDY OF LIPEGFILGRASTIM COMPARED WITH PEGFILGRASTIM IN PATIENTS WITH BREAST CANCER WHO ARE RECEIVING CHEMOTHERAPY

O.A. Gladkoy1, I.M. Bondarenko2, R. Elsaesser3, A. Buchner4 and P. Bias4

1Chemotherapy, Regional Oncology Center, Chebaksyn, RUSSIAN FEDERATION, 2Oncology, Dnipropetrovsk State Medical Academy, Dnipropetrovsk, UKRAINE, 3Biostatistics, Teva Ratiopharm, Ulm, GERMANY, 4Clinical Research, Teva Ratiopharm, Ulm, GERMANY

Background: Cancer chemotherapy frequently causes neutropenia, leading to an increased risk of infections and delays in subsequent chemotherapy treatments. In a randomized, double-blind, phase 3, active-controlled, noninferiority trial, the efficacy and safety of lipegfilgrastim, a glycosylated and pegylated recombinant granulocyte colony stimulating factor (G-CSF), was compared with pegfilgrastim, a pegylated recombinant G-CSF. Here we report the results of the absolute neutrophil counts (ANC) from this study.

Methods: Patients with high-risk stage II, III, or IV breast cancer and an absolute neutrophil count ≥1.5x10^9 cells/l were randomly assigned to lipegfilgrastim 6 mg (n = 101) or pegfilgrastim 6 mg (n = 101). Study medication was injected subcutaneously on day 2 of the chemotherapy cycle (4 cycles maximum). The primary efficacy endpoint, the duration of severe neutropenia, was reported previously. Secondary endpoints included ANC nadir and time to ANC recovery and were analyzed using a Poisson regression. The intent-to-treat (ITT) analysis population included all randomized patients.

Results: ANC nadir and time to ANC recovery for cycle 1 (ITT population) are summarized in the table.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Lipegfilgrastim (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 (10^9/L)</td>
<td>1.2 (1.3)</td>
<td>1.0 (1.2)</td>
<td>0.146 (0.169 to 0.461)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.6 (0.0 to 5.5)</td>
<td>0.4 (0.0 to 5.2)</td>
<td>p = 0.3610</td>
</tr>
<tr>
<td>Time to ANC recovery (days)</td>
<td>5.8 (3.3)</td>
<td>7.4 (3.6)</td>
<td>-1.570 (-2.547 to -0.592)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.0 (0.0 to 12.0)</td>
<td>8.0 (0.0 to 21.0)</td>
<td>p = 0.0018</td>
</tr>
</tbody>
</table>

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


1549PD TREATING DIABETIC PATIENTS WITH CHEMOTHERAPY: SINGLE CENTRE EXPERIENCE OF TOXICITY AND OUTCOMES

J.F. Seligmann1, A. Young2, G. Heath3, D. Cains3, A. Anthony2, G. Hal2, M. Seymour2 and D. Swinson2

1Medical Oncology, St. James Institute of Oncology, Leeds Teaching Hospitals NHS Trust, Leeds, UNITED KINGDOM, 2Medical Oncology, The Leeds Teaching Hospital NHS Trust St. James University Hospital, Leeds, UNITED KINGDOM, 3Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UNITED KINGDOM

Background: Diabetes is a common comorbidity in cancer patients, and is associated with poorer survival in colorectal cancer (CRC). However, there is little data to describe the experience of diabetic patients during chemotherapy. We have compared a diabetic population of cancer patients with matched controls receiving chemotherapy in a single centre.

Methods: We performed a retrospective case note analysis using an electronic patient record database (Patient Pathway Manager) and chemotherapy prescription software (ChemoCare) between 2001 and 2011. Diabetic patients starting first line chemotherapy for advanced CRC and adjuvant therapy were identified. For each case a non-diabetic control was selected, matched for age (<65 vs ≥65), disease site (GC vs CRC) and chemotherapy type (single agent vs combination). Data for dose adjustments, acute admissions, stoppages, subsequent therapy and survival were compared, corrected for performance status (PS), comorbidity and primary site.

Results: 146 diabetic patients and 146 matched controls were included. Median age was 67 years; 95% of diabetic patients had type 2 diabetes, 18.5% were receiving insulin. Performance status was similar (diabetic 66% PS0-1, 29% PS2-3; non-diabetic 64% PS0-1, 34% PS2-3). More diabetic patients had comorbidity (60% vs 45%). A non-significant difference was observed in dose reductions (upfront 31.5% vs 23.9% p = 0.15; on-treatment 23.3 vs 13.7% p = 0.35). Only 5% of diabetic patients had upfront steroid reduction. Diabetes was independently associated with an increased risk of acute admission (OR = 3.32, 95% CI 1.8-5.8, p < 0.0001), early stopping of chemotherapy (OR = 2.17, 95% CI 1.25-3.85, p = 0.006) and reduced use of 2nd line treatment (OR = 0.56, 95% CI 0.34-0.95, p = 0.03). The most common causes of admission in the diabetic group were infection (41%) and poor glycaemic control (17%). Poor PS was also an independent risk factor for the above factors in multivariable analysis. Primary site, PS and age, but not diabetes, were independently prognostic for survival.

Conclusions: Diabetic patients experienced more acute complications on chemotherapy possibly limiting further treatment options. A prospective study would clarify the contributing factors and inform planning and monitoring of diabetic patients with cancer.

Disclosure: All authors have declared no conflicts of interest.
Role of Temporary Ovarian Suppression Obtained with GnRH Analog in Reducing Premature Ovarian Failure (POF) Induced by Chemotherapy in Premenopausal Breast Cancer Patients: A Meta-Analysis of Randomized Studies

L. Del Mastro\textsuperscript{1}, A. Levaggi\textsuperscript{2}, F. Poggio\textsuperscript{3}, S. Giraud\textsuperscript{4}, G. Bighin\textsuperscript{5}, A. D’Alonzo\textsuperscript{6}, M. Lambertini\textsuperscript{7}, P. Pronzato\textsuperscript{2} and P. Bruzzi\textsuperscript{8}\\\textsuperscript{1}SìSviluppo Terapie Innovative, IROCS AOI San Martino - IST-Istituto Nazionale per la Ricerca sul Cancro, Genova, ITALY, \textsuperscript{2}Oncologia Medica A, IROCS AOI San Martino - IST-Istituto Nazionale per la Ricerca sul Cancro, Genova, ITALY, \textsuperscript{3}Clinical Epidemiology, IST-San Martino, Genoa, ITALY

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

Methods: Studies were retrieved by searching the PubMed database and the proceedings of major conferences. Odds ratios (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 + GnRHa: 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 (G-CSF) in Chinese Breast Cancer Patients Receiving Docetaxel, Epirubicin, and Cyclophosphamide

M. Hei\textsuperscript{1}, S. Huang\textsuperscript{1}, L. Yu\textsuperscript{1}, G. Shi\textsuperscript{1}, J. Deng\textsuperscript{1}, X. Zhang\textsuperscript{1}, X. Wang\textsuperscript{1}, J. Chen\textsuperscript{1}, X. Ning\textsuperscript{1} and P. Shen\textsuperscript{1}\\\textsuperscript{1}Medical Oncology, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, CHINA, \textsuperscript{2}Department of Medical Oncology, 1st Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, CHINA

Background: Docetaxel, Epirubicin, and 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 prophylactics 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 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 = 0.001) and anemia, thrombosis, anorexia, myalgia and dysgeusia. Patient’s QOL decreased during chemotherapy, more in TEC without PPG than TEC 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.
Biosimilar Filgrastim Initiation in Patients Enrolled in the Monitor G-CSF Observational Study Relative to EORTC Guidelines


1Institut Multidisciplinaire d’OncoLOGie, Clinique de GénoLOGie, GenoLOG, SWITzerLAND. 2Medical Oncology, Hospital Clínic y Provincial de Barcelona, Barcelona, Spain. 31st Department of Medicine, Wilhelminenhospital, Wien, aUSTRIA. 4Head of The Department for Oncology, Haematology and Bone Marrow Transplantation, UKL II. Medizinische Klinik und Poliklinik, Klinikum der Universität München, Munich, Germany. 5Section of Haematology, Università degli Studi di Torino, Torino, Italy. 6Sandoz International GmbH, Sandoz Biopharmaceuticals, Holzkirchen, GERMANY. 7Matri 45, Tucson, AZ, UNITED STATES OF AMERICA

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). This analysis describes treatment initiation with biosimilar filgrastim in the MONITOR G-CSF observational 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 predominately 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 ≥21, 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 2 presents other risk factors on CT regimens with 10-20% FN risk.

Table 1. All patients

<table>
<thead>
<tr>
<th>Prophylaxis (%)</th>
<th>Initiation (%)</th>
<th>Duration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Haematology</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>CT toxicity:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;20%</td>
<td>76</td>
<td>24</td>
</tr>
<tr>
<td>10-20%</td>
<td>74</td>
<td>26</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>56</td>
<td>44</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>Primary</td>
<td>Secondary</td>
</tr>
<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 GCSE</td>
<td>73</td>
</tr>
<tr>
<td>Poor performance (ECOG &gt;2)</td>
<td>83</td>
</tr>
<tr>
<td>Female</td>
<td>76</td>
</tr>
<tr>
<td>HB &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 maybe indicative of changing practice trends to optimise patient well-being and minimise FN risk needs to be further 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/leukemia (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 analyzed.

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.


EFFECTIVENESS OF INFLUENZA VACCINE (FLUvAX) IN PATIENTS UNDERGOING CHEMOTHERAPY

R. Kumar1, D. Gordan2, C.S. Karapetis3, B. Koczwara4, G. Kichnadasse1, D. Dua1, H. Táňchar1, J. Kain1, Y. Honda-Kubok3 and S. Sukumaran1

1Department of Medical Oncology, Finders Medical Centre, Adelaide, AUSTRALIA, 2Department of Medicine, Finders University, Adelaide, AUSTRALIA, 3Department of Microbiology and Infectious Diseases, Vachez Pte Ltd, Adelaide, AUSTRALIA

Background: Influenza virus related illness is a common seasonal respiratory infection. Cancer patients undergoing chemotherapy are advised to be immunised against influenza, however, the efficacy of vaccination has not been well studied. This study aimed to demonstrate the efficacy of the 2011/2012 trivalent FluVax in patients undergoing chemotherapy in comparison to healthy historical controls.

Method: Twenty-six patients with solid tumours were given one dose of 2011/2012 trivalent FluVax containing A/California/7/2009(H1N1), A/Perth/16/2009(H3N2), B/Brisbane/60/2008 strains (WHO), at least 3 days before chemotherapy. Efficacy was determined by measurement of haemagglutination inhibition (HA) titres against component viruses in serum collected at baseline, 3, 6 and 24 weeks to assess baseline and following immune protection (SP) (HA ≥ 40) and seroconversion (SC) (2-fold increase titre).

Results: 78 events were evaluable. The mean age was 57.6 years, with 44% of patients being male. The majority of patients had colorectal cancer (29.6%), followed by breast cancer (25.9%), non-small cell lung cancer (14.8%), ovarian cancer (7.4%). Nearly half the patients had stage IV disease (48%).32.1% had baseline SP, with an additional 19.2% achieving SP during the study. Only 23.1% had SC. The majority of those with baseline SP maintained immunity during treatment. Prior FluVax was independent of achieving SP during treatment (p = 0.93). Patients ≥65 years were more likely to achieve SP (p = 0.016), as were men (p = 0.022). Tumour type was not predictive of SP. Patients having palliative treatments were just as likely to achieve SP compared those having curative treatments (p = 0.38).

The likelihood of achieving SP was not affected by type of cytotoxic treatment, however those having monoclonal antibodies were more likely to achieve SP. The likelihood of achieving SP was not affected by type of cytotoxic treatment, however those having monoclonal antibodies were more likely to achieve SP.

Conclusion: FluVax efficacy is suboptimal in patients with cancer undergoing chemotherapy, compared with the expected SP rate of 85-100% in healthy individuals. New approaches to improving vaccine efficacy are needed.

Disclosure: All authors have declared no conflicts of interest.

EPIGENOMICS, RESISTANCE PROFILE AND ORIGIN OF BACTERIA IN NON-NEUTROPENIC PATIENTS WITH SOLID TUMOR

M. Merad, E. Chachaty, B. Gachot, A.T. Albay, M. Dipla and A. Sami

Ambulatory Care, Gustave Roussy Institute, Villejuif, FRANCE

Background: Few microbiological data are available in feasible patients with solid tumors without neutropenia. Recently we have observed an increase in bacteria resistance in immuno compromised patients and particularly with hematological diseases. The aim of this study is to describe the bacteria occurring in solid tumors, and to identify a potential association with other sites of infection.

Methods: This retrospective study was conducted in an emergency oncology department (EOD) in a cancer hospital (2010-2011). In our EOD, 5200 patients with cancer are admitted for an unexpected event/year; 15% of them are admitted for exploration of fever. The records of bacteremia and positive microbiological sample from these patients were analyzed. Tumors samples were taken at the same time. Urinary skin and/or sputum samples were analyzed according to clinical symptoms. Central venous catheter infection (CVC) was defined with the differential time to positivity between hub-blood and peripheral-blood cultures.

Results: We reported 290 episodes of bacteremia. Gram-positive represented 58% of the organisms isolated from blood culture; coagulase-negative staphylococci (CNS) (n = 105), Staphylococcus aureus (SA) (n = 38) (only one was methicillin-resistant), S. pneumoniae (n = 7), Streptococcus sp (n = 29). The majority of gram-negative were Enterobacteria (E) (n = 97) and most of them were E. coli (n = 62). Only 2 E. coli developed extended spectrum beta-lactamases resistance. Pseudomonas sp, other gram-negative, anaerobes and Candida sp counted, respectively, 12, 12, 6 and 6 bacteremia. One microorganism was identified in 270 bacteremia cases. Two more microorganisms were found in 35 and 6 bacteremia cases, respectively. All the bacteremia were related to CVC when CNS, SA and Candida sp were identified excepted 3/38 of SA linked to a skin infection. For the E, 25/98 were attributed to a catheter infection and 45 to a urinary tract infection. It is important to highlight that all the bacteremia cases were not associated with another site of infection.

Conclusion: In patients with solid tumors without neutropenia, all bacteremia are associated with documented sites of infection. It is important to point out that the bacteria resistance in our department is the exception (1%) and 58% of the bacteremia were gram-positive microorganisms.

Disclosure: All authors have declared no conflicts of interest.

THE NEUTROPTENIA PROPHYLAXIS EVALUATION PROGRAM IN PATIENTS RECEIVING MYELOSUPPRESSIVE CHEMOTHERAPY WITH MODERATE OR HIGH RISK OF FEBRILE NETROPENA – AN INTERIM ANALYSIS OF THE DIEPP STUDY

T. Cosszi1, M. Saffandi2, G. Mazur3, G. Mihaylo4, J. Benkovics5 and E. Tóth6

1Hétényi G Korhaz Orvostagyi Kozpont, Hétényi G Korhaz, Orvostagyi Kozpont, Szoft, HUNGARY, 2Ódödelli Klinikai Orvostagyi, Nemocnice Na Homolce, Prague, CZECH REPUBLIC, 3Hematology Blood Neoplasm and Bmt, Klinika Hematologii i Nowotworów Krwi i Transplantacji Szpiku, Wroclaw, POLAND, 4Clinic of Hematology, Specialized Hospital for Active Treatment of Hematology Diseases, Sofia, BULGARIA, 5Clinical Oncology, Sv. Vincent s.r.o., Převidza, SLOVAK REPUBLIC, 6Amgen Slovakia s.r.o., Piestany, SLOVAK REPUBLIC

Background: Pégfilgrastim is a pegylated granulocyte colony stimulating factor (G-CSF) indicated for the prophylaxis of febrile neutropenia (FN) in patients (pts) treated with myelosuppressive chemotherapy (CT). The DIEPP study was designed to evaluate FN incidence and risk assessment in pts at high overall risk of FN receiving myelosuppressive CT with pegfilgrastim prophylaxis (PP).

Methods: This prospective observational study collected data from pts within Central and Eastern Europe and Austria having the following malignancies: early stage breast cancer (stages I-III), diffuse large B-cell lymphoma, lung, gastric or ovarian cancer. To be eligible, pts had an investigator-assessed overall risk of FN ≥20% (CT plus patient risk factors), and were planned to receive pegfilgrastim according to the SmPC and to receive CT for ≥4 cycles. The primary objective was to estimate FN incidence and secondary objectives included assessment of which risk factors (RF) from the ASCO/EORTC guidelines most often contributed to the decision to use pegfilgrastim primary (PP) or secondary (SP) prophylaxis. The final planned sample size is 1,200 pts; this interim analysis includes data collected from the Czech Republic, Poland, Hungary, Romania, and Austria between 08/2011 and 01/2012.

Results: At the interim cut off time 268 enrolled pts (mean age 58 ± 12 years, 25% male) received 1334 CT cycles; 237 pts (88%) received PP, 10 pts (4%) SP, and 21 pts (8%) delayed or other pégfilgrastim administration. Overall 9 pts (4%; 95% CI [2%, 6%]) reported FN in a total of 10 (1%; 95% CI [0.4%, 1%]) cycles. Five pts (2%; 95% CI [1%, 4%]) reported FN in the first CT cycle. The high FN risk of planned CT was the most common reason reported by physicians for pegfilgrastim use: 65% pts (95% CI [74%, 84%]). The three most common pt-related RFs were: female gender, 54% (95% CI [48, 60]), advanced disease stage, 41% (95% CI [35%, 47%]); and age ≥65, 21% (95% CI [17%, 27%]). No SADR and 2 ADR cases (neutropenia and bone pain) were registered.

Disclosure: Based on data from the CEE and Austria, rates of FN were low with FN incidence and risk assessment in pts at high overall risk of FN receiving myelosuppressive CT with pegfilgrastim prophylaxis.
H.W. Tessen5, M. Reiser6, K. Severin1 and S. Schmitz1

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 anaemia 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 anaemia (hemoglobin (Hb) < 11 g/dL), received a chemotherapy, gave written informed consent, and had a pretherapeutic diagnostics of anaemia: Ferritin (F), transferrin saturation (TSAT), endogenous erythropoietin (eEPO) and soluble transferrin receptor (sTFR) on day 1 and 14. All pts were treated with Darbepoetin alfa (DA, 500 μg, q3w) with or without iv-III-hydroxyl-succanath (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, Fe < 11μg/ml) 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 9.53g/dL (SD 0.78) and increased in average 1.23g/dL (SD 1.34) and 1.53 g/dL (SD 1.49) till weeks 6 and 9, respectively. The rate of response 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 a 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 for response to DA than TSAT. Supported by Amgen, Munich, Germany.


1Hematology and Oncology, Outpatient Clinic, Cologne, GERMANY, 2University, Institut für Medizinische Statistik, Informatik und Epidemiologie, Cologne, GERMANY, 3Hematology and Oncology, Outpatient Clinic, Krefeld, GERMANY, 4Hematology and Chemotherapy, Outpatient Clinic, Cologne, GERMANY, 5Hematology and Oncology, Outpatient Clinic, Goslars, GERMANY, 6Hematology and Oncology, PICH - Outpatient Clinic, Cologne, GERMANY

Background: Darbepoetin 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 to 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 BLC had Hb in the target 9 - 11 g/dL range, while 4284/4760 (90.0%) pts enrolled ALC 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 withheld 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 darbeapoetin alfa. This study was sponsored by Amgen GmbH CEE Headquarters.


1Hematology, Warsaw Medical University, Warsaw, POLAND, 2Oncology Department, Szpital Ss, Budziszówski Bednarz Kózda, Budapest, HUNGARY, 3Radiation Oncology and Oncology, East Slovakian Cancer Institute, Košice, SLOVAK REPUBLIC, 4Department of Laboratory Medicine, Medical University of Lodz, Lodz, POLAND, 5Hematology Department, Faculty Hospital, Pliva-Czech Republic, 6Medical Oncology, Institute of Oncology, Ljubljana, Slovenia, 7Amgen Slovakia s.r.o., Piešťany, SLOVAK REPUBLIC

** Table: 1561P

<table>
<thead>
<tr>
<th>Predictive factor for response*</th>
<th>to DA (OR (95% CI))</th>
<th>to DA with additional iv-iron (OR (95% CI))</th>
<th>to DA without iv-iron (OR (95% CI))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin (F) ≥ 100 ng/ml</td>
<td>1.80 (0.85–3.81)</td>
<td>4.60 (1.62–13.09)</td>
<td>0.13 (0.02–0.76)</td>
</tr>
<tr>
<td>TSAT &lt;20%</td>
<td>1.28 (0.72–2.27)</td>
<td>1.10 (0.80–1.59)</td>
<td>0.65 (0.24–1.76)</td>
</tr>
<tr>
<td>sTFR ≥ 1.76 mg/dL</td>
<td>1.51 (0.87–2.60)</td>
<td>1.70 (0.87–3.30)</td>
<td>1.13 (0.43–2.99)</td>
</tr>
<tr>
<td>FL sTFR/log ≤ 3.2**</td>
<td>3.92 (0.43–35.70)</td>
<td>7.29 (0.38–140.76)</td>
<td>0.57 (0.02–17.60)</td>
</tr>
<tr>
<td>eEPO &lt;100 U/L</td>
<td>1.76 (0.80–4.80)</td>
<td>2.26 (0.65–7.89)</td>
<td>0.29 (0.01–8.35)</td>
</tr>
<tr>
<td>Δ sTFR d14 ≤ 1.25%</td>
<td>1.75 (0.75–4.03)</td>
<td>1.85 (0.73–4.86)</td>
<td>1.98 (0.35–11.35)</td>
</tr>
<tr>
<td>Δ Hb d21 ≥ 2.06 g/dL</td>
<td>6.09 (3.23–11.49)</td>
<td>8.20 (3.71–18.10)</td>
<td>3.11 (1.05–9.23)</td>
</tr>
<tr>
<td>** Hb d42 ≥ 11 g/dL or Δ Hb d42-d1 ≥ 1.5 g/dL, no transfusion d21-d42</td>
<td>** Odds ratio, confidence interval, and number of pts with †</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The approval of epoetin biosimilars in the European Union requires extensive scientific evaluation and stringent regulatory procedures, including post-marketing studies. The ORHEO (place of biOsimilaRs in the therapeutic management of anaemia secondary to chemotherapy in HaEmatology and Oncology) study was an observational, longitudinal, multicentre study performed in France to evaluate the efficacy and safety of biosimilar epoetins for the treatment of CIA in the clinical setting. Patients >18 years with CIA (haemoglobin [Hb] <11g/dL) in association with solid tumours, lymphoma or myeloma and eligible for treatment with an epoetin biosimilar were included in this study. Patient characteristics were recorded at time 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 treatments. Patients were then followed-up at 3 and 6 months. Analyses included adverse events, achievement and target Hb responder 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).2310 patients (mean age 66.5 years) from 232 centres were included, of whom 79.6% had solid tumours, 13.0% had lymphoma and...
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 was 9.6 g/dL, with 35.6% of patients having moderate anemia (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 CEA in patients with solid tumours, lymphoma and myeloma.

Disclosure: 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 anemia (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 LI. The mean age was 63.2 years old (range 35-75 years old). fortnightly for 8 weeks. Primary endpoint of the study was Hb response (increase 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 evaluated 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 hemoglobin levels between 9-10 g/dL. None of the patients required red blood cell transfusion and supplemental 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 anemia receiving supplemented epoetin alfa, daily supplemental protein of LI is safe and produces a significant increase in Hb anemia with 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.

Disclosure: All authors have declared no conflicts of interest.

Background: Quality of life in cancer patients is significantly reduced by anaemia and associated fatigue. Fatigue is one of the most common symptoms of cancer and cancer therapy. The aim of the present study was to evaluate fatigue in treatment-naïve patients with solid tumours and after four months of cancer therapy using the Functional Assessment of Cancer Therapy-Fatigue (FACT-F) questionnaire.

Methods: Multicenter, prospective and observational study that included newly diagnosed cancer patients. Patients completed the FACT-F questionnaire at baseline and after four months of cancer therapy. Anaemia status (haemoglobin <12 g/dL) was also recorded before and after cancer therapy. Hb levels were compared according to the presence or absence of severe fatigue (FACT-F < 30 points).

Results: The study included 295 patients (153 females), mean age was 61.6 ±12.5. FACT-F score decreased by a mean of 2.4 points over the four months of cancer therapy (p< 0.001). The proportion of patients with severe fatigue was higher after cancer therapy: 23.6% vs 15.5% at baseline (p< 0.001). Most of the patients with severe fatigue had anaemia at baseline (69.8%) and at the four-month visit (71.2%). The proportion of patients with both anaemia and severe fatigue not receiving treatment was 26.2% at baseline and 24.3% after cancer therapy. According to type of cancer, the proportion of patients with severe fatigue at baseline was 21% in gastrointestinal cancer (GI), 18% in lung cancer and 4% in breast cancer. After therapy, these proportions were 24% and 15%, at 3 and 6 months respectively. In conclusion, Retacrit was effective and well tolerated in the management of CEA in patients with solid tumours, lymphoma and myeloma.

Disclosure: All authors have declared no conflicts of interest.
Medians (IQR) or n (%). Information available for 984°, 588

Prior chemotherapy 387 (53%) a

Hb level

Performance status 1

Hb level, g/dL 9.6 (9–10.1)°

Female 617 (63%)°

1.1%, the rate of clinically significant adverse events was 16.7%, while the rate of

1.4 g/dL and 1.7 g/dL at 3 and 6 months, respectively. At 6 months, the transfusion rate

30.8% a stage IV tumour, while metastases were identified in 71.5% of patients. At

291 patients with gynecologic malignancy. Median age was 60 years (24-84).

2.4% (n = 350) of the patients received epoetin zeta (Retacrit®, Hospira UK Ltd.)

Conclusion: In patients with lung cancer, epoetin biosimilars were effective and well tolerated.

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

1569P

adverse drug reactions, the investigators classified 12 as DA related. Of these, 1

clinically important difference was only found using FACIT-F. Of 30 reported

transfusion was required by 32% of pts from wk1 to wk9; 16% of pts required

levels rose from 9.6 g/dL at baseline (BL) to 10.8 g/dL at wk9. 519 pts (53%) of DA

treatment. Median time to Hb level ≥10 g/dL was 14 days (IQR 9–12 days). RCC

transfusion was required by 32% of pts from wk1 to wk9; 16% of pts required

Results: In total, 984 pts met the protocol criteria and were included into the

Median age was 60 years (24-84). Median duration of inclusion was 14.8 months.

Transfusion was required by 32% of patients from wk1 to wk9; 16% of patients required

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 86.8% and 91.7% of patients with breast cancer 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 clinically significant adverse events was 9.1%, while the rate of thrombocytopenia was 0.8%. In conclusion, 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. P. Soubyean: I have received honoraria from Hospira for advisory boards and consulting. H. Albrand: Employed by Hospira.

1568P

THE USE OF BIOSIMILAR EPOETINS IN THE MANAGEMENT OF CHEMOTHERAPY-INDUCED ANAEMIA (CIA) IN PATIENTS WITH LUNG CANCER: A SUBANALYSIS OF THE ORHEO STUDY

M. Michallet1, E. Luporsi2, P. Soubyean3 and H. Albrand4

1Service d'Hématologie, Pavillon Marcel Bérard 1g, Centre Hospitalier Lyon Sud, Lyon-Pierre Bénite, FRANCE; 2Medical Oncology, Centre Alexi Vautrin, Vandœuvre-lès-Nancy, FRANCE; 3Department of Medical Oncology, Institut Bergonie and Université Bordeaux Segalens, Bordeaux, FRANCE; 4Medical Director, Laboratoire HOSPIRA France, Meudon La Forêt, FRANCE

An observational, longitudinal, multicentre study (ORHEO) of biosimilars in the therapeutic management of anaemia secondary to chemotherapy in France 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, myeloma 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 epoetins 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 1.4 g/dL and 1.7 g/dL at 3 and 6 months, respectively. At 6 months, the transfusion rate was 1.1%, the rate of clinically significant adverse events was 16.7%, while the rate of thrombocytopenic events was 2.4%. In conclusion, biosimilar epoetin was effective and well tolerated in patients with lung 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. Soubyean: I have received honoraria from Hospira for advisory boards and consulting. H. Albrand: Employed by Hospira.
A pooled analysis of 562 women receiving highly emetogenic chemotherapy (HEC) in prospective clinical trials of palonosetron (PALO)

L. Celio1, F. Longo2, S. Brugnatelli3, G. Mansueti3, E. Bonizzoni4, F.G.M. Braud5 and M.S. Aapro6

Background:
STATES OF AMERICA

MODERATELY EMETOGENIC CHEMOTHERAPY (MEC) in highly emetogenic chemotherapy (HEC) in prospective clinical trials of palonosetron (PALO).

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

Conclusion:

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.

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

Disclosure:

All authors have declared no conflicts of interest.

Methods:

POLYCHEMOTHERAPY

The acute-phase efficacy of APD421 in combination with ondansetron (ON) in moderately emetic chemotherapy (MEC)

J. Herrstedt1, Y. Summers2, G. Daugaard3, T.B. Christensen4, K. Holmsovs5, P.D. Taylor2, G. Fox5 and A. Molassiotis6

Conventional dopamine D2 antagonists are among the oldest antineuctics 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 testing, APD421, a potent D2 and D3-antagonist, showed some single-agent efficacy in preventing vomiting and especially nausea caused by cisplatin. We therefore investigated its efficacy in combination with ondansetron at preventing acute-phase CINV.

Methods:

Chemotherapy-naïve patients receiving cisplatin ≥ 50 mg/m² were given single IV CR 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.

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

D. Voisin1, 2 and S. Grunberg2

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 [0.125 mg IM or rectal]) prior to MEC (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-naïve) 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).

Conclusion:

The acute-phase efficacy of APD421 in combination with ondansetron effectively prevents acute cisplatin-induced nausea and vomiting (CINV).

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 1-day regimen comparison was significant (DN, 58.9% vs. 46.4%; P < 0.0001). For 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 acute-phase efficacy of APD421 in combination with ondansetron is reached (expected to be completed July 2012). Final results will be presented.

Disclosure:

All authors have declared no conflicts of interest.

The dopamine D2/D3 receptor antagonist APD421 in combination with ondansetron effectively prevents acute cisplatin-induced nausea and vomiting (CINV)

J. Herrstedt1, Y. Summers2, G. Daugaard3, T.B. Christensen4, K. Holmsovs5, P.D. Taylor2, G. Fox5 and A. Molassiotis6

Conclusions:

The acute-phase efficacy of APD421 in combination with ondansetron (ON) in moderately emetogenic chemotherapy (MEC) compared favourably with historical data on other 5-HT3-based combinations. Randomised trials in acute and delayed phase CINV are merited.

Disclosure:

G. Fox: The author is an employee and stock-holder of Acacia Pharma.

All authors have declared no conflicts of interest.

Downloaded from https://academic.oup.com/annonc/article-abstract/23/suppl_9/ix499/218718 on 31 May 2018

Volume 23 | Supplement 9 | September 2012
doi:10.1093/annonc/mds416 | i507
compared to older 5HT3-RAs. The primary objectives were to investigate the bioequivalence of two oral PALO 0.75 mg formulation(s) (F(s)) b1 and b2 and their absolute bioavailability when compared to b3, 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 F(s).

Methods: 36 male and female hv were randomized in this open-label, 3-treatment, randomised order (14-day interval set between periods). Treatments b1 and b2 were analyzed for bioequivalence by ANOVA CIs and defined bioequivalence if the 90% confidence intervals (CI) for the AUC and Cmax treatment ratios lie within 80% to 125% range CI Absolute Ratios. Absolute bioavailability of the oral F0 was calculated using the extent of exposure AUC0-24h and AUC0-∞.

Results: The oral 0.75 mg F0 b1 and b2 showed bioequivalence in terms of rate and extent of absorption: The 90% CI for PALO AUC0-24h and Cmax treatment ratios lie within 80% to 125% range. Absolute bioavailability of the oral F0 was calculated using the extent of exposure AUC0-24h and AUC0-∞.

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.

Disclosure: D. Vossen: The Author is an Helsinn Employee, C. Giuliano: The Author is an Helsinn Employee, All other authors have declared no conflicts of interest.

Table: 1574P

<table>
<thead>
<tr>
<th>Pharmacokinetic parameter palonosetron</th>
<th>Ratio</th>
<th>Point estimate</th>
<th>Test/Ref. ratio</th>
<th>90% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC(0-72h) [ng h/L]</td>
<td>b1 / b3</td>
<td>96.56</td>
<td>91.47 - 101.93</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b2 / b3</td>
<td>99.88</td>
<td>94.61 - 105.44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b1 / b3</td>
<td>97.26</td>
<td>92.33 - 102.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b2 / b3</td>
<td>98.99</td>
<td>93.98 - 104.27</td>
<td></td>
</tr>
<tr>
<td>Cmax [ng/L]</td>
<td>b1 / b3</td>
<td>72.60</td>
<td>67.01 - 78.67</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b2 / b3</td>
<td>71.71</td>
<td>66.18 - 77.70</td>
<td></td>
</tr>
</tbody>
</table>

b1: oral administration of 0.75 mg palonosetron as a softgel capsule (formulation A, clinical trial formulation).
b2: oral administration of 0.75 mg palonosetron as a softgel capsule (formulation B, Proposed commercial formulation).
b3: intravenous administration of 0.75 mg palonosetron (3 ± 0.25 mg i.v. Aloxi® - reference for the bioavailability analysis).

ANOVA and 90% CIs for log-transformed.

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)

Department of Medicine, Division of Medical Oncology, Hematology and Infectious Diseases, Fukuoka University, Fukuoka, JAPAN

Aim: 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.

Result: The pharmacokinetic studies of 6 patients showed mean Cmax values on day 1 and 3 were 2.05 and 2.90ng/mL, respectively, with coefficients of variation (CV) of 30.9% and 32.4%. Mean AUC0–4h values were 42.4 and 58.3ng·h/mL on day 1 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 AUC0–4h.

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.

ADME STUDY OF [14C]NETUPIPAT ADMINISTERED AS AN ORAL 300 MG SUSPENSION TO HEALTHY MALE SUBJECTS

C. Giuliano, S. Calcagnile, S. Mair, L. Stevens and I. Nisbet
Quotient Bioresearch, Nottingham, UNITED KINGDOM

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 is rapidly absorbed with peak in plasma concentration ranging between 2h and 5.5h post dose. Elimination is mainly via the feces, with approximately half of the administered dose was recovered within 120h and, based on an extrapolation, elimination was completed by 696h. NETU undergoes extensive metabolism forming phase I and II metabolites. The main metabolites of NETU are M1 (N-demethylated NETU), M2 (NETU-N-oxide) and M3 (monohydroxy NETU) which, on average, account respectively for 29%, 14% and 33% of the NETU plasma exposure.

Results: Total radioactivity was greater 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 696h. NETU undergoes extensive metabolism forming phase I and II metabolites. The main metabolites of NETU are M1 (N-demethylated NETU), M2 (NETU-N-oxide) and M3 (monohydroxy NETU) which, on average, account respectively for 29%, 14% and 33% of the NETU plasma exposure. Phase I metabolites are formed through hydroxylation, 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.

Results: 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.

EVALUATION OF SUBCUTANEOUS (SC) VERSUS INTRAVENOUS (IV) PALONOSETRON IN CANCER PATIENTS TREATED WITH PLATINUM-BASED CHEMOTHERAPY: A RANDOMIZED PHARMACOKINETIC ASSAY

Clinical Oncology, Clinica Universitaria de Navarra, Pamplona, SPAIN

Background: 5-HT3 antagonists are one of the more effective antiemetic preventions in patients who are receiving platinum-based chemotherapy. Some of these 5-HT3 antagonist are available for oral use, however the therapeutic formulations with more bioavailability and middle course which have been traditionally administrated by the intravenous route, have a limited use in the hospital environment. Up to now, no study has examined the pharmacokinetics of these drugs when administered subcutaneously. We have compared pharmacokinetics of palonosetron in the two different routes, SC and IV.

Methods: Patients under platinum-based chemotherapy were randomized to receive before the first cycle of chemotherapy, palonosetron by the SC or the IV route. In the second cycle, the drug was administrated by the other route. The main endpoint was Area Under the Curve between 0-24 hours (AUC 0–24h). Blood samples were drawn at 10, 15, 30, 45, 60, 90 min and 2, 3, 4, 8, 12, 24 h after palonosetron. Drug levels were determined by HPLC with fluorescence detection after liquid extraction of the samples, with a quantification limit of 0.1 ng/ml.

Results: We included 26 patients, from October 2009 to May 2010. We found no statistically differences in the Area Under Curve at 24 hours after the drug administration (AUC 0–24) between both routes. Maximum concentration (Cmax) reached after its administration was significantly lower via the SC route than by IV. The time to reach the Cmax (Tmax) by the SC route was superior than the IV route. The elimination of unmetabolized drug in urine (Ae 24h) was similar in both routes.
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 control in the prevention of early and late emesis, which can benefit the management of outpatient treatments.

Disclosure: All authors have declared no conflicts of interest.

1578P
CORRELATION BETWEEN CYCLOPHOSPHAMIDE-INDUCED HYPONATREMIA AND THE USE OF APREPANT
Y. Tono, T. Mizuno, K. Saito, S. Tamanu, Y. Yamashita, H. Oda, S. Kageyama and N. Katayama
Medical Oncology, Mie University Hospital, Tsu, JAPAN

Background: For prevention of emesis during anthracyline (A)/cyclophosphamide (CPA) therapy breast cancer, use of aprepitant(AP) combined with serotonin receptor antagonist(5HT3) and dexamethason(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 cases 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 anthracylin 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 which the median age was 53(33-64) and 52(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 in the 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% v 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.

Disclosure: All authors have declared no conflicts of interest.

1579P
THE EFFICACY OF TRIPLET ANTIEMETIC THERAPY FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN LUNG CANCER PATIENTS RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY: PALONOSETRON (PALO), APREPANT (APR), AND DEXAMETHASONE (DEX)
H. Yoshizawa1, K. Sato2, M. Makino2, O. Kobayashi2, H. Tanaka2, S. Miura2, K. Zarogoulidis2, A. Feng1, Z. Cong1 and A. Braun1
1Bioscience Medical Research Center, Nigata University Medical and Dental Hospital, Nigata, JAPAN, 2Department of Respiratory Medicine, Nagaoka Red Cross Hospital, Nagaoka, JAPAN, 3Department of Internal Medicine, Nigata Prefectural Chiba Hospital, Chiba, JAPAN, 4Department of Internal Medicine, Nigata Prefectural Central Hospital, Joetsu, JAPAN, 5Department of Internal Medicine, Nigata Cancer Center Hospital, Nigata, JAPAN, 6Department of Medicine (II), Nigata University Medical and Dental Hospital, Nigata, JAPAN, 7Department of Health Promotion Medicine, Nigata University Graduate School of Medical and Dental Sciences, Nigata, JAPAN

Background: Chemotherapy-induced nausea and vomiting (CINV) is one of the most problematic symptoms experienced by patients undergoing cancer treatments. Triplet therapy with PALO, APR, and DEX, is a guideline-recommended antiemetic prophylaxis for highly emetogenic chemotherapy (HEC). However, the efficacy and safety of this therapy for lung cancer patients has not yet been well investigated.

Methods: Chemotherapy naïve lung cancer patients scheduled to receive HEC were enrolled in this study. The eligible patients were pretreated with the triplet therapy (PALO 0.75 mg day 1, APR 125 mg day 1 and 80 mg day 2-3, DEX 9.9 mg day 1 and 8 mg day 2-4) before receiving HEC. The efficacy and safety of these substances were assessed during an observation period starting from the administration of HEC to 120 hours. A questionnaire diary documented patients’ complaints. The primary endpoint was the proportion of the patients who did not experience emesis or rescue antiemetic (Complete Response rate; CR rate) during any part of the whole observation period. The secondary endpoints were (1) the CR rate during the acute phase (0-24hrs) and the late phase (24-120hrs), (2) the proportion of patients who experienced no emetic episodes and significant nausea with no rescue medication (Complete Control rate; CC rate), and (3) safety.

Results: A total of 72 patients were enrolled with 65 assessable patients at the time of submission. The median age was 64 years. The CR rate during the whole observation period, the acute and late phase was 75.8%, 95.4% and 80.0%, respectively. The CC rate in the late phase was 62.9%. No severe side effects were observed. In the subset analysis, the CC rate in late phase was significantly lower in female subset (71.4% vs. 45.0%). Another subset analysis regarding to chemotherapy regimen, the proportion of vomiting event was higher in the patients used cisplatin.

Conclusion: Triplet therapy using PALO, APR and DEX, was shown to be safe and effective in preventing CINV in lung cancer patients treated with HEC. Further investigation is needed for to reduce nausea in the late phase.

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

**A RANDOMIZED PHASE II TRIAL COMPARING STANDARD PAIN CONTROL WITH OR WITHOUT GABAPENTIN FOR THE TREATMENT OF PAIN RELATED TO RADIATION-INDUCED MUCOSITIS IN HEAD AND NECK CANCER**


1Division of Oral and Maxillofacial Surgery, Shizuka Cancer Center, Shizuka, JAPAN, 2Medical Oncology and Hematology, Kobe University Hospital, Kobe, JAPAN, 3Oral Radiology and Head and Neck Surgery, Kobe University Hospital, Kobe, JAPAN, 4Oncology Service, Hospital General Universitario de Alicante, Zaragoza, SPAIN, 5Radiation Oncology, Kobe University Hospital, Kobe, JAPAN

**Background:** Radiation-induced mucositis (RIM) in chemoradiation (CRT) for head and neck cancer (HNC) causes severe pain and worsens CRT compliance and outcome. Following retrospective reports that gabapentin might improve RIM-associated pain during CRT, we conducted a randomized phase II trial to analyze the safety and efficacy of gabapentin for RIM-associated pain.

**Methods:** HNC patients (pts) receiving CRT were randomized to receive standard pain control (SPC) or SPC plus gabapentin (SPC + G). Pts in the SPC arm received acetaminophen and opioids as analgesic, while those in the SPC + G arm received gabapentin in addition to SPC. Gabapentin maintained at dose of 900 mg/day till 4 weeks after CRT. The prescribed RT dose was 66-74 Gy/33-35Fr. Concurrent chemotherapy consisted of a three-week cycle of cisplatin. Primary endpoint was maximum VAS score during CRT. Secondary endpoints were total dose of opioids, change in QOL (EORTC QLQ-C30 and EORTC QLQ-HN 35) from baseline to 4 weeks after CRT, and adverse events.

**Results:** From Apr 2010 to Oct 2011, 22 eligible pts were randomly assigned to receive SPC (n = 11) or SPC + G (n = 11). All pts were Stage III or IV. Twelve were treated in a locally advanced setting and 10 in a postoperative setting. No statistically significant differences were seen in median maximum VAS scores between arms (47 in SPC vs. 74 in SPC + G, p = 0.317). Median total dose of opioids at maximum VAS and total dose of opioids at 4 weeks after CRT did not statistically differ but appeared higher in the SPC + G arm (215 mg vs. 745.3 mg; p = 0.880, 1260 mg vs. 1537.5 mg; p = 0.9438). QOL analysis showed significantly worse scores in the SPC + G arm for weight gain (p = 0.005). Adverse events related to gabapentin were manageable. One-year survival rate in both arms was equivalent.

**Conclusions:** This is the first prospective randomized trial to analyze the safety and efficacy of gabapentin for RIM-associated pain. While survival data was equivalent in both groups (NRS 0-10-2.7 and -2.2 points respectively, p = 0.08), it was confirmed a significant improvement of bowel function (p<0.01) in patients treated with oxycodone/naloxone versus those treated with other strong opioids, which worsened their bowel function.

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

---

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


1Radio-Oncology Service, Hospital Virgen del Rocío, Sevilla, SPAIN, 2Oncology Service, Hospital Povisa, S.A, Vigo, SPAIN, 3Oncology Service, Hospital San Juan de Dios, Yecla, SPAIN, 4Oncology Service, Complejo Hospitalario Regional Carlos Haya, Málaga, SPAIN, 5Radio-Oncology Service, Hospital Clínico Universitario Lozano Blesa, Zaragoza, SPAIN, 6Oncology Service, Hospital General Universitario de Alicante, Alicante, SPAIN, 7Oncology Service, Hospital Clínico Universitario Lozano Blesa, Zaragoza, SPAIN, 8Oncology Service, Hospital Universitario Puerta de Hierro de Majadahonda, Madrid, SPAIN

**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.

**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 the 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 I: 54%; receiving chemotherapy 64% and radiotherapy 41%. Main location of the primary tumour: lung (28%), colon/rectum (12%), head and neck (11%). Metastatic cancer: 79% 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 (NRS0-2.7 and -2.2 points respectively, p = 0.08). It was confirmed a significant improvement of bowel function (p<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.

---

**PROSPECTIVE STUDY OF TREATMENT PATTERN, EFFECTIVENESS, AND SAFETY OF ZOLEDRONIC ACID (ZOL) THERAPY BEYOND 24 MONTHS IN PATIENTS (PTS) WITH MULTIPLE MYELOMA (MM) OR SOLID TUMOR BONE METASTASIS (STM)**

T. van den Wyngaert1, M. Delforge2, C. Doyen3, L. Duck2, K. Wouters6, I. Delabaye7, C. Wouters8, H. Wildiers9 and on behalf of BSMO/BHS and Lotuz Investigators.1

1Nuclear Medicine, Antwerp University Hospital, Edegem, BELGIUM, 2Hematology, University Hospitals Leuven, Leuven, BELGIUM, 3Hematology, Cliniques Universitaires UCL, Groene, BELGIUM, 4Oncology, Clinique St. Pierre, Ottignies, BELGIUM, 5Biostatistics, Antwerp University Hospital, Edegem, BELGIUM, 6Novartis Oncology, Novartis Pharmaceuticals, Wóodroo, BELGIUM, 7Oncology, University Hospitals Leuven, Leuven, BELGIUM

**Background:** Trial data documenting ZOL treatment is currently limited to approximately 2 years of therapy.

**Methods:** Pts with MM or STM and with at least 24 months of regular q3-4w ZOL therapy were followed for 18 months. ZOL could be continued, interrupted or stopped at the discretion of the treating physician. End-points included ZOL exposure, incidence of skeletal related events (SRE), and safety.

**Results:** In all, 298 evaluable pts were enrolled (female n = 201; median age 66y). Pts had MM (31.2%), breast- (52.7%), prostate cancer (11.7%), or another solid tumor (4.4%). The mean continuation rate of ZOL was 90.6%, even though only 28.0% of pts who completed follow-up (n=218) received uninterrupted per-label ZOL therapy. Exposure to ZOL decreased steadily with time in all pts, but was on average lower (50.0% vs 67.6%; p < 0.001) with higher discontinuation rates (IRR 1.95; p < 0.002) in MM compared to STM pts. ZOL infusions were extended beyond 15 minutes in 39.5%, and the treatment interval exceeded 4 weeks in 29.3% of pts. ZOL continued to suppress the rate of SREs similarly during the 18 months study period (0.14 per person-year) as compared to the 18 months before inclusion (0.13 per person-year; p = 0.9). At 18 months, 82.7% (95% CI 77.4 – 87.6%) of pts were SRE free. The rate of SREs was lower in MM compared to STM pts (IRR 0.48; p = 0.03). In STM pts, persistent ZOL therapy reduced the SRE risk (HR 0.42; p = 0.01) compared to interrupted treatment. Renal deterioration occurred in 11 pts (3.7%), with a higher risk when ZOL dose was not adjusted for renal function (HR 3.96; p = 0.03), as observed in 12.5% of pts. Symptomatic hypocalcemia was not reported, although adherence to supplemental calcium and vitamin D was only 18.5%. Acute phase reactions were infrequent (6.4%) and ONJ developed in 6.0% of pts. Invasive dental procedures or trauma were associated with increased ONJ risk (HR 4.67; p = 0.002), with a 20% risk of ONJ after any of these events.

**Conclusion:** The continuation rate of ZOL beyond two years of therapy is high and ZOL demonstrated continued effectiveness in maintaining low SRE rates. Nevertheless, ZOL treatment patterns were heterogeneous and interrupting ZOL therapy in pts with STM was associated with a higher SRE risk. The long-term safety profile of ZOL was favorable, but adequate prevention strategies for ONJ remain important.

**Disclosure:** T. van den Wyngaert: Advisory board Novartis, M. Delforge: Lecture fees from Novartis, I. Delabaye: Employee of Novartis Pharmaceuticals, C. Wouters: Employee of Novartis Pharmaceuticals. All other authors have declared no conflicts of interest.
HOME-BASED ZOLEDRONIC ACID (ZOL) INFUSION THERAPY IN PATIENTS WITH SOLID TUMOURS: COMPLIANCE AND PATIENT-NURSE SATISFACTION

T. Lebret1, J. Mouysset2, A. Lortholary3, C. El Kouri4, L. Basit4, M. Khouri5, K. Slimane2, F. Muracciole6 and S. Guérif7

1-Urology, Hôpital Foch, Suresnes, FRANCE, 2-Oncology, Psychiatrie Parc Rambot-Provence, Aix en Provence, FRANCE, 3-Medical Oncology, Catherine de Sienne Institute, Nantes, FRANCE, 4-Radiothérapie, Centre de Radiothérapie, Evreux, FRANCE, 5-Oncology, Novartis Pharmaceuticals, Rueil-Malmaison, FRANCE, 6-Servizio di Radiotherapia, CHU La Timone APHM Marseille, Marseille, FRANCE, 7-Radiothérapie, CHU Poitiers, Poitiers, FRANCE

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 Zometa5, 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 763 met inclusion criteria. Overall, 343 nurses (97.5% community) took part. 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, 343 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; 97.9% felt that home therapy promoted a good relationship with patients, and 73% were either highly satisfied or satisfied with their hospital contacts. Among patients, 95.3% were either very satisfied or satisfied with home ZOL therapy. Causes for satisfaction were quality of the nurse-patient relationship (57.8%) in addition to expected reasons (e.g. less time travelling/waiting (68.8%), less disruption to daily routine (36.6%)). ZOL therapy was well tolerated (discontinuation due to adverse events 6.1%; osteonecrosis of the jaw 0.6%, fractures 0.2%). Practitioner compliance with recommendations was 73% for dental hygiene checks at inclusion and 48-56% thereafter, 66% for dental hygiene who must undergo preventive dental treatment. When reparative phenaema are compromised by B, the healthy oral environment prevents infections and subsequent mortality. In our opinion, this type of preventive program should be encouraged.

Conclusions: Our study demonstrates that ONJ can be effectively prevented with a systemic preventive program focused primarily on reducing its incidence and, wherever it develops, the need for demolitive surgery with permanent sequelae. In our opinion, this type of preventive program should be encouraged.

Disclosure: All authors have declared no conflicts of interest.

QOL AND SURVIVAL SURVEY OF CANCER CACHEXIA IN ADVANCED NSCLC PATIENTS - NJUG-LC STUDY, TORG0912

S. Aitai1, F. Imamura2, A. Yokoyama3, K. Minato4, T. Harada5, N. Katakami6, T. Yokoyama7, Y. Ohashi8, K. Watanabe9 and K. Eguchi10

1-Department of Thoracic Oncology, Kinki-chuo Chest Medical Center, Osaka, JAPAN, 2-Department of Thoracic Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, JAPAN, 3-Department of Internal Medicine, Nigata Cancer Center Hospital, Nigata, JAPAN, 4-Department of Respiratory Medicine, Gunma Prefectural Cancer Center, Ota, JAPAN, 5-Center for Respiratory Disease, Hakaido Social Insurance Hospital, Sapporo, JAPAN, 6-Division of Integrated Oncology, Instituto de Biomedical Research and Innovation Hospital, Kobe, JAPAN, 7-Department of Respiratory Medicine, Kyorin University Hospital, Tokyo, JAPAN, 8-Department of Biostatistics, School of Public Health, The University of Tokyo, Tokyo, JAPAN, 9-Department of Respiratory Medicine, Yokohama Municipal Citizen’s Hospital, Yokohama, JAPAN, 10-Internal Medicine, Division of Medical Oncology, Tokyo University School of Medicine, Tokyo, JAPAN

Background: Cancer cachexia, mainly characterized by muscle atrophy and subsequent cancer induced weight loss (CIWL), is attributed to 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.

Method: Untreated stage IV NSCLC patients with ECOG PS of 0-2 were registered. (Continued...)

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: 56.3kg, PS 0: 39.2%, and PS 1: 51.5%. The patients with BW loss ≥ 5% (n = 219) reported more early deaths than those without (n = 166, p = 0.0001). Patients without 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 attributes: more weight on anaemia, 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 attributes 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 and treatments based on the further elucidation of its pathology are needed.

Disclosure: All authors have declared no conflicts of interest.
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. Anorexin is an investigational orally active ghrelin receptor agonist with orexigenic and anti-cachectic 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 not previously treated with oxaliplatin. Patients were randomized to treatment with placebo (PL) or 50mg anorexin (AN) once daily for 12 weeks. Eighty-two patients were assessed total LBM by DXA, handgrip strength (HGS) and Quality of Life (QoL; ASAS scale) at baseline, 4, 8 and 12 weeks. For 72 subjects (N = 38, AN; N = 34, PL), data was also available for aLBM. Solid 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 aLBM 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.


Disclosures: All authors have declared no conflicts of interest.

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

Y.H. Yun1, Y.N. Cho2, Y.A. Kim3 and E.J. Choi4

1Department of Medicine, Seoul National University, Seoul, KOREA, 2School of Medicine, Seoul National University, Seoul, KOREA, 3Public Health, Korea University, Seoul, KOREA, 4Family Medicine, Seoul National University Hospital, Seoul, KOREA

Purpose: Although the suicide rate of cancer-survivors is higher compare to that of general population, there are few studies examined on the suicide related risk factors. To evaluate 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 suicide ideation among 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, dyspnea, 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 (adjusted odds ratio[aOR] 2.84; 95% confidential interval[aCI] 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

T. Amano1, Y. Shimada2, T. Nishia2, K. Shinoda4, T. Esaki2, Y. Komatsu2, H. Akita1, K. Shimozuma2, Y. Ohashi4 and F.H. Hausheer5

1Medical Oncology, Hokkaido University Graduate School of Medicine, Sapporo, JAPAN, 2Gastrointestinal Oncology, National Cancer Center Hospital, Tokyo, JAPAN, 3Gastrointestinal Oncology, National Hospital Organization Shikoku Cancer Center, Matsuyama, JAPAN, 4Clinical Pharmacology, Hiroshima Prefectural Hospital, Hiroshima, JAPAN, 5Gastrointestinal and Medical Oncology, National Kyushu Cancer Center, Fukuoka, JAPAN, 6Cancer Center, Hokkaido University Hospital, Hokkaido, JAPAN, 7Biomedical Sciences, College of Life Sciences, Ritsumeikan University, Shiga, JAPAN, 8Department of Biostatistics, School of Public Health, The University of Tokyo, Tokyo, JAPAN, 9BioNumerik Pharmaceuticals, Inc., San Antonio, TX, UNITED STATES OF AMERICA

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 subscale, 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
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)

M. Nakamura, K. Nakamura, T. Onikubo, H. Kamikawa and K. Tauchi
Aizawa Comprehensive Cancer Center, Aizawa Hospital, Matsumoto, JAPAN

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 systemic 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, tinnitus, 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), capetibine (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 = 0.03; paired t test) and 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

S. Vasquez1, M. Guidon2, E. McHugh2, O. Lennon2 and O.S. Breathnach3
1Physiotherapy, Beaumont Hospital Cancer Centre, Dublin, IRELAND; 2Medical Oncology, Beaumont Hospital Cancer Centre, Dublin, IRELAND

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 Spearman's 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.

significance correlations were found between mTNS and BERG (r = -0.289, p = 0.05), TUG (r = 0.136, p = 0.05), and FACT-G (r = 0.050, 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.

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

L. Traldi Macedo1 and A. Sasse2
1Medical Oncology, State University of Campinas (UNICAMP), Campinas, BRAZIL; 2Devon Centre for Evidences in Oncology, UNICAMP - Univesidate Estadual de Campinas, Campinas, BRAZIL

Introduction: Hand-foot syndrome (HFS) is a distinctive adverse event relatively frequent to some chemotherapeutic agents as capecitabine, pegylated liposomal doxorubicin, docetaxel or sorafenib, and often recognized as a dose-limiting reaction. The prevention of HFS 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 TJ-14 rinse appears to have a significant ability to treat grade 2 COM and reduce the risk of developing grade 3 COM. Our results are encouraging and warrant further phase III trials.

Conclusions: From all available possibilities for prevention of HSF, celecoxib appears to be the most promising agent, with statistically significant results. Larger, multicentric studies would be ideal to reinforce this hypothesis.

Disclosure: All authors have declared no conflicts of interest.

Topical Application of TJ-14 (Hangeshashinto) in the Treatment of Chemotherapy-Induced Oral Mucositis: A Randomized, Placebo-Controlled, Double-Blind, Phase II Trial

N. Nagata1, C. Matsuda2, Y. Munemoto3, M. Oshiro4, M. Kataoka5, Y. Shindo6, S. Morita7, T. Kono8, J. Sakamoto9 and H. Mishima10

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 (hangeshashinto) may be useful for COM via downregulating pro-inflammatory prostaglandins in the cyclooxygenase pathway (ASC0-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 dissolve 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 expec troitating 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 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 incidence of grade 2 or higher COM, the duration of grade 2 or higher COM, and the healing time of COM.

Results: Ninety patients (43 in the TJ-14 group, 47 in the placebo group) were included in the statistical analysis. The incidence of grade 3 COM was 9.5% vs. 17%, while no significant difference in the incidence of grade 2 or higher COM was found between the two groups. The median duration of grade 2 or higher 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.

Maintenance of Quality of Life in Patients with Malignant Ascites During Treatment with the Trifunctional Antibody Catumaxomab: Results from the Phase III B CASIMAS Trial

F. Lordick1, J. Sehouli2, I.B. Vergote3, P. Roosendaal4, A. Schneeweiss5, A. Blox6, D. Bertoni-Rigaudo7 and P. Wimberger8

Background: Malignant Ascites (MA) is associated with a poor prognosis and a major deterioration in quality of life (QoL). To demonstrate the value of a new treatment the assessment of QoL is of particular importance. Results from the pivotal study demonstrated catumaxomab’s potential to stabilize QoL and prolong the time to first deterioration of QoL in these patients. Observations from the two-arm, open-label, multicentre CASIMAS trial now give evidence that QoL remains unaffected during catumaxomab treatment.

Methods: In our trial, 219 patients were randomized to receive catumaxomab plus premedication of 25 mg prednisolone (CP, 111 pts) or catumaxomab alone (C, 108 pts). QoL was measured using the EQ-VAS during the treatment period (d 0, 3 and 10) and follow-up (d 8, 28). Descriptive analyses were performed according to EQ-SD User Guide (Version 4.0). In addition, ascites-related symptoms were measured with a disease specific patient questionnaire (Functional Assessment of Chronic Illness Therapy, FACIT).

Results: Longitudinal analysis of the EQ-VAS for the pooled population (CP and C) showed no relevant changes in mean score during the treatment period with catumaxomab (d5: 51.5; d3: 50.9; d10: 51.0) and compared to screening (52.7). During the follow-up period (d5: 53.9, d28: 57.1), an increase in mean values was observed. Descriptive comparison of both treatment groups revealed no major differences in QoL and ascites-related symptoms during the treatment and follow-up period, indicating that prednisolone has no impact on patient’s self-rated health.

Conclusions: Quality of Life as measured by EQ-VAS remains unchanged during treatment with catumaxomab and improves after the treatment period. The improvement is plausible due to the prolonged puncture-free survival and is consistent with previous observations of QoL changes during and after intraperitoneal treatment with catumaxomab.


Prophylactic Topical Adapalene and Oral Minocycline for Panitumumab-Induced Skin Toxicity

T. Yamada1, H. Hashimoto1, N. Yamaizaki2, H. Yasui2, G. Sakai3, S. Akatsuka4, K. Ogawara5, H. Yamaoka5, T. Hamaguchi5

Background: Panitumumab (Pmb) has been associated with a high incidence of skin toxicity. The STEP study evaluated whether prophylactic treatment with a topical steroid and oral doxycycline during the first 6 weeks of Pmb-containing therapy could prevent grade 2 skin toxicity. The current study evaluated the efficacy and safety of adding topical adapalene and oral minocycline to this regimen.

Results: From all available possibilities for prevention of HSF, celecoxib appears to be the most promising agent, with statistically significant results. Larger, multicentric studies would be ideal to reinforce this hypothesis.
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 adapalene and oral minocycline in patients receiving Pmb.

Methods: Patients with KRAS wild-type unresectable/recurrent colorectal cancer enrolled in a prospective phase II clinical trial of third-line Pmb plus irinotecan (CPT-11) or Pmb monotherapy were included. Prophylactic therapy with topical adapalene, 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. Adapalene 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 the STEPP trial results (29%). The median adherence to topical adapalene was 90% (range, 0-100%), while minocycline was 100% (range, 17-100%). In the good adapalene adherence group (≥median), the incidence of the skin toxicity of grade 2 or higher was 20.8% compared to 37.3% 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 adapalene may be an effective prophylactic treatment option for management of Pmb-related skin toxicity.

Disclosure: All authors have declared no conflicts of interest.

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

T. Yoshida1, S. Nito1, M. Toda1, T. Ogawa2, S. Matsumoto1, S. Umemura1, K. Yoh1, R. Goto1, H. Ohnatsu1 and Y. Ohe1

1Division of Thoracic Oncology, National Cancer Center Hospital East, Chiba, JAPAN, 2Division of Pharmacy, National Cancer Center Hospital East, National Cancer Center Hospital East, Chiba, JAPAN

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)-contained 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 (CrCl) (<50ml/min), co-administration of non-steroidal anti-inflammatory agents (NSAIDs), and treatment methods [cisplatin dose (≥80mg/m²), concurrent topical radiotherapy, use of apprenitant, non-preloading 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 apprenitant as antimetic 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.

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

**CONCLUSION:**

Pmab was 95%.

**DISCUSSION:**

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 the STEPP trial results (29%). The median adherence to topical adapalene was 90% (range, 0-100%), while minocycline was 100% (range, 17-100%). In the good adapalene adherence group (≥median), the incidence of the skin toxicity of grade 2 or higher was 20.8% compared to 37.3% 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:**

In our study nearly 50% of patients with metastatic or locally advanced diagnosis of cancer are overweight and more than 25% of them are obese. The incidence of BMI ≥55 in a European cancer population seems to be negligible, otherwise all classes of overweight seems to be related to a higher risk of TE. A formal study is needed to evaluate the risk of all BMI classes as independent risk factors of TE among cancer patients.

Disclosure: T. Perrone: TP is employee of Italfarmaco S.p.A. All other authors have declared no conflicts of interest.

**EXPLORING THE TYPES OF QUALITY OF LIFE TRAJECTORIES AND RELATED FACTORS IN ADVANCED LUNG CANCER PATIENTS – A 6 MONTHS LONGITUDINAL STUDY**

Y. Lai1, Y. Lee1, Y. Liao2, W. Liaor, G. Chi2, Y. Liu1, P. Yang1 and J. Chan1

1School of Nursing, National Taiwan University College of Medicine & Hospital, Taipei, TAIWAN, 2Department of Nursing, Yuan-Pei University, Shing-Jui, TAIWAN, 3Department of Interna Medicine, National Taiwan University Hospital, Taipei, TAIWAN

Background: Quality of life (QOL) is one of the major outcomes to reflect lung cancer patients’ general condition. However, the individually physical and psychological differences may affect and cause different types of QOL trajectories. The aims of this study were to (1) explore the potential types of QOL trajectories in advanced lung cancer patients during the first 6 month of diagnosis, and (2) identify factors related to each type of the QOL trajectories.

Methods: A prospective longitudinal study was conducted in a medical center in Taiwan. A total of 170 newly diagnosed non-operable lung cancer patients were recruited and completed 4 assessments during pre-treatment and 1, 3, 6 months from receiving treatments (T1-4, respectively). QOL trajectory was measured by the overall QOL item from the EORTC QLQ-C30. Physical function and symptoms, depression, uncertainty (about illness) land self-efficacy (level of confidence) in coping with cancer were assessed and analyzed as potential related factors of each QOL trajectory. We used Latent Class Growth Analysis (LCGA) to identify the types of QOL trajectory and their related factors.

Results: Three types of QOL trajectories were identified. The first type of QOL type covered 41.8% of patients which represented a “declining form moderate level of QOL to lower QOL and then back to moderate levels of QOL.” The second type of QOL covered 19.6% of patients and represented “the relatively higher level of QOL...”
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, uncertainty, and self-efficacy: 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 for clinical effectiveness in enhancing advanced lung cancer patients’ QOL during the most distressful first 6 months of having lung cancer. Acknowledge This study is supported by National Health Research Institute (NHRHI) in Taiwan.

Disclosure: All authors have declared no conflicts of interest.
grade 4 toxicity were observed, hemoglobin and non hemoglobin grade 3 toxicities were observed in 12.21% and 13.8% of pts, respectively. In the adults, grade 4 hematological and non hematological grade 3 toxicities were observed in 3.8% and 1.9% of pts, respectively. For grade 4 hematological toxicities in 2.32% 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 were 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.

1605P
OPINIONS OF NURSES ON THE APPLICATION AND IMPLICATIONS OF DNR/DNI ORDERS

Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX, UNITED STATES OF AMERICA, 2Palliative Care, Albert Einstein Medical Center, Philadelphia, PA, UNITED STATES OF AMERICA, 3Department of Palliative Care and Rehabilitation Medicine, MD Anderson Cancer Center, Houston, TX, UNITED STATES OF AMERICA, 4Palliative Care and Rehabilitation Medicine, M. D. Anderson Cancer Center, Houston, TX, UNITED STATES OF AMERICA

Background: Although do not resuscitate (DNR) do not intubate (DNI) orders have a technically limited mandate, the implication of such orders may be broad. Moreover, the patient factors that may influence healthcare providers’ decisions may be debated. This study aimed to evaluate nurses’ opinions on DNR/DNI orders.

Methods: The study was conducted as an anonymous, single institution survey. Fulltime nurses (RN) were identified by payroll and received a questionnaire.

Nurses’ demographics and background, their rating of factors leading to DNR/DNI and rating of appropriateness of treatments were obtained.

Results: Of the 350 distributed surveys, 83% were returned. Work locations included general floors (47%), intermediate care (21%) and ICU (32%). Sixty-seven percent were ≤40 years old. Eighty percent were female, and 73% had ≥10 years of work experience. 204 RNs felt that DNR/DNI orders influence treatment choices of physicians, 81% felt they should be more included in the discussion process. Female RNs were more likely to change the amount of time spent at bedside (OR 0.32, 95%CI 0.12-0.92) and they felt that physicians treatment choices were influenced by DNR orders (OR 0.36, 95% CI 0.17-0.74) compared to males. From an RN view, most important factors leading to a DNR/DNI order were patients’ wishes (99%), untreated/untreatable cancer (94%) and quality of life before admission (89%). For less experienced RNs, there was a general trend to support the administration of blood products, antibiotics, feeding tube placement, invasive procedures, vasopressors, and ICU transfer. Their support for hemodialysis was the only variable that was statistically significant (OR 1.74, 95% CI 1.03-2.97). Pool analysis demonstrated that less experienced were more likely to support a more aggressive treatment approach (OR 1.14, 95% CI 1.17-1.71, p=2.6%).

Conclusion: Nurses regard patients’ wishes, quality of life, serious diseases as the most important factors leading to a DNR/DNI order. Less experienced nurses favor a more aggressive treatment approach. Nursing staff feel that they should be a vital part of the DNR/DNI decision. Further continuous education of the whole health care team on the meaning and implication of DNR/DNI orders is mandated.

Disclosure: All authors have declared no conflicts of interest.

1606P
PARENTAL CANCER: REVIEWING THE CONCERNS OF BREAST CANCER PATIENTS WITH CHILDREN

E. Mura and T. Ishida
Child Support, St.Luke’s International Hospital, Tokyo, JAPAN

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 under 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” (36%), 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 emotional states (≥10%) and doing 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 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 for 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.

Disclosure: All authors have declared no conflicts of interest.

1607P
FAMILY PHYSICIANS (FP) ARE RARELY INVOLVED IN MANAGING ACUTE ONSET SYMPTOMS DURING CANCER TREATMENT

K. Yaocubene, M. Merad, A. T. Albayd, M. Di Palm and A. Sami
1Ambulatory Care, Gustave Roussy Institute, Villejuif, FRANCE, 2Ambulatory Care, Gustave Roussy Institute, Villejuif, FRANCE

Objectives: 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 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 FP 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 FP and 85% for SP.

Conclusions: Our study shows that an assessment was required by a well trained physician in supportive care for more than 4/5 of the acute onset symptoms.

Disclosure: All authors have declared no conflicts of interest.

1608P
BRONCHOSCOPIC INTERVENTION FOR AIRWAY STENOSIS CAUSED BY THYROID TUMOR

1Medical Oncology & Respiratory Medicine, National Hospital Organization Nagoya Medical Center, Nagoya, JAPAN, 2Department of Respiratory Medicine, National Hospital Organization Nagoya Medical Center, Nagoya, JAPAN

Background: Although, bronchoscopic intervention has become a widespread way to palliate respiratory symptoms due to airway stenosis, only a few studies have focused on the utility of bronchoscopic treatment for 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.

Methods: We retrospectively investigated patients who underwent bronchoscopic treatment using rigid and flexible bronchoscopes under general anesthesia from July 2000 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 7, silicone stent placement followed by expandable metallic stent placement in 1), and the remaining 4 patients underwent bronchoscopic airway recanalization using argon plasma coagulation, electrocautery or rigid bronchoscopic coaxing 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. Acute complications occurred in 4 patients (airway injury during bronchoscopic procedure in 1, stent migration in 1, respiratory failure in 1, and obstruction by secretion in 1). Median survival was 117 days (range 1 – 1951).

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

Disclosure: All authors have declared no conflicts of interest.

Downloaded from https://academic.oup.com/annonc/article-abstract/23/suppl_9/ix499/218718 by guest on 31 May 2018
Background: We performed a prospective longitudinal single-center pilot study to investigate physical activity (PA) and physical fitness (PF) in Hodgkin Lymphoma (HL) and Non-Hodgkin-Lymphoma (NHL) patients before, during and after first-line systemic chemotherapy. Further aims were to correlate different patient-, disease- and treatment-related factors with the possible decline or increase of PA and PF and to identify patients at risk of developing a significant decline in PA and PF who might be candidates for an individualized exercise training program.

Methods: PA was assessed with an activity monitor (Dynaport MiniMod McRoberts, The Hague, The Netherlands), PF by incremental cycle ergometry and by a 6-minute walking test (6MWD). Isometric quadriceps strength was measured using a Cybex II dynamometer (Lumes, Bay Shore, United States). Pulmonary function tests, electrocardiography, echocardiography, blood pressure measurements were routinely performed.

Results: The pilot study involved a total of 22 lymphoma patients (19, ♀: 3, median age 57 years, NHL: 14, HL: 8) from 10/2010 to 01/2012. At baseline, PA, 6MWD, maximal inspiratory pressure, quadriceps strength, diffusion capacity at pulmonary function tests were significantly lower than predicted. In contrast, forced expiratory volume in one second (FEV1), forced vital capacity (FVC), maximal oxygen consumption (VO2max), maximal expiratory force and hand grip strength were not significantly different. We observed a broad variation in the different test results between patients at baseline. After 2-3 cycles of chemotherapy we did not identify a significant decrease in PA, whereas VO2max decreased significantly after 2-3 cycles but recovered after completion of chemotherapy (6-8 cycles). Importantly, a huge interpatient variability could be observed at all different time points.

Conclusions: Preliminary results of the PAFILP pilot study suggest that levels of PA and PF probably evolve very differently between lymphoma patients. The study is ongoing to identify possible risk factors predictive for decline in PA and PF. Such a screening tool would allow us to identify early in the course of treatment patients at risk of developing a significant decline in PA and PF who might benefit from an individualized exercise training program.

Disclosure: All authors have declared no conflicts of interest.
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% (124/1676 BTP) and 82.4% (137/1668 BTP) respectively. Patients’ quality of life and functional status [modified Brief Pain Inventory-short version 7 item subscale (BPI-7S)] improved after treatment with FBT [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 FBT was rated “very easy/convenient” and “easy/convenient” for 82.5% (117/421) of patients. Safety data do not indicate concerns with use of FBT and were as expected for cancer patients with opioid treatments. These results demonstrate that FBT was safe and efficacious in a real-world clinical practice setting with a large number of cancer patients experiencing BTP.


The majority of cancer patients with complications are admitted in hospital for cancer and/or treatment in 73% of patients and it was unclear/unknown in 23%. The causes of admission were: Dyspnoea 14%, Neutropenic sepsis 8%, CNS related 9%, metastatic spinal cord compression 6%, pain 12%, miscellaneous/unclear 51%. Admission was attributed to 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 (MHPH) and referred to the AOS.

Materials and method: We collected the data of patients admitted to MHPH because of cancer or treatment-induced complications or diagnosis cancer. Patients were referred via the inpatient referral system and were registered daily in a purpose built database. We reviewed 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/unclear 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.

The most common reported OAEs were increased lacrimation, dry eye, blurred vision, ocular hyperemia, eyelash changes, eye pain, eye irritation, eye pruritus, eyelid irritation, conjunctivitis, eyelid 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, papillae disease, uveitis, cataract, iriditis, 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

S. Barri1, K.F. Bongonovo1, M. Ginardi1, M. Cabiddu1, F. Maspero1, F. Cremonesi1 and F. Petrelli1
1Medical Oncology Division, Azienda Ospedaliera Treviglio-Caravaggio, Treviglio, ITALY
2Medical Oncology Division, A.O. Treviglio-Caravaggio, Treviglio, ITALY

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 So and Su 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 Su. Comparison arms were: Axitinib in 1 trial, Bevacizumab/ INF or Bevacizumab/Tensiromius 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 = 0.0001). 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

N.J. Neesser1, M. Na’Amad2 and A.A. Gabizon2
1Department of Oncology, Rabin Medical Centre (Beilinson Campus), Petach Tikva, ISRAEL
2Hematology, Shaare Zedek Medical Centre Oncology Institute, Jerusalem, ISRAEL
3Oncology, Shaare Zedek Medical Centre Oncology Institute, Jerusalem, ISRAEL

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 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 doses 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 hr 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: NCT00716898. 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.

1617 EDMONTON SYMPTOM ASSESSMENT SCALE (ESAS) FOR ROUTINE SYMPTOM ASSESSMENT OF NON-ADVANCED PATIENTS WITH SOLID OR HAEMATOLOGICAL MALIGNANCIES ON ONCOLOGICAL THERAPIES

C.I. Ripamonti1, S. Boldini1, L. Buonaccorso2, E. Bandieri3, A. Marcelli4, M. A. Pettinetti1 and G. Miccinesi1

1Supportive Care in Cancer Unit, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milano, ITALY, 2Supportive Care in Cancer, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milano, ITALY, 3Psychology, AIMO Assisiocazione of Oncological Patients from nine towns and villages in the Northern Area of Modena, Mirandola, ITALY, 4Oncological Unit, Azienda USL Modena CelEAS Modena, Mirandola Modena, ITALY, 5Psychology Unit, UILT and Centre for Oncological Rehabilitation CERON of Florence, Firenze, ITALY, 6Supportive Care in Cancer, Fondazione IRCCS, Istituto Nazionale Tumori, Milano, ITALY, 7Epidemiology, Cancer Prevention and Research Institute ISP Florence, Florence, ITALY

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 (10/11) in respect to those below. The intensity of psychological suffering was higher for patients who requested psychological support. The correlation (rho of Pearson) between the anxiety and depression items of ESAS with HADS was > 5, whereas the feeling of well-being in ESAS inversely strongly correlated with all the other ESAS symptoms (rho > 4); anorexia with nausea and drowsiness; drowsiness with fatigue; and anxiety with depression. As the ESAS assesses the most frequent symptoms referred to by the patients during oncological treatments, its administration to the patients in the routine practice before each visit with the oncologist can give him/her the information on the presence and intensity of physical and emotional symptoms.

Disclosure: All authors have declared no conflicts of interest.

1618 IN VITRO DRUG-DRUG INTERACTION STUDIES WITH THE ANTIEMETIC DRUG NETUPITANT AND ITS MAJOR METABOLITES M1 AND M2, INVOLVING SEVERAL HUMAN CYTOCHROME P450 ISOENZYMES

G. Giulian1, E. Lovati1, C. Funk2, M. Potthast3 and G. Pietra4

1Preclinical R&D, Helsinn Healthcare SA, Lugano, SWITZERLAND, 2Non-clinical Drug Safety, Hoffmann La-Roche Ltd., Basel, SWITZERLAND

Introduction: Nausea and emesis are significant adverse events of chemotherapy. Substance P plays a major role in the emetic process especially in the delayed emesis occurring 24h after treatment and beyond. Antagonism of substance P effect at the neurokinin 1 (NK1) receptor level is a validated target in showing a broad antiemetic activity in animal models of emesis and also in humans. Within the new NK1 activity in animal models of emesis and also in humans. Within the new NK1-activity in animal models of emesis and also in humans. Within the new NK1 isoenzyme is the major enzyme involved in the oxidative metabolism of Netu. In vitro studies have shown that the CYP3A4 isozyme is the major enzyme involved in the oxidative metabolism of Netu.

Methods: The in vitro inhibition potential of Netu and its major metabolites M1 and M2 has been studied for the human cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP3A4, CYP2D6 and 3A4 using human liver microsomes and isoform selective substrates.

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 hydroxylation of dexamfenac, 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, CYP19 and 2D6 (IC50, >100 µM).

Conclusions: Significant metabolic drug-drug interactions in human are not anticipated for compounds metabolized mainly by CYP1A2, CYP19 and 2D6 and are very unlikely for CYP2C9 metabolized drugs based on the expected human plasma concentration of Netu in the low micromolar 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 as 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 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.

| Table: 1620 Survival results according to glutamine supplementation (GLT) and weight loss (WL) |
|---------------------------------|---------------------------------|---------------------------------|
| **Median OS (Months)** | **GLT+ and KK+** | **GLT+ and KK-** | **GLT- and KK+** | **GLT- and KK-** |
| (95%CI) | 15.7 (11.8-19.6) | 21.7 (12.1-31.3) | 13.5 (9.8-17.2) | Not reached yet |
| 1-year OS | 65.1 | 93.3 | 60.6 | 98.0 |
| 2-year OS | 12.1 | 44.9 | 3.8 | 58.3 |

1622 A PROSPECTIVE STUDY OF 5% LIDOCAINE PATCH IN PATIENTS WITH CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY

D. Niederniess-Beke1, T. Puntus2, J.-. Ferrari3, A. Flam-Ahorak2 and J. Meran2
1Department of Medicine I, Center for Oncology and Hematology, Wilhelminenspital, Vienna, AUSTRIA, 2Department of Internal Medicine, Barmherzige Brüder Hospital, Vienna, AUSTRIA, 3Department for Neurology, Barmherzige Brüder Hospital, Vienna, AUSTRIA

Introduction: Chemotherapy induced peripheral neuropathy (CINP) is a common problem in oncological patients. With an incidence of 30% - 40% CINP is the major cause for dose reductions and one of the leading causes for treatment discontinuation. Especially taxans, platins derivatives, Thalidomid and vincaincaloids are frequently causing CINP. Depending on the substance used, a pure sensory and painful neuropathy or a mixed sensormotor neuropathy can occur. Currently no standard of care is established.

Methods: 21 patients with CINP Grade > 2 (NCCN-CTCAE v4.0) were included in the study. Up to 4 patches containing 5% lidocain (Versatis®), a locally acting topical anesthetic, were simultaneously applied on the affected areas for a maximum of 12 hours a day. Pain was documented according to the Visual Analogue Scale (VAS) by the patients during the entire treatment phase. Other symptoms like paresthesia were also documented daily.

Results: 21 out of 26 patients were included in the final analysis (7 male and 14 female). In the total study group the VAS score improved in 8 subjects (38.1%). The non-responder group included 13 participants (61.9%). The VAS score remained equal in 7 (33.3%) of the subjects and worsened in 6 (28.6%). In the female subgroup (14 participants) 4 (28.6%) reported an improvement of the VAS. 5 patients (35.7%) reported an intensification of symptoms while using the patch. 4 male patients (57.1%) showed an improved VAS after the application of the lidocaine patch. There were 3 (42.9%) non responders in the male group. No correlation between efficacy and the applied cytostatic agent was found.

Efficacy of lidocain patch

<table>
<thead>
<tr>
<th>Male (%)</th>
<th>Female (14)</th>
<th>N (21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>better</td>
<td>4 (57.1%)</td>
<td>4 (28.6%)</td>
</tr>
<tr>
<td>equal</td>
<td>2 (28.6%)</td>
<td>5 (35.7%)</td>
</tr>
<tr>
<td>worse</td>
<td>1 (14.3%)</td>
<td>5 (35.7%)</td>
</tr>
</tbody>
</table>

The median duration of therapy was 10 days. No participants suffered skin toxicities or any other treatment related adverse events.

Conclusion: Only some patients benefited from treatment with 5% lidocain patch (Versatis®). Due to excellent tolerability and lack of alternative treatments, lidocain patches should still be an option for patients with CINP.

Disclosure: J.-. Meran. Member of the advisory board of Grünenthal company. All other authors have declared no conflicts of interest.

1623 PROPHYLAXIS OF NEUTROPENIA DURING ADJUVANT DAC (DOCETAXEL, DOXORUBICIN, CYCLOPHOSPHAMIDE) CHEMOTHERAPY WITH DICARBAMIN IN PATIENTS WITH EARLY BREAST CANCER

M.V. Kopp1, I.A. Koroleva2, L.V. Shaplygin2 and A.S. Machalova1
1Chemotherapy, Samara Regional Clinical Oncology Dispensary, Samara, RUSSIAN FEDERATION, 2Samara Oncology Center, Samara, RUSSIAN FEDERATION

Background: One of the most serious potential side effects of chemotherapy is neutropenia. Grade 3 and 4 neutropenia is especially problematic because of increased incidence of infections, hospitalization, antibiotic treatment, necessity to reduce therapy intensity. Dicarbamin is agent for the prevention of chemotherapy-induced neutropenia. We conducted an analysis of efficacy of Dicarbamin in patients during Docetaxel-based chemotherapy.

Materials and methods: Between May 2011 and February 2012, 76 patients with early breast cancer were treated with adjuvant DAC regimens (docetaxel 75 mg/m2, doxorubicin 50 mg/m2, cyclophosphamide 500 mg/m2) every 3 weeks. All patients were female. All patients were treated with these regimens without prophylactic growth factor support. 42 patients (244 cycles of chemotherapy) were given...
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 giver 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 special toxicity.

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

---

**1624 NEXT AND VENICE: DESIGN OF TWO MULTICENTRE, PHASE IV, PROSPECTIVE, LONGITUDINAL STUDIES EVALUATING THE SAFETY PROFILE OF A BIOSIMILAR FILGRASTIM IN PATIENTS TREATED WITH CYOTOXIC CHEMOTHERAPY**

S. Fruehaufl, C. Berthou2, S. Lepreterl, L. Cals3, F. Maloisefl and D. Karionem

1Haematolo/Oncologie, Paracelsus Klinik Center for Tumor Diagnostics and Therapy, Osnabrück, GERMANY, 2Département d’Clinique Hématologie, Hôpital Morvan, Brest, FRANCE, 3Département D’Hématologie, 3Centre Henri Becquerel, Rouen, FRANCE, 4Department of Medical Oncology, CHRU de Besançon, Besançon, FRANCE, 5Department of Hematology and Oncology, Clinique Saint Anne, Strasbourg, FRANCE, 6Oncologique Médical et Hématologie, Hôpital Privé de l’Ouest Parisien, Trappes, FRANCE

**Introduction:** 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 in clinical trials. However, the safety of biosimilars in general is closely scrutinised. We present designs for two observational phase IV studies that will examine the safety profile of prophylactic and curative Nivestim™ in patients treated with cytotoxic chemotherapy in real-world clinical-practice.

**Method:** NEXT (Tolérance de Nivestim™ chez les patients traités par une chimiothérapie anticancéreuse en pratique courante) and VENICE (Vérification de l’Éfficacité et de l’Économie de Nivestim™ en pratique courante) are multicentre, prospective, longitudinal, observational studies that aim to monitor 2000 adult and 700 adult and paediatric patients respectively 12 months. The primary objective of the studies is to assess the safety of Nivestim™ in patients undergoing cytotoxic chemotherapy for malignancy through the evaluation of adverse events in all organ system classes, as required by EU pharmacovigilance guidelines. Secondary objectives include obtaining data on efficacy outcomes, lab values, patterns of use of Nivestim™, dose intensity, indications for treatment, patient characteristics, physician knowledge of filgrastim prescribing, and the reasons for choosing Nivestim™. VENICE will also be able to data on levels of CD34+ cells to assess predictive value as a marker of response. Data will be gathered over 3 patient visits: 1) inclusion visit, 2) first follow-up after first course of Nivestim™, and 3) second follow-up after completion of chemotherapy.

**Results:** Accrual figures as of 1 May 2012 are 630 (NEXT) and 136 (VENICE). Completion dates are June 2013 and June 2014 respectively.

**Conclusion:** Data from NEXT and VENICE will provide additional information on the long-term safety and efficacy of Nivestim™ in patients receiving cytotoxic chemotherapy in clinical practice.

**Disclosure:** S. Fruehaufl: Receiving support from Hospira for the conduct of the NEXT study, C. Berthou: Receiving support from Hospira for the conduct of the VENICE study, S. Lepreter: Receives support from Hospira for the conduct of the NEXT study, L. Cals: Received support from Hospira for the conduct of the NEXT study, F. Maloisef: Receives support from Hospira for the conduct of the NEXT study, D. Karionem: Receives support from Hospira for the conduct of the NEXT study.

---

**1625 NEUTROPENIA IN LUNG CANCER PATIENTS TREATED WITH CHEMOTHERAPY IN A ROUTINE CLINICAL PRACTICE – AN INSTITUTIONAL EXPERIENCE**

N.T. Hii1, K. Mohorcic1, A. Sadikov2 and T. Cufer1

1Department of Medical Oncology, University Clinic Golnik, Golnik, SLOVENIA, 2Department of Artificial Intelligence, Faculty of Computer and Information Science Ljubljana, Ljubljana, SLOVENIA

**Background:** Febrile neutropenia (FN) is a serious complication of chemotherapy (ChT). Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Febrile neutropenia (FN) is a serious complication of chemotherapy (ChT). Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT. Lung cancer patients are fragile with much comorbidity mostly receiving ChT.

**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 pts received platinum based chemotherapy (cisplatin 64.7%, carboplatin 20.0%), only 15.3% received other ChT schemas. For most of the pts it was first line ChT (68.8%). Majority of the pts received 6 cycles of ChT (46.3%), 53.7% of pts received 2-6 cycles. Only one patient received ChT 1 cycle.

**Results:** Neutropenia at any time during ChT was reported in 100/190 (52.6%) of pts, in 60/190 (31.6%) of pts it was grade 3 or 4. FN was found in 16/190 (8.4%) of pts. Mostly, neutropenia developed after the first three cycles of ChT (76.0%). One patient died due to FN. There was no correlation between occurrence of neutropenia and Nivestim® vs. carboplatin ChT, nor the line of 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 with FN received standard antibiotic treatment, while secondary prophylaxis with G-CSF has not been initiated in 8 pts due to the dose reductions 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 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.
RETROSPECTIVE ANALYSIS OF CANCER AND CHEMOTHERAPY INDUCED ANAEMIA TREATED WITH FERRIC CARBOXYMALTOSE ONLY, AN INTRAVENOUS IRON THERAPY

B. Tschechne1, S. Broszeit-Lüft2, O. Harlin3, W.O. Jordan4 and H. Zakaria5


Chemotherapy induced anemia is often treated with ESAs and/or blood transfusions. Oral or intravenous iron substitution represent alternatives for both cancer and chemotherapy induced anemia. Current discussions focus on intravenous treatment to increase Hb levels in cancer patients, as oral treatments are often associated with limited response rates and gastrointestinal side effects. This retrospective, single centre analysis investigates the effectiveness of an iv iron compound, ferric carboxymaltose (Ferinject®) as the only anaemia treatment in an unselcted, routinely treated anaemic cancer patient population between 2009 and 2012. Patients fulfilling the following criteria were included in the analysis: malignant cancer diagnosis, anaemia, FCM treatment > 2 weeks, complete available documentation > 12 weeks, no ESA or other iron medication and no blood transfusion during the observation period. At baseline, sex, age, tumour history, anti-tumour treatment and history of anaemia treatment during the four weeks prior to the respective analysis were recorded. Modality of FCM treatment and serum levels of available relevant laboratory parameters (e.g. Hb, transferrin saturation [TSAT], ferritin, haematocrit) were recorded at baseline and throughout the observation period. Treatment response, tolerability and adverse reactions for a total of 59 cancer patients were investigated. The median age was 61 (20-91) years, of these 14 were male and 45 female. During the FCM therapy, 52 patients were not treated actively for cancer and 7 patients were on anticancer treatment. Median Hb increase was 2.0 g/dl compared to baseline (range: 0 to 6.2 g/dl). Patients received an average 336 mg iron (range: 100-1760mg). No adverse events related to FCM were recorded. The results of our retrospective analysis demonstrate the safety and effectiveness of FCM therapy in correction of anaemia in cancer patients prior, during or after completed chemotherapy. More long-term data on FCM exposure in cancer patients with iron deficiency are needed in order to characterize patients benefit most from this therapy and to determine optimal dosing and frequency of FCM use.

Disclosure: B. Tschechne: I am a member of the Advisory Board of Vifor Pharma Deutschland. Harlin: employee of Vifor Pharma Germany. Harlin: employee of Vifor Pharma Germany. H. Zakaria: The data analysis shown was sponsored by Vifor Pharma Deutschland. All other authors have disclosed no conflicts of interest.

ANEMIA POINT PREVALENCE IN PATIENTS RECEIVING CHEMOTHERAPY IN 56 CENTERS IN ITALY AND AUSTRIA

L. Merlini1, G. Carteri2, S. Iacobelli3, C. Stelitano4, M. Airoldi5, P. Balke6, F. Keil7, F. Hinterseer8, L. Belton9 and B. Pujol10

1Medical Oncology, Oncologica Civile S. Bartolomeo, Verona, ITALY; 2Oncology, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, ITALY; 3Medical Oncology, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, ITALY; 4Medical Oncology, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, ITALY; 5Medical Oncology, Azienda Ospedaliero Universitaria di Ferrara, Ferrara, ITALY; 6Medical Oncology, Hospital Universitario La Fe, Valencia, SPAIN; 7Medical Oncology, Hospital Universitario La Fe, Valencia, SPAIN; 8Medical Oncology, Hospital Universitario La Fe, Valencia, SPAIN; 9Medical Oncology, Hospital Universitario La Fe, Valencia, SPAIN; 10Medical Oncology, Hospital Universitario La Fe, Valencia, SPAIN

Purpose: To evaluate the point prevalence of anaemia in patients with non-myeloid tumors being treated with chemotherapy 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 anemic based on 1) hemoglobin (Hb) ≥10 g/dL on/within 3 days prior to visit, 2) ongoing anemia treatment at visit, or 3) physician diagnosis of anaemia together with ≥1 anaemia symptom at visit. Results: For visit, patient demographic, tumor type, systemic chemotherapy, 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 = 642; Austria n = 770). Of these, 14% were men, median age was 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 chemotherapy cycles. The point prevalence of anaemia was 32% (95% CI 29.4%, 34.2%); 14% of patients were defined anemic based on Hb levels ≥10 g/dL, 9% based on evidence of anaemia treatment and 8% based on physician assessed prevalence of anaemia with ≥1 anaemia symptom. Overall, 82% of patients had Hb data; the mean (SD) Hb level was 117 (17.2) g/dL. 32% of patients had anaemia symptoms, the most common were fatigue (28%), dizziness and dyspnea (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 one-third of patients with non-myeloid tumors undergoing chemotherapy were found to be anemic on the prespecified study day. Disclosure: L. Belton: Contract worker for Amgen Ltd, B. Pujol: Employed by Amgen Europe. All 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

N.T. Hilti1, K. Mohoric1, A. Sadikov2 and T. Cufer1

1Department of Medical Oncology, University Clinic Golnik, Golnik, SLOVENIA; 2Department of Artificial Intelligence, Faculty of Computer and Information Science, Ljubljana, Ljubljana, SLOVENIA

Background: Anaemia 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-naive patients with solid tumours, the incidence of anaemia 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 chemotherapy. The primary endpoint 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 61.5 (±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 48.3% 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, 59.3% for lung and 75.5% 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-naive 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.
Physical and Emotional Symptoms in Patients with Solid Haematologic Malignancies Without Metastases: on Cure or Follow-Up: Are They Overlapping?

C.L. Ripamonti1, M.A. Pessi2, A. Maruelli3, G. Muccino4, E. Bandieri6, and B. Buonaccorsi6

1Supportive Care In Cancer Unit, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milano, ITALY, 2Supportive Care in Cancer, Fondazione IRCCS, Istituto Nazionale Tumori, Milano, ITALY, 3Psychology Unit, ILIT and Centre for Oncological Rehabilitation, Azienda Ospedaliero Universitaria, Piacenza, ITALY, 4Supportive Care in Cancer, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milano, Milano, ITALY, 5Epidemiology, Cancer Prevention and Research Institute ISPO Florence, Florence, ITALY, 6Oncological Unit, Azienda USL Modena Ospedale Modena, Mirandola Modena, ITALY

In a prospective study carried out on 88 patients with solid cancer on cure and on 20 and 86 patients with haematologic malignancies (68 on cure) (Group B), we assessed the presence and intensity of physical and emotional symptoms through the Edmonton Symptom Assessment Scale (ESAS). In both groups, whereas no correlation was observed between age or religiosity and ESAS symptoms, a score above the clinical cut off for HADS score above the cut off. Being on cure (rather than in follow up) was associated with dyspnoea for group B only. Uncontrolled pain and drowsiness (score ≥5; p = 0.054 and p = 0.013 respectively) were reported more often in patients with KPS >70 vs those with KPS <70 for group A only. Whereas, for group B the associations with low KPS were for uncontrolled anxiety, not well being and dyspnoea (p = 0.002; p = 0.018 respectively). In both groups patients with higher proportion of uncontrolled depression or drowsiness were significantly associated to receiving psychological support. Pain, anxiety and not-well being were correlated with psychological support. The routine assessment of physical and emotional symptom in patients with both malignancies is mandatory to recognize all the symptoms with a particular attention to the emotional ones. Physical and emotional symptoms in patients with solid and haematologic malignancies without metastases, on cure or follow-up: are they overlapping

Disclosure: All authors have declared no conflicts of interest.

Hemodialysis in Cervical Cancer Patients: Clinical Aspects and Outcome in 95 Patients from the Brazilian National Cancer Institute (INCA)

D.G. Candido Reis1, L.M.O. Soares2, D. Hencherhorn1, I.S. Martins1 and E. Rocha3

1Medical Oncology, Brazilian National Cancer Institute, Rio de Janeiro, BRAZIL, 2Servicio de Infectología, Universidad Federal Fluminense, Niterói, BRAZIL, 3Departamento de Nefrologia, Hospital Universitário Clementino Fraga Filho-UFPR, Rio de Janeiro, BLOUET ISLAND

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 unknown, and it should be better clarified due to its cost and morbidity.

Material and methods: Data were retrospectively assessed from all 95 consecutive patients diagnosed with cervical cancer submitted to renal substitute therapy in the years of 2007/2008, with a follow-up until March 2010. Statistical analysis was performed using software SPSS v11.0. Median Age of Diagnosis and at 1st Hemodialysis (HD) were, respectively, 50.72y (25.39-95.13) and 52.06y (25.41-95.70), 70 pts (73.7%) had stage III or IV at the moment of diagnosis and 81 pts (85.3%) had disease progression between 2007 and 2010. Main reason for the HD was post-renal kidney failure in 84pts (88%). 34 pts (36%) received any kind of chemotherapy at the moment of HD and 5 pts (5%) developed nephrotoxicity due to chemotherapy. 87pts (91.6%) were dead at the moment of analysis, and 67pts (71%) died within the first 3 months after the HD. The Median Survival for the entire cohort was 41 days (CI95: 25.57-55). The main causes of death were cancer (83%) and sepsis (5%). In a Multiple Logistic Analysis using Cox Model, a significant difference was found in the Median Survival in the following categories: Age at First HD (<55 years: 62 days (CI95: 29-970); >55 years: 25 days (CI95: 9-41), HR = 0.259, p = 0.020); Tumor Status at the moment of HD (stable disease/partial response/no evidence of disease: 52 days (CI95: 30-74); Disease Progression/active disease: 39 days (CI95: 20-58), HR = 0.052, p = 0.003); Renal Drainage (not performed: 20 days (CI95: 7-33); performed: 67 days (CI95: 39-95), HR = 2.287, p = 0.003)

Conclusions: Overtreatment is common in oncology, from anti-cancer therapy to supportive care, and this can be hazardous to the patients. Most patients who were submitted to HD in this cohort had active advanced disease, and renal failure seemed to be a surrogate of poor prognostic outcome. Patients who were benefited from HD was those younger than 55y and those with controlled disease.

Disclosure: All authors have declared no conflicts of interest.

Bisphosphonates in Bone Metastatic Patients: Experience of a Bone Metastases Expertise Centre, University of A’Lquila over 17 Years

E. Ricevuto1, A. Iresi1, K. Caronita1, G. Brusa1, P. Laruffa Baldi1, V. Coccione1, E. Piazzu1, L. Rinaud1, A. Teti1 and C. Ficorella1

1Oncologic Division, S. Salvatore Hospital, University of L’Aquila, L’Aquila, ITALY, 2Department of Experimental Medicine, University of L’Aquila, L’Aquila, ITALY

Three hundred and twenty-nine bone metastatic patients (BMP) followed at Medical Oncology Division, San Salvatore Hospital L’Aquila from 1995 were evaluated. Primary tumors were: breast 113, 55%; prostate 29, 14%; lung 26, 13%. Treatment with bisphosphonates was administered in 204 patients, 62% (male/female, 80/124); zoledronic acid and/or intravenous pamidronate 178, 87%; ibandronate 16, 8%; and ibandronate followed by intravenous bisphosphonate 10, 5%. Median duration of treatment was 7 months (range 1-47months), 19.5 months (range 1-57months) and 27 months (range 9-44months), respectively. Features of bone metastases: multiple bone sites 193 (95%), one bone site 11 (5%), osteolytic 124 (61%), osteosclerotic lesions 35 (17%), mixed 28 (14%), underdiagnosed 17 (8%). Involved sites: spinal column, 172 (84%); pelvis/hip, 146 (72%); long bones, 102 (50%); other skeletal sites, 156 (76%). Overall skeletal-related events (SREs) during follow up were 140 (69%); pathologic fracture, 45 (22%); spinal cord compression, 6 (3%); bone RT, 120 (59%); bone surgery, 1 (7%). The first occurring SRE was: pathologic fracture in 28 patients (20%); spinal cord compression, 3 (2%); bone RT, 108 (77%); bone surgery, 1 (1%). Number of SREs in individual patient was: 1 in 54%; 2 in 25%; 3 in 17%; 4 in 7%; 6 in 5% of patients. The most frequent SREs were: pathological fracture, 137 (53%); bone RT, 120 (59%); bone surgery, 1 (1%); spinal cord compression, 6 (3%). Median duration of treatment was from 10 days (range 1-116 days); 3 months (range 1-9 months); 6 months (range 1-18 months). Median time to first SRE after diagnosis of bone metastases was 32 months. Median time to first SRE after diagnosis of bone metastases was 15 days. Median survival after first SRE was 29 months. Events related to bisphosphonate were: acute phase reactions (first 3 days), 6 (2.5%); pyrexia, 5 (2%); bone pain, 2 (0.8%); arthralgia, 1 (0.4%); hypercalcemia, 4 (1.7%); hypocalcemia, 7 (2.9%); toothache, 3 (1.25%); osteonecrosis of the jaw (ONJ), 6 (2.5%); aurita, 1 (0.4%). ONJ before and after introduction of baseline mouth assessment, 4/65 patients (6.1%) and 2/139 patients (1.4%). Our experience confirms the relevance of SREs and efficacy of bisphosphonate treatment in BMP.

Disclosure: All authors have declared no conflicts of interest.

Meeting the Challenge of Oral Anti-Cancer Therapy Education – An Irish Perspective

D.M. Graham, E. Duignan, A. Campbell and K. O’Byrne

Medical Oncology, St James’s Hospital, Dublin, IRELAND

Background: Prescription of oral anti-cancer therapy (OAT) is increasing. Safety and adherence issues surrounding OAT are causing a shift in the traditional roles and responsibilities of oncologists, nurses and pharmacists. The aim of this study was to evaluate education provided to patients receiving OAT and to develop a standardised tool to improve the education process and its documentation.

Methods: Over a 1-month period patients attending St James’s Hospital oncology department for OAT were identified. Charts were reviewed for each of these patients. Analysis: Criteria were established to assess standards of documentation. 1. All charts should have documentary evidence of patient education for OAT. 2. Documentary
evidence should include: side effects, schedule of treatment, support services, storage, handling, disposal and interactions.

Results: During the review period, 35 patients receiving OAT were identified. Of these, 12 patients had documentation of education by a doctor (34%), 15 (43%) by a nurse. Documentary evidence of education about side effects was noted in 22 cases (63%), schedule of treatment in 16 cases (46%), support services in 16 (46%), safe storage in 3 cases (9%), safe disposal, safe handling and interactions in 2 cases (6%). Recommendations for additional training for health care staff included: further training for nurses; education for patients about the tool and clinic; and, following a pilot period, a repeat audit will be performed to assess the effectiveness of the tool. These results will also be presented.

Disclosure: All authors have declared no conflicts of interest.

1635 INTENSIVE CARE AS A KEY PLAYER IN THE CHANGING PARADIGM OF MODERN CANCER CARE: A SINGLE INSTITUTION EXPERIENCE

L. C. Connell1, F. Othman2, B. Marshi3, D. N. Carney1, J. A. McCaffrey4, P. O’Gormann2 & C. M. Kellya

1Medical Oncology, Mater Misericordiae University Hospital, Dublin, IRELAND; 2Department of Intensive Care, Mater Misericordiae University Hospital, Dublin, IRELAND; 3Haematology, Mater Misericordiae University Hospital, Dublin, IRELAND; 4Medical Oncology, Mater Misericordiae University Hospital, Dublin, IRELAND.

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. Clinical-pathological 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 most frequent reasons for admission were sepsis (n = 16, 31%) & had received multiple lines of CT previously. The ICU-specific mortality rate was 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: We performed a retrospective analysis of all patients with cancer treated with cisplatin-based chemotherapy. We also examined the prognostic value of patients baseline and treatment characteristics in predicting TEE occurrence.

Disclosure: All authors have declared no conflicts of interest.

1636 A PROSPECTIVE STUDY OF SUBACUTE THYROID DYSFUNCTION FOLLOWING SUPRACLAVICULAR IRRADIATION IN THE MANAGEMENT OF CARCINOMA OF THE BREAST

S. Akyurek1, I. Babaloglu1, S. Yucel2 & S. Cakir Gokce3

1Radiation Oncology, Ankara University School of Medicine, Ankara, TURKEY; 2Biostatistic, Ankara University School of Medicine, Ankara, TURKEY.

Purpose: To evaluate the relationship between irradiation and early thyroid dysfunction, focusing on radiation dose-volume factors.

Patients and methods: Between December 2010 and January 2012 a total of 21 patients with breast cancer received supraclavicular irradiation were evaluated. Thyroid function tests, including serum thyroid stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), were analyzed prior to irradiation and every three months the first year and then 18th month after radiotherapy. Based on each patient’s dose-volume histogram (DVH), total volume of the thyroid, mean radiation dose the thyroid and percentages of thyroid volume which received radiation doses 10-60Gy (V10-V60) were considered for statistical analysis.

Results: Mean TSH levels before irradiation, at 3, 6 and 12 months were 1.4 μIU/ml, 1.5 μIU/ml and 1.7 μIU/ml, respectively. Serum TSH levels did not change significantly at 3 and 6 months after irradiation (p = 0.1). However, a significant elevation was noted at 9 months (p = 0.005). Mean thyroid dose was 32 Gy (19-48 Gy) and mean thyroid volume was 35 cc (24-64 cc). Median values were 8 Gy, 20:30-40:50-90, were 68%, 58%, 55%, 53%, 48% and 0%, respectively. With a median follow-up was 9 months (range, 3-18 months), only one patient (5%) developed clinical hyperthyroidism requiring thyroid replacement treatment.

Conclusion: As we expected, gastric and pancreatic cancers had the highest incidence of TEE. We verified a very high incidence of TEE in patients treated with cisplatin-based chemotherapy. We also examined the prognostic value of patients baseline and treatment characteristics in predicting TEE occurrence.

Disclosure: All authors have declared no conflicts of interest.

1637 COMBINATION OF SERUM PROCALCITONIN AND C-REACTIVE PROTEIN LEVEL AS A DIAGNOSTIC MARKER OF DISCRIMINATING INFECTION FROM NEOPLASTIC FEVER IN FEBRILE LUNG CANCER PATIENTS

K. Miyamoto1, R. Seki2, D. Taniyama1, H. Kamata1 & F. Sakamaki1

1Pulmonary Medicine, Saiseikai Central Hospital, Minato-ku, Tokyo, JAPAN; 2Pathology, Saiseikai Central Hospital, Tokyo, JAPAN.

Background: Neoplastic 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 neoplastic fever and infection.

Methods: We reviewed the medical records of 112 consecutive febrile episodes of 52 patients (39 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 neoplastic 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/ml were the most sensitive from ROC curve for discriminating infection to neoplastic fever.

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

Disclosure: All authors have declared no conflicts of interest.

1638 INCIDENCE OF THROMBOEMBOLIC EVENTS IN PATIENTS TREATED WITH CISPLATIN-BASED CHEMOTHERAPY

A.C. Fernandes1, S.R. Meireles2, I. Augusto3, L. Aguias4 & M. Damasceno5

1Oncologia Médica, Hospital de São João, Porto, PORTUGAL, 2Medical Oncology Department, Hospital São João, Porto, PORTUGAL.

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 examined 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 were deep vein thrombosis (DVT) in 9.9% (14), pulmonary embolism (PE) in 5.7% (8), DVT plus PE in 0.7% (4) and arterial thrombosis in 2.8%. The majority of DVT (51.9%) had a TEE after 63 days, and after the 3rd dose of cisplatin, with a cumulative dose of 160 mg/m2. By univariate analysis, active smoking (p = 0.016), hypertension (p = 0.007), site of cancer (p = 0.025), Khorana site of cancer (p = 0.001), Khorana score (p = 0.004) and risk group (p = 0.004) were all identified as risk factors. However, by multivariate analysis, only hypertension (p = 0.18; HR 3.95; 95% CI, 1.25 to 10.34) and Khorana site of cancer (p = 0.03) retained statistic significance.

Conclusions: As we expected, gastric and pancreatic cancers had the highest incidence of TEE. We verified a high very incidence of TEE in patients treated with cisplatin-based regimens, also described in other published studies. It is therefore
Between June 2009 and October 2010, 102 patients aged ≥65 years who received chemotherapy at Northern Health. For each patient, age, treatment dose at onset, ECOG, presence of metastases, and the reason for admission were documented. Univariate and multivariate logistic regression analysis was used to assess the association between a factor and subsequent hospitalization. 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 aged ≥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-related reason. After adjusting for age there was a trend for patients on full chemotherapy to have a decreased risk of admission (OR 0.50, 95%CI 0.21-1.12, p = 0.116). A multivariate model found that after adjusting for age and treatment dose, there was a trend for the presence of metastases at baseline (OR 2.6, 95%CI 0.88-4.85, p = 0.095) and the presence of cardiac comorbidities (OR 2.35, 95%CI 0.90-6.11, P = 0.080) to be associated with an increased risk of admission.

Conclusion: In this cohort 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.

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 amiphostine and melatonin as radioprotectants 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 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 rat to a total dose of 24 Gy in 3 fractions with the contralateral right leg as the non-irradiated control. 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 ZA to the irradiated groups reduced the mean percent overall limb growth loss and the mean percent overall limb discrepancy to 28.5 ± 5.6 and 4.4 ± 3.3, 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.
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.

**1705**

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

H. Kato¹, T. Mineta², K. Chikamori², N. Hamajima², S. Koyama³, H. Kushihara³, B. Hiroshiki⁴, M. Yamauchi⁴, K. Kawada¹ and F. Nomura¹

¹Medical Oncology, Japanese Red Cross Nagoya First Hospital, Nagoya, JAPAN
²Nursing, Japanese Red Cross Nagoya First Hospital, Nagoya, JAPAN
³Pharmacy, Japanese Red Cross Nagoya First Hospital, Nagoya, JAPAN
⁴Nutrition, Japanese Red Cross Nagoya First Hospital, Nagoya, JAPAN

**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.