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supportive care

988O PROPHYLAXIS OF CHEMOTHERAPY-INDUCED ORAL MUCOSITIS: DOUBLE BLIND PLACEBO-CONTROLLED RANDOMIZED STUDY OF CHLORHEXIDINE VERSUS PLACEBO AND WITH NONBLINDED RANDOMIZED COMPARISON TO ORAL COOLING (CRYOTHERAPY)

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Purpose: Oral mucositis is a frequent complication to many chemotherapy regimens in conventional doses. Chlorhexidine prophylaxis has been beneficial in some studies and suggested detrimental in others, but never compared to oral cooling (cryotherapy). This 3-arm randomized study compared all these prophylactic measures.

Methods: Previously untreated patients (pts) with GI-cancer receiving bolus 5-FU 425 mg/m^2 with leucovorine 20 mg/m^2 daily in five days were randomized, pending informed consent, to either chlorhexidine 0.1% 15 ml mouthrinse one minut TID for 3 wks. (regimen A), or to double blind placebo (normal saline with same taste additive as in A) with same dose and frequency (reg. B), or to cryotherapy with crushed ice 10 min. before to 35 min. after chemotherapy start (reg. C). Pts self-reported on severity (CTC-grading) and duration of oral mucositis.

Results: Among 225 pts randomized, 206 answered the questionnaire (70, 64, and 63 pts in reg.A, reg.B, and reg.C) There were no differences between the regimens with respect to diagnoses, stage, age, gender, smoking habits, or performance status. Mucositis grade 3–4 (impaired oral nutrition/need of artificial nutrition) occurred in 13%, 33%, and 11% in regimens A, B, and C, respectively. Reg. B was significantly worse than A ($p<0.01$) and C ($p<0.005$). Median mucositis durations were A: 3 days (0–17), B: 5 (0-20), and C: 1 (0–20). Duration was significantly longer in B than in both A ($p=0.035$) and C ($p=0.003$).

Conclusions: Frequency and duration of oral mucositis may be significantly improved by either prophylactic chlorhexidine or by cryotherapy. The latter is easy and inexpensive but is drug- and schedule-dependent as it cannot be used with infusional 5-FU or with chemotherapy with substantially longer half-lifes than 5-FU.

989O IDENTIFYING POTENTIAL MUCOSITIS-RELATED INFECTION RESOURCE USE IN SOLID TUMOR CANCER PATIENTS

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Objective: Mucositis is a common side effect of therapies used to treat solid tumors. Most research has focused on a small set of healthcare resource utilization (HCRU) variables: hospitalization days, total parenteral nutrition (TPN), gastronomy tube placement, pain medication, and antibiotics. The objective of this study was to explore HCRU connected with inpatient diagnostic or surgical procedures associated with mucositis-related infections.

Methods: This was a claims-based analysis of the Premier Prospective Comparative Database, a compilation of inpatient diagnostic, treatment and cost data from >13 million patients from >400 hospitals in the U.S. This analysis included hospitalizations between 10/1/04 and 9/30/05 with the following cancers (ICD-9 codes): head & neck (140–149, 160–161), colorectal (153–154), lung (162), breast (174), ovary (183). Two cohorts were defined: (1) Any hospitalization with a 2° diagnosis of the cancers listed (N=70,458); (2) Patients with a 2° diagnosis of these cancers and a 1° diagnosis of an infection possibly attributable to chemotherapy-induced mucosal barrier injury as the inductive event, including septicemia (due to escherichia, pseudomonas, other gram negative organisms or streptococci), bacteremia, and disseminated candidiasis (N=737). ICD-9 procedures were listed by prevalence for each cohort.

Procedure	All hospitalizations N=70,458 Percent (95% CI)	Mucositis-related infection hospitalizations N=737 Percent (95% CI)
Transfusion	10% (9.8–10.2)	36% (32.5–39.5)
Vascular catheterization	7% (6.8–7.2)	23% (20.0–26.0)
TPN/G tube/Other nutritional	4% (3.9–4.1)	10% (7.8–12.2)
Mechanical ventilation	3% (2.9–3.1)	8% (6.0–10.0)
GI scope or imaging	5% (4.8–5.2)	7% (5.2–8.8)

Results: Table 1. Most common procedures among patients hospitalized with probable mucositis-related infections vs. all hospitalized patients

Conclusion: Transfusions, vascular catheterizations, TPN and other nutritional supplementation, mechanical ventilation, and GI scoping/imaging were all higher in the cohort of patients with likely mucositis-related infections. Studies examining the economic impact of mucositis need to consider the use of HCRU (and potential costs) associated with mucositis-related clinical conditions like septicemia, bacteremia and disseminated candidiasis.

990O RISK ASSESSMENT MODEL FOR FIRST-CYCLE CHEMOTHERAPY-INDUCED NEUTROPENIA (CIN) IN PATIENTS WITH SOLID TUMOURS (ST). ON BEHALF OF THE DELFOS STUDY GROUP

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Background: CIN, the major dose-limiting toxicity of chemotherapy (CT) is directly associated with concomitant morbidity, mortality and costs having strong impact both on health and on health care systems.

Objective: to determine a predictive model for first-cycle CIN in patients (pts) with ST to help establishing appropriate protocols in routine patient care, hence improving clinical decision-making.

Methods: Data was obtained from the Delfos Study, a multicentre non-interventional prospective-cohort study in Spain. This study has completed enrolment and data are available for this planned analysis. To obtain the predictive logistic regression model (LRM), the hierarchical principle was followed as a way to enable results replication. The model was implemented for CIN defined as neutropenia grade ≥3 (with or without body temperature ≥38 C°). A ROC Curve was used to determine the model's sensitivity and specificity.

Results: A total of 1,194 pts (56% female; mean age: 58 yrs (SD: 12); 93,9% ECOG status ≤ 1) with ST(breast, 37,9%; lung 17.6%; colorectal, 15%; other 29.5%) were included in 88 Spanish oncology health centres. The LRM obtained predicted the CIN (pChi-sq<0.0005) containing the following factors: gender, treatment intention, ECOG status, baseline lymphocyte count (BLC), baseline neutrophil count (BNC) and the interaction gender-treatment intention. From those, the following were statistically significant: ECOG status 2 vs 0- ($p=0.003$; OR=3.12), BLC ($p=0.011$; OR=0.67), BNC ($p=0.026$; OR= 0.90) and the interaction between gender and treatment intention ($p = 0.012$). Inherent sensitivity and specificity of the equation were, respectively, 62.6% and 67.1%.

Conclusions: A risk prediction model for first-cycle CIN in pts with ST has been implemented. Four prediction factors were identified. BNC and BLC were inversely associated with toxicity. Toxicity increased with higher ECOG values. The interaction gender-treatment intention reflects the weight of the breast cancer female population in the study sample.

991O PYRIDOXINE IS NOT EFFECTIVE FOR THE PREVENTION OF CAPECITABINE-INDUCED HAND FOOT SYNDROME (HFS): RESULTS OF A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

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Background: Although pyridoxine has been used empirically for the prevention of capecitabine-induced HFS, its efficacy has not been proven yet.

Method: Chemotherapy-naive patients with gastrointestinal tract cancers who will have capecitabine-containing chemotherapy were randomized to receive either oral pyridoxine (200 mg/day) or placebo daily during chemotherapy after stratified by chemotherapy regimen: 1) capecitabine alone, 2) capecitabine and cisplatin, or 3) capecitabine, docetaxel, and cisplatin. The patients were observed until grade 2 or 3 HFS (by NCI CTC version 2.0) developed or capecitabine-containing chemotherapy ended. When grade 2 or 3 HFS developed in patients in placebo group, they were randomized again to receive either pyridoxine or placebo for next cycle of chemotherapy in order to determine whether pyridoxine could prevent the recurrence of severe HFS.

Result: From July 2004 to March 2006, total 382 patients were entered onto the study. Twenty nine patients (15 in placebo group and 14 in pyridoxine group) were excluded because of ineligibility or patients' refusal. Patients' characteristics were well balanced except more female in placebo group. Grade 2 or 3 HFS developed in 55 of 176 (31.3%) patients in placebo group and in 57 of 177 (32.2%) in pyridoxine group. (p=.91) The median number of chemotherapy cycles to grade 2 or 3 HFS was 3 in both groups. The cumulative dose of capecitabine until occurrence of grade 2 or 3 HFS was not different between the two groups. (116720.6 mg/m2 vs 116184.2 mg/m2, p=.83) Among the 44 patients in placebo group who had grade 2 or 3 HFS and were randomized again, there was no significant difference between the placebo and pyridoxine groups in the proportion of patients with improvement of HFS (43% vs 48%, p=.94). Prognostic factor analyses showed that age and the development of stomatitis during the first cycle were independent risk factors for the development of grade 2 or 3 HFS (OR: 1.57, 95% C.I.:1.05-2.36, p=.03, OR: 1.51, 95% C.I.:1.00-2.36, p=.00, respectively).

Conclusion: These results indicate that pyridoxine is not effective for the prevention of capecitabine-induced HFS.

992O ELTROMBOPAG, A NOVEL, ORAL PLATELET GROWTH FACTOR, IS WELL TOLERATED AND INCREASES PLATELETS IN PATIENTS (PTS) WITH IDIOPATHIC THROMBOCYTOPENIA PURPURA (ITP)

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Background: Eltrombopag is an investigational oral thrombopoietin receptor agonist that stimulates proliferation and differentiation of megakaryocyte progenitors.

Methods: A prospective, global, double-blind, placebo-controlled, dose-ranging phase II trial, randomized adults with chronic previously-treated ITP and platelet counts <30,000/μL to placebo, eltrombopag 30 mg, 50 mg, or 75 mg administered once daily for 6 weeks. Pts were stratified by splenectomy status, use of concomitant ITP therapy, and baseline platelet counts. The primary efficacy endpoint was the proportion of pts with platelets ≥50,000/μL after 42 days of dosing.

Results: In 95 evaluable pts, platelets increased to ≥50,000/μL in 16% (4/25) of pts on placebo; 28% (7/25) on 30 mg, 67% (16/24, p<0.001) on 50 mg and 86% (18/21, p<0.001) on 75 mg eltrombopag, respectively. Median platelet counts after 6 weeks of dosing were 16,000/μL, 29,000/μL, 132,000/μL, and 202,000/μL for the placebo, eltrombopag 30 mg, 50 mg, and 75 mg arms, respectively. The dose-dependent effect was not affected by any stratification variable. Adverse events (AEs) were similar in all arms, with headache, AST elevation, constipation, and epistaxis as the most common AEs (in ≥5% of pts) in any eltrombopag arm; and fatigue, headache, constipation, diarrhea, peripheral edema, arthralgia, hemorrhoids and dysguesia as most common AEs (in ≥5% of pts) in the placebo arm. During treatment, two serious AEs (SAEs) were reported in 2 pts on placebo; 6 SAEs were reported in 2 pts on 50mg, with no SAEs reported on the 30 mg or 75 mg eltrombopag arms. No other dose-dependent safety concerns were identified.

Conclusions: Eltrombopag was generally well tolerated and associated with increased platelet counts in ITP pts with severe thrombocytopenia. Eltrombopag is currently being examined in other pt populations, including chemotherapy-induced thrombocytopenia.

993P LOW MOLECULAR WEIGHT HEPARIN (LMWH) IN CANCER PATIENTS (PTS) CARRYING BRAIN METASTASES (BM): A RETROSPECTIVE ANALYSIS

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Background: Bm and deep vein thrombosis (dvt) are life treatening conditions because of the risk of endocrinic complications and pulmonary embolism. Post mortem studies show a higher than clinical incidence of bm (25%) and dvt (30-50%) in cancer pts. No literature data are available about the incidence of clinically overt and/or autoptic evidence of both conditions. Anticoagulants are discouraged due to the risk of intra and/or perilesional hemorrage. Brain irradiation enhances the risk of bleeding acting on fragile vessels of bm or surrounding tissue. The authors evaluated the occurrence of intracranial adverse events in pts treated with lmwh.

Methods: The charts of all pts with cancer and bm who underwent lmwh therapy from October 2002 to December 2005 were retrospectively reviewed, collecting data regarding heparin characteristics, anticoagulatory treatment and intracranial adverse events.

Results: A total of 23 patients with bm were treated with lmwh. Gender: m/f 13/10. Mean age: 55 (range 53–73). Lmwh molecules: nadroparin (20 pts); enoxaparin (1); reviparin (2). Tumor type: nsclc (13 pts); breast (6 pts); colon (1 pt); pancreas (1pt); sclc (1 pt); melanoma(1 pt). Indications for lmwh therapy were: dvt and secondary prophylaxis (5 pts); superficial thrombophlebitis (9 pts); intracardiac thrombus (1 pt); mild disseminated intravascular coagulation (4); acute disseminated intravascular coagulation (1); Raynaud phenomenon (1); atrial fibrillation (1 pt); pulmonary embolism (1 pt). Timing of brain radiotherapy administration: before lmwh (11 pts); during lmwh (5 pts); never irradiated (7 pts). Median lmwh drug therapy duration after bm diagnosis: 11.6 weeks (range: 1–36). No patient was affected by intracranial hemorrage and no neurologic status deterioration was recorded.

Conclusion: There are no standard approaches for pts suffering from coagulatory complications and concomitant bm. Prospective studies should be undertaken using hospital databases, analyzing incidence and outcome of intracranial bleeding in a larger cohort of pts. Despite anticoagulatory therapy is not recommended for cancer pts carrying bm, when necessary these pts could safely be anticoagulated with lmwh.

994P THE IMPACT OF ''LAYING ON HANDS'' ON WELL BEING IN PATIENTS WITH ADVANCED CANCER

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Objective: To determine whether the impact of ''laying on of hands'' on well being of patients with advanced cancer is more efficient when performed by a person with ''healing powers'' as compared to an actor.

Patients and methods: A total of 80 patients was registered to participate in a randomized, single-blind phase III trial to evaluate the difference in efficacy of ''laying on hands'' by either a ''healer'' or a sham person (actor). Both arms were designed to consist of a total of 40 patients, divided into 5 groups including 8 patients each. Each patient should receive treatment for 5 minutes, 3 times a week. A ''Well-being scale'' was used to measure differences in treatment outcomes. The primary and secondary endpoint evaluated the difference in the total sum score of the ''Well-being scale'' between the two arms on day 10 or day 5, respectively.

Results: The first run was unblinded by the ''healer''. Hence, only the second run was available for comparison. There was no significant difference in sum-score values between the ''healer'' and the actor (p=0.34) with regard to the primary endpoint or the secondary endpoint (p=0.94). After the second run, the ''healer'' quit and a major protocol violation occurred. Despite this major obstacle, the study was completed by the actor as a descriptive, explorative study. There was a significant decrease in total sum score values after each single treatment (day 1, 3 and 5, p<0.0001, respectively) for all patients. In addition, a significant improvement in symptoms could be found on day 5 (p<0.001) after treatment and day 10 (p=0.0002) as compared to day 1 before treatment.

Conclusion: ''Laying on of hands'' resulted in a significant improvement of cancer related symptoms or cancer-therapy associated symptoms. The magnitude of improvement obtained was similar when 'treatment' was provided by a self declared healer or an actor, although the comparison was hampered by protocol violations by the healer.

995P USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN CANCER PATIENTS: RESULTS OF SURVEY IN THE SINGLE CANCER CENTRE IN POLAND (OLSZTYN)

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Background: The aim of this study was to explore the use of complementary and alternative medicine (CAM) in cancer patients (pts) in the our cancer centre.

Patients and methods: In the April 2006 descriptive questionnaires was collected from 121 pts in the in-patient and out-patient clinic. The mean of age of pts is 54 years (range: 22 - 80), the male/female ratio: 1/3. 32% of responders live in the rural area. 32% of them is the cancer survivors, 30% actually received chemotherapy due to metastatic disease, and 38% as adjuvant setting.

Results: Data suggest that CAM is popular among cancer patients. Current CAM use was reported by 27.6% of responders. Most often shark cartilage and fish oil were used (38%). In the subsequent position mind-body intervention and herbs (Chinese herbs, Vilca cora) were placed. Energy therapies, acupuncture and homeopathy were used uncommonly. 24% of CAM-users reported that used more than one CAM therapy

together. The analysis of responders group showed that the profile of the CAM user in our centre was that of elder people (mean of age: 57 vs 51), female (71%) and city occupier (62%). Pts during adjuvant treatment used CAM most often (52%) than pts during palliative treatment (24%) and survivors (24%). It was interesting that only 86% of CAM-users discussed with their doctor about CAM therapy.
Conclusion: In our centre more than one third (31%) cancer pts used CAM during conventional treatment (adjuvant or palliative) and 20% during follow-up visit. Health-care staff need to be aware of such use of CAM and to be able to educate pts appropriately.

996P A FRENCH NATIONAL SURVEY OF ANAEMIA MANAGEMENT IN PATIENTS UNDERGOING CHEMOTHERAPY – FACTORS AFFECTING SUCCESSFUL TREATMENT WITH DARBEPOETIN ALFA

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Darbepoetin alfa effectively manages chemotherapy (CT)-induced anaemia, a common side effect in cancer patients (pts) receiving CT. This observational study aimed to identify factors leading to successful darbepoetin alfa treatment. A large, retrospective multicentric survey of adult pts with non-myeloid cancer, who had received darbepoetin alfa treatment for ≥3 CT cycles, was conducted between September 2004 and February 2005. WHO status, cancer type, presence of metastases, and haemoglobin (Hb) levels were assessed at baseline, weeks 3 and 6 (CT cycles of 21 days) or weeks 4 and 8 (CT cycles of 15 or 28 days). Evaluable pts (Hb measurements available from baseline to week 6/8) were grouped and classified according to their haemoglobin increase. The primary endpoint of the study was to identify predictive groups representing the overall variation in the patient population. Of 2017 pts in the ITT population, 1865 (92.5%) were evaluable. During the study, 15.9% of pts received blood transfusions; the proportion of pts who reached target Hb of 11g/dL is 77.2% (ITT). Haemoglobin increase in the different groups was found to be correlated with baseline Hb level, indicating that groups with a baseline Hb level <10 g/dL achieved a greater increase than groups with a baseline Hb level >10g/dL. Haemoglobin increase was not correlated with age, sex, presence of metastases, or baseline WHO status. WHO status changes were associated with an increased Hb level; the percentage of pts with a WHO status <2 increased from 68.6% at baseline to 75.4% at week 6/8. Patient subgroups were identified based on the variation in Hb increase, with the best responders achieving a mean Hb gain of 1.65 g/dL at week 6/8. A response was also observed in pts who presented a Hb > 10g/dL. This is important because improving Hb to the range of 11g/dL −12g/dL may yield optimal improvement in health-related quality of life. Darbepoetin alfa treatment was associated with an improvement in WHO status in the patient groups studied.

997P IBANDRONIC ACID IS MORE EFFECTIVE THAN ZOLADRONATE IN LOWER SERUM CALCIUM IN PATIENTS SUFFERING FROM BREAST CANCER AND SEVERE HYPERCALCEMIA

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The aim of this study was to compare the safety and efficacy of ibandronic acid and zoladrodronate in breast cancer patients with severe hypercalcemia. A total of 36 patients suffering from breast cancer with severe hypercalcemia (corrected serum calcium (CSC) 2.7 mmol/L was stratified according to baseline CSC and randomised to treatment with ibandronic acid (n=19) or zoladronate (n=17). Within each treatment group, the dose of bisphosphonate administered was determined by baseline CSC, according to approved dosing recommendations. Ibandronic acid (6 mg) was infused in 15min and zoladronate 4mg in 15 min. and CSC monitored daily. The mean reduction from baseline CSC after four days (primary efficacy variable) was -0,73 mmol/L for ibandronic acid and -0,57 mmol/L for zoladronate (intent-to treat population). Rates of response, time to response and time to onset of calcium lowering were similar. However, in the two strata of patients with higher baseline CSC (3,5 - <4,0 mmol/L and >4,0 mmol/L) (n=11), mean reduction from baseline CSC was significantly greater in the ibandronic acid group (-1,30 and -1,52% than in the zoladronate group (-0,47 and -0,76) (p=0.044 per-protocol analysis). The number of adverse events and their profile did not differ between the ibandronic acid and the zoladronate group. In conclusion, treatment of tumor-associated hypercalcemia with ibandronic acid is at least as effective as therapy with zoladronate. In breast cancer patients with severe hypercalcemia, ibandronic acid therapy appears to be superior to zoladronate treatment in restoring normocalcemia.

998P DENOSUMAB SUPPRESSES BONE TURNOVER MARKERS IN BREAST CANCER PATIENTS (PTS) WITH BONE METASTASES (METS) NAÏVE TO INTRAVENOUS BISPHOSPHONATES (IV BP) REGARDLESS OF ANTI-NEOPLASTIC TREATMENT

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Elevated bone resorption due to excess osteoclast activity is common in pts with bone mets who are at risk for skeletal-related events. Receptor activator of NF-κB ligand (RANKL) is a key mediator of osteoclast formation, function, and survival. Denosumab, a fully human monoclonal antibody, binds and neutralizes RANKL, thus inhibiting osteoclast-mediated bone resorption. An earlier analysis of a phase 2, randomized, active-controlled trial showed denosumab significantly reduced the level of the bone turnover marker (BTM) urine N-telopeptide at week 13 from baseline levels in breast cancer pts with bone mets naïve to IV BP. We now report results of an exploratory analysis evaluating the effects of denosumab on other BTMs by type of cancer-specific therapy. Eligible pts (female; ≥ 18 years-old; breast cancer with confirmed bone mets; naïve to IV BP) were stratified by hormonal therapy (HT) or chemotherapy (CT; classified as CT if receiving both), and randomized to 1 of 6 treatment arms (1 IV BP [zoledronic acid, pamidronate, or ibandronate; open label]; 5 denosumab [double blind]; see table below). The percent change in BTMs from baseline to week 13 was assessed by stratification group. In total, 255 pts were enrolled. The mean age was 57.8 years for all denosumab groups versus 52.0 years for the IV BP group. A majority of pts had bone mets at > 2 sites (74% denosumab; 81% IV BP). Similar numbers of pts received concurrent CT (n=131 [51%]) or HT (n=124 [49%]). Percent change in BTMs is shown (Table). At week 13 denosumab treatment suppressed BTMs to similar levels as IV BP regardless of the type of anti-neoplastic

Percent Change in Bone Turnover Markers From Baseline to Week 13 in Breast Cancer Patients. See abstract 998P

Bone Turnover Markers in Patients Receiving Chemotherapya	IV Bisphosphonate Q4W[b,c] (n=23)	Denosumabd 30 mg Q4W (n=21)	Denosumab 120 mg Q4W (n=22)	Denosumab 180 mg Q4W (n=23)	Denosumab 60 mg Q12W (n=19)	Denosumab 180 mg Q12W (n=23)	Denosumab Total (n=108)
Serum C-telopeptidee (ng/mL)	−78.6 (−89.1, 8.4)	−82.3 (−96.6, −45.2)	−87.6 (−93.2, 76.2)	−85.1 (−95.6,−31.9)	−83.7 (−92.9, 121.1)	−80.2 (−94.1,−7.5)	−84.1 (−96.6, 121.1)
Bone Specific Alkaline Phosphatasee (units/mL)	−36.5 (−78.7, 18.2)	−47.2 (−81.3, 2462.5)	−41.5 (−78.2, 32.7)	−37.0 (−73.9, 30.4)	−33.9 (−72.0, 62.2)	−30.0 (−80.4, 40.7)	−36.3 (−81.3, 2462.5)
Bone Turnover Markers in Patients Receiving Hormonal Therapya	IV Bisphosphonate (n=20)	Denosumab 30 mg Q4W (n=21)	Denosumab 120 mg Q4W (n=20)	Denosumab 180 mg Q4W (n=20)	Denosumab 60 mg Q12W (n=23)	Denosumab 180 mg Q12W (n=20)	Denosumab Total (n=104)
Serum C-telopeptidee (ng/mL)	−81.2 (−91.7, 164.4)	−85.1 (−95.2, −46.1)	−86.2 (−95.3,−52.7)	−83.5 (−97.0,−64.4)	−86.4 (−95.2, 19.1)	−83.7 (−96.7,−53.3)	−85.3 (−97.0, 19.1)
Bone Specific Alkaline Phosphatasee (units/mL)	−41.4 (−72.7, 16.8)	−40.3 (−62.6, 76.0)	−49.9 (−82.2, 12.8)	−43.2 (−81.1, 13.0)	−37.7 (−81.2, 0.3)	−39.9 (−64.3, 19.0)	−40.5 (−82.2, 76.0)

[a]Values reported are median (minimum, maximum); [b]Q4W is dose administered every 4 weeks, Q12W is dose administered every 12 weeks;
[c]Bisphosphonates were administered according to the country-specific product inserts; [d]Denosumab was administered as a subcutaneous injection;
[e]At data cut-off, not all patients randomized to each treatment group had a week 13 value for the indicated bone turnover markers.

therapy received, confirming the osteoclast inhibitory activity of denosumab. Phase 3 trials evaluating the effects of denosumab on skeletal-related events are in progress.

999P OSTEONECROSIS OF THE JAW (ONJ) DURING TREATMENT WITH BISPHOSPHONATES (B) IN CANCER PATIENTS: A RETROSPECTIVE STUDY

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ONJ is a serious complication of B treatment. To assess the incidence and the outcome of ONJ, we evaluated retrospectively 135 pts (82 females, 53 males), who received from 10/2003 to 3/2006 pamidronate (P) 90 mg monthly or zoledronate (Z) 4 mg monthly. Primary tumors: 63 breast, 25 prostate, 16 lung, 6 urogenital, 8 haematological, 17 other sides. ONJ was diagnosed in 14/135 (10%) pts, 64.5 years (49-77), 7 females and 7 males. All pts were treated with Z (total 277 cycles, range 8-43; median cycles/pt 19.7) and 4 pts were pretreated also with P (total 124 cycles, range 12-43, median cycles/pt 31). Primary tumors: 7 breast, 1 kidney, 2 lung, 1 head-neck, 1 thyroid, 1 NHL, 1 sarcoma. Concomitant therapies: 13 pts were treated with chemotherapy (CT); 7 hormonotherapy; 2 radiotherapy, one encephalic and one head-neck region; 4 pts received steroids. Significant medical history: 4 pts had diabetes and 8 pts had a recent history of dentoalveolar procedures. The presenting symptoms of ONJ were: multiple recurrent alveolar abscesses 9 pts, oral pain (without abscess) 3 pts, dental mobility 1 pt, paresthesia of the lower lip 1 pt. The diagnosis was histological in 6 pts, radiological (loss of bone density at sites of osteonecrosis) in 3 pts and clinical (exposed bone) in 5 pts. The treatments were: antibiotics 10 pts, curettage 3 pts, hyperbaric oxygen therapy 3 pts (one pt had a pneumotorax), surgical resection 3 pts (one partial maxillectomy, complicated by septic shock and large oroantral communication, one partial mandibulectomy, one segmental mandibular resection). All pts underwent suspension of treatment with B. We remark the increased rate of ONJ related to delivery of B, with an incidence of 10%. Recommendations for cancer patients are preventive dental evaluation prior CT and B administration, good oral hygiene, avoid dental extractions or elective jaw procedures; recommended treatments are non-surgical approach, antibiotics and antifungal agents, antiseptic-containing oral rinses, cessation of B if oral surgery is required.

1000P DENOSUMAB SUPPRESSES BONE TURNOVER IN PATIENTS (PTS) WITH BONE METASTASES AND ELEVATED BONE TURNOVER MARKERS (BTM) WHILE RECEIVING INTRAVENOUS BISPHOSPHONATE (IV BP) THERAPY

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Bone metastases (mets) cause elevated levels of BTM and risk of skeletal-related events (SRE) regardless of the blastic (prostate cancer [PC]) or lytic (breast cancer [BC], multiple myeloma [MM]) aspect of the bone disease. Receptor activator of NF-κB ligand (RANKL), a primary mediator of osteoclastogenesis, is implicated in cancer-related bone disease. Denosumab, a fully human monoclonal antibody, inhibits bone destruction by binding RANKL. Preliminary results of this ongoing, randomized, open-label trial suggest that in pts with elevated urine N-telopeptide (uNTx) levels while on IV BP more achieve normalized uNTx levels after treatment with denosumab than with IV BP. In this analysis, we report the effect of denosumab on additional BTM by tumor type.

Eligible pts (aged ≥ 18 years; solid tumors [except lung] or MM; confirmed bone mets; high uNTx levels at screening [>50 nM bone collagen equivalents/mM creatinine]; ≥ 8 weeks IV BP therapy) are stratified by tumor type and baseline uNTx (50 - 100; > 100), and randomized to 1 of 3 arms: continuation of IV BP every 4 weeks (Q4W) or subcutaneous denosumab injections (180 mg) Q4W or Q12W.

Data from 49 pts are currently available (n=33 denosumab; n=16 BP), of whom 96% had > 2 sites of bone mets. Median time (months) on IV BP was 3.9 for PC (n=24) versus 6.8 for BC (n=20) and 7.9 for MM/other (n=5). Absolute changes in BTM are shown in the Table. In general BTM were suppressed to similar levels in both denosumab treatment groups, and denosumab caused greater decreases in the median absolute change of BTM than IV BP at week 13.

These preliminary data suggest that denosumab decreases bone turnover in pts with elevated BTM receiving IV BP regardless of tumor type.

1001P BISPHOSPHONATES AND JAW OSTEONECROSIS: UPDATED EXPERIENCE WITH IBANDRONATE

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Background: Osteonecrosis of the jaw (ONJ) has recently been associated with the use of bisphosphonates in cancer patients, particularly zoledronic acid and pamidronate. The underlying pathological mechanism for ONJ is uncertain. We investigated the reporting of ONJ following treatment with intravenous and oral ibandronate (Bondronat®), a single-nitrogen, non-cyclic bisphosphonate, for the treatment of bone metastases.

Methods: An electronic search of Roche safety database was conducted of all ONJ or similar events reported cumulatively to Roche by January 31, 2006. The safety database comprises of serious adverse events from clinical trials and serious/non-serious spontaneous reports. Cases were included if ONJ or related conditions including osteomyelitis of the jaw were documented.

Results: Of approximately 720, 000 patients treated with ibandronate, there have been 18 reports (reporting rate=0.0026%): breast cancer, n= 11 (61%), prostate cancer, n=2 (11%), multiple myeloma, n=2 (11%) and immuno/plasmacytoma, n=3 (17%). Ten patients received intravenous ibandronate, five patients received oral ibandronate and information was unavailable for three patients. Seven patients (39%) had previously received an alternative bisphosphonate: zoledronic acid only, 4/18 cases (22%), zoledronic acid and pamidronate, 2/18 cases (11%), clodronate, 1/18 case (6%). In the other 11 cases, prior bisphosphonate exposure cannot be excluded based on the available information. Time to ONJ onset following ibandronate treatment ranged from 2.4 months to 5 years.

Discussion: As with other bisphosphonates, the time to ONJ onset after ibandronate exposure varied from months to years. ONJ associated with ibandronate is a serious, though rare adverse reaction.

1002P RENAL IMPAIRMENT IN CANCER PATIENTS FOLLOWING ZOLEDRONIC ACID OR IBANDRONATE TREATMENT

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Absolute Change From Baseline to Week 13 of BTM in PC Pts or BC and MM/Other Cancer Pts. See abstract 1000P

Prostate Cancer Pts					Breast and MM/Other Cancer Pts				
Bone Turmover Markers	IV BP Arm Baseline	IV BP Arm Absolute Change at Week 13	Denosumab Arms Baseline	Denosumab Arms Absolute Change at Week 13	Bone Turmover Markers	IV BP Arm Baseline	IV BP Arm Absolute Change at Week 13	Denosumab Arms Baseline	Denosumab Arms Absolute Change at Week 13
Serum C-telopeptide (bone resorption) ng/mL					Serum C-telopeptide (bone resorption) ng/mL				
n	6	4	16	12	n	8	8	17	14
Median	1.07	−0.49	1.75	−1.63	Median	0.85	−0.25	0.97	−0.43
(minimum, maximum)	(0.3, 10.5)	(−5.9, 0.4)	(0.2, 6.0)	(−4.7, −0.1)	(minimum, maximum)	(0.4, 2.7)	(−0.6, 0.1)	(0.2, 4.0)	(−3.9, −0.1)
Osteocalcin (bone formation) µg/L					Osteocalcin (bone formation) µg/L				
n	8	5	15	11	n	8	8	17	14
Median	9.85	−2.10	19.00	−8.50	Median	15.35	−1.65	12.10	−2.40
(minimum, maximum)	(6.9, 131.2)	(−11.4, 3.5)	(5.1, 51.8)	(−33.4, 1.0)	(minimum, maximum)	(6.9, 28.0)	(−16.2, 4.4)	(4.3, 28.1)	(−14.0, 11.5)

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Background: This retrospective study compared renal impairment rates in breast cancer (BC), multiple myeloma (MM), prostate cancer (PC) and non-small cell lung cancer (NSCLC) patients treated with ibandronate (IB) or zoledronic acid (ZO).

Methods: Medical records in two German oncology clinics from May 2001 to March 2006 were retrospectively reviewed. Creatinine measurements were analyzed from baseline (before ZO or IB treatment) to last evaluation for each patient. Renal impairment was defined as (1) a serum creatinine (SCr) increase of ≥0.5 mg/dL or ≥1.0 mg/dL from baseline values of <1.4 mg/dL or ≥1.4 mg/dL, respectively, or (2) a ≥25% decrease in glomerular filtration rate (GFR; abbreviated MDRD formula) from baseline. Patients treated sequentially with both ZO and IB were included as separate observations. The Cox proportional hazards (PH) model and the Andersen-Gill (A-G) extension of the Cox model for multiple events analysis were used for multivariate analysis, with controls for: age, clinic site, primary cancer type, baseline SCr or GFR, prior bisphosphonate use, concomitant use of drugs associated with acute renal failure, and renal-related comorbidities.

Results: In 333 patients (BC 188, MM 84, PC 40, NSCLC 21), 257 received ZO and 108 received IB (32 patients had both drugs). Compared with IB, the ZO group had a significantly better baseline renal function (mean SCr 0.86 vs 1.09, p=0.0003; mean GFR 86.7 vs 69.8, p<0.0001). ZO treatment increased the relative risk (RR) and the incidence rate (IR) of renal impairment by ∼2-fold compared with IB (renal impairment rates: ZO 19.1% vs IB 12.0%, RR=1.6, p=0.103 [SCr]; 44.7% vs 34.3%, RR=1.3, p=0.064 [GFR]; IR: 0.53 vs 0.19 events per person-year (PPY) [SCr]; 1.82 vs 1.02 events PPY [GFR]; both p<0.0001). Multivariate analysis using the Cox PH and A-G models consistently found significantly higher hazards ratios for ZO over IB, after adjusting for differences in characteristics between the two treatment groups (SCr: Cox=2.4, p=0.032; A-G=7.3, p<0.0001; GFR: Cox=2.0, p=0.012; A-G=3.3, p<0.0001).

Conclusions: In this retrospective review, patients were significantly more likely to experience renal impairment with ZO than with IB.

1003P RAPID REDUCTION IN BONE PAIN FOLLOWING LOADING-DOSE IBANDRONATE IN PATIENTS WITH NEWLY DIAGNOSED BONE METASTASES

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Background: Severe bone pain is often the first symptom of metastatic bone disease. For many patients, analgesics including opioids and radiation therapy are insufficient and are associated with considerable side effects. Several trials have demonstrated that bisphosphonates can provide relief from metastatic bone pain. In particular, phase III studies (in breast cancer) with ibandronate (Bondronat®) show long-term pain relief for up to 2 years with standard doses (intravenous ibandronate 6mg every 3–4 weeks or daily oral ibandronate 50 mg). In addition, phase II studies in patients with urologic cancers suggest that loading-dose ibandronate (intravenous ibandronate 6 mg infused on 3 consecutive days) provides rapid and significant metastatic bone pain relief within days. The aim of the present study was to further evaluate the effects of loading-dose ibandronate in patients with bone metastases from other tumor types.

Patients and methods: Fifteen patients with metastatic bone pain from breast (n=11), lung (n=2) or kidney (n=2) cancer were treated with loading-dose ibandronate. All patients were bisphosphonate-naïve and had received symptomatic pain therapy with opioids or NSAIDs. Patients rated bone pain severity on a daily basis using a numerical rating scale (NRS; from 0 to 10). Within 3 weeks, all patients received further therapy.

Results: Loading-dose ibandronate significantly reduced pain scores within 5–7 days of first infusion. NRS scores were reduced at Day 7 (NRS= 3–4) compared to Day 0 (NRS= 6–7). Reductions in pain scores were achieved without additional palliative therapy. Treatment with loading-dose ibandronate was well tolerated.

Conclusions: Here we report that loading-dose ibandronate results in a rapid reduction in metastatic bone pain (within days). This pilot study, in other tumor types, is in agreement with earlier trials evaluating loading-dose ibandronate. Further clinical trials with loading-dose ibandronate, in a range of tumor types, are warranted.

1004P RENAL IMPAIRMENT (RI) IN MULTIPLE MYELOMA (MM), BREAST CANCER (BC), OR PROSTATE CANCER (PC) PATIENTS RECEIVING ZOLEDRONIC ACID OR PAMIDRONATE: A RETROSPECTIVE STUDY

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Background: Zoledronic acid (ZO) and pamidronate (PA) are associated with an increased risk of RI. We compared RI rates in cancer patients treated with ZO, PA, or no bisphosphonate (NB).

Methods: Medical and pharmacy claims and laboratory data were reviewed from >35 managed care plans from 01/2000 to 12/2004. Inclusion criteria were ≥2 claims for MM, BC, or PC, no gap in health coverage, and serum creatinine readings before and after first ZO or PA infusion. Pts receiving NB served as a reference group. Observation periods extended from initial bisphosphonate (BIS) infusion to health plan disenrollment or BIS switch. RI was defined as ≥25% decrease in glomerular filtration rate (GFR, abbreviated MDRD formula). Cox proportional hazards (COX) models adjusted for demographics, baseline comorbidities, and nephrotoxic drugs were used to analyze time to first RI event. The multivariate Andersen-Gill (AG) extension of the COX model was used to analyze multiple events in a given pt.

Results: There were 561 ZO-treated, 287 PA-treated, and 5,597 NB pts. Compared to the PA group, the ZO group had greater baseline GFR and chemotherapy exposure (both < 0.001). Compared to NB, the ZO group had higher rates of bone metastasis, exposure to chemotherapy/nephrotoxins, and baseline GFR (all p<0.0001). ZO and PA groups had similar RI rates that were significantly higher than the NB group and increased with treatment duration (ZO 19.5%, PA 17.1%, NB 7.3% in pts treated for <6 months; and ZO 48.3%, PA 41.1%, NB 15.5% in pts treated for ≥18 months). Mean RI events per person per year were higher for ZO than PA (1.11 vs. 0.92, p=0.03), and both were greater than the NB group (0.23, p< 0.001). COX and AG models found an increased risk of RI with ZO or PA use vs NB (ZO: Hazards Ratio (HR)=1.92, p<0.0001, PA: HR=1.46, P<0.01 in COX model; and ZO: HR=2.39, p<0.0001, PA: HR=1.62, p<0.0001 in AG model). In both models ZO had a higher risk of RI than PA (HR=1.31, p=0.07 COX model; HR=1.39, p<0.0001 AG model).

Conclusion: This retrospective observational study suggests that both ZO and PA are associated with an increased risk of RI vs NB. There is a significantly higher risk of RI with ZO than PA.

1005P RELATIONS BETWEEN ZOLEDRONIC ACID AND QUALITY OF LIFE IN METASTATIC PROSTATE CANCER

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Background: Bisphosphonates reduced the bone morbidity in patients with cancer and bone metastasis, relief pain and improved the quality of life. Bone metastasis are frequently in prostate cancer patients. Zoledronic acid is the only bisphosphonate who can significantly reduce pain and skeletal-related events in bone metastasis prostate cancer patients.

Purpose: In our study we evaluated the correlation between zoledroanic acid administration and pain relief in symptomatic bone metastasis prostate cancer patients.

Patients and methods: Between feb 2003 and mar 2004 we included 43 patients with a median age of 69,5 years (range 58–81) with bone metastasis. We assess time to pain score decrease, analgesic score decrease and number of skeletal related events. We administrated 4 mg i.v zoledronic acid at 28 days for up to 12 months. The patients were evaluated at baseline and then at 4 weeks interval. We use the visual analogue scale for pain assessment. We also search for adverse events and skeletal related events. The patients complete quality of life questioner every three month.

Results: Among this patients baseline score was 5.1 (range 3 to 8). 9 patients had score 3, 7 patients score 4, 8 patients score 5, 12 patie4nts score 6, 4 patients score 7, 3 patients score 8. After the first dose the median pain score was 4.6. After 6 month the main pain score decrease at 1.8. 9 patients have no pain at this time (6 month). The median time to response was 4.2 months (2- 9 months) and median response duration 6 months (2–13 months). We had only one skeletal-related event. We have no major toxicities.

Conclusions: Zoledronic acid is an effective treatment for bone metastasis, with decrease of pain score, with a response in 4.2 months and a good maintenance of response for 6 months. Our data suggest that such treatment may improve the quality of life in this subgroups of patients.

1006P RENAL SAFETY AND TOLERABILITY OF IBANDRONATE IN CLINICAL PRACTICE: POST-MARKETING EXPERIENCE IN GERMANY

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Background: In November 2003 ibandronate (Bondronat®) was launched in Germany for the treatment of skeletal complications in breast cancer patients with bone metastases. We report here an interim analysis of renal safety and tolerability data (from the perspective of physicians and the patients) from a post-marketing surveillance of ibandronate.

Patients and method: In this interim analysis, 551 patients were evaluated (aged 62.8 ± 11.9 years). A further 1000 patient records are planned for the final analysis (1500 total). Approximately 40% of patients had prior bisphosphonate therapy, and 2% were completely without prior therapy. In this 24-week study all patients received standard-dose ibandronate (intravenous 6mg every 4 weeks [86%] or daily oral 50mg [11%]). Renal safety was monitored using serum creatinine levels. Tolerability was assessed using a standard scale (range: poor, moderate, good, excellent).

Results: Initial creatinine levels were lower (non-significant) for bisphosphonate naïve and ibandronate pre-treated patients (0.9 ± 0.3 mg/dL) versus pre-treatment with other bisphosphonates (1.0 ± 0.4mg/dL). Mean (± SD) baseline creatinine values (0.9 ± 0.3 mg/dl) remained stable throughout ibandronate treatment (maximal average variation 0.1 ± 0.2mg/dl per patient). No renal failure was observed during the study. Nearly all physicians (98%) rated ibandronate as good or excellent. Patient-assessed tolerability was also high (97% rated ibandronate as good/excellent). Patients with a history of bisphosphonate pre-treatment showed a clear preference for oral ibandronate (15% ibandronate pre-treatment, 16% other bisphosphonate pre-treatment, 8% with bisphosphonate naïve).

Conclusion: These data suggest that the renal safety profile of ibandronate in clinical trials transfers to actual clinical practice. Both formulations of ibandronate were rated as well tolerated by both physicians and patients, with the oral formulation preferred by long-term patients. A total of 1500 patients are planned for the final analysis. This represents a large patient group in the clinical setting and is likely to provide further evidence of the safety and tolerability of ibandronate.

1007P REDUCTION OF MYOCARDIAL MASS FOLLOWING ANTHRACYCLINE TREATMENT FOR HAEMATOLOGICAL MALIGNANCY OR SOLID TUMORS

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Aim: The long-term survival from haematological malignancy or solid tumors results in the development of a population of cancer patients with a history of a previous exposure to anthracyclines during their chemotherapy course. We evaluated the impact of anthracycline chemotherapy in the myocardial mass growth, short term following anthracycline treatment for haematological malignancy or solid tumors.

Patients and method: The population studied were 34 asymptomatic patients with haematological malignancy or solid tumors (20 male, 14 female, mean age 68 + 5 yrs) with a history of anthracycline chemotherapy for hematologic malignancy or solid tumors, diagnosed at a mean age of 71,2 years. The average cumulative anthracycline dose was 275 mg/m^2 (range 50–600 mg/m^2).

Left ventricular myocardial mass (LVM) was determined by echocardiography, using the Devereux formel, and indexed on height (H). The normal values of LVM/H were determined in our population, using as controls a group of 118 healthy adults, evaluated for innocent heart murmur. The resulting regression of LVM on height was used to derive the expected value of LVM for each patient. The difference of the two values of LVM (expected and measured) for each patient, was expressed as percentage of the expected LVM, with negative values corresponding to LVM reduction.

Results: All patients had a normal systolic ventricular function (FS>31%). 22 patients (64,7%) had lower than expected values of indexed myocardial mass (-22%, range -55% to -6%). The median difference (%) of the two values in the whole population studied was -16%. Patients having received higher anthracycline cumulative dosis had significantly lower than expected myocardial mass (correlation coefficient r = -0.64, P=0.001).

Conclusions: The reduction of myocardial mass in asymptomatic cancer patients having a normal left ventricular systolic function, following anthracyclines for haematological malignancy or solid tumors might had a substantial impact in long-term survivors.

1008P MONITORING OF CARDIO-SPECIFIC MARKERS AND MARKERS OF THYROID GLAND FUNCTION IN ONCOLOGICAL PATIENTS

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Aim of the study: The aim of this study was to assess the changes of cardio-specific enzymes in patients treated with radiotherapy and chemotherapy and also to evaluate the incidence rate of the pathological values of the thyroid function markers in cancer patients treated by 5 fluorouracil (5-FU) regimen.

Materials and methods: Cardio-specific enzymes were assessed in a total of 37 patients treated with radiotherapy (group I) and in a total of 42 colorectal cancer patients treated with 4 cycles of adjuvant or palliative chemotherapy with 5-FU regimen (group II). In 30 patients of the group of colorectal cancer patients we also evaluated the markers of thyroid function (group III). The following markers were assessed: cardio-specific enzymes (BNP, NT- pro BNP, Troponin I, Seristra) and markers of thyroid function (TSH, fT4, anti TPO).

Results: In group I 30% of patients (11/37), after completion of radiotherapy, had pathological values of BNP (above 100 pg/L) suggestive of cardiovascular disease. In group II we confirmed an increase in serum levels of BNP and Troponin I with a high incidence rate. In group III we confirmed hypothyroidism in 15% of patients (3/20) and hyperthyroidism also in 15% of cases (3/20).

Conclusions: Based on our results we can conclude that is very important to monitor the side effect of anti- cancer therapy using laboratory methods. It is very important in a situation where conventional imaging methods are not available or their prompt interpretation is missing.

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1009P PHARMACOKINETICS OF ESCALATING DOSES OF DARBEPOETIN ALFA IN PATIENTS WITH SOLID TUMORS UNDERGOING CHEMOTHERAPY

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Background: Darbepoetin alfa (DA), the long-acting erythropoiesis-stimulating protein, is administered at various dosages and intervals. The pharmacokinetic (PK) profile of DA, however, is limited. We, therefore, conducted two studies in patients receiving multiple cycles of chemotherapy to evaluate the PK, safety, and haemoglobin (Hb) - increasing effects of escalated doses of DA in Japan.

Patients and methods: Anemic patients (Hb ≤ 11.0 g /dL) with solid tumors undergoing multiple chemotherapy cycles were administered DA subcutaneously (SC) at doses of 1.0, 2.25, or 4.5 mcg/kg once a week (QW) or 6.75 or 9.0 mcg/kg every 2 weeks (Q2W). DA was withheld if Hb increased to 14 g/dL in women or 15 g/dL in men. PK profiles were estimated after the first DA injection.

Results: A total of 37 patients were registered and recieved DA. Serum concentrations of DA were slowly absorbed after SC administration with a mean time to reach maximum serum concentration (t_{max}) of approximately 3 to 4 days for all DA dosages. The elimination half-life of DA was long and estimated to be 92.5 ± 39.2 and 107.9 ± 71.9 hours (mean ± SD) for 6.75 and 9.0 mcg/kg/Q2W, respectively, however the duration was insufficient to estimate the terminal half-life in QW DA administration. The maximum serum concentrations (C_{max}) and areas under the time-concentration curve (AUC) increased with dose in a linear manner across the dose range of 1.0 to 9.0 mcg/kg DA (see table below), and there was no unexpected accumulation. Hb was increased at all DA dosages. No dose-dependent adverse events or adverse effects associated with a drug-induced maximum Hb concentration were observed.

Conclusions: SC administration of DA at a dose ranging from 1.0 to 4.5 mcg/kg/QW and from 6.75 to 9.0 mcg/kg/Q2W was well-tolerated and the PK parameters of DA were linear. DA can be administered at various dosages and intervals to patients with chemotherapy-induced anemia.

Summary statistics for non-compartmental PK parameters, cycle

Dose (mcg/kg)	1.0 (n=8)	2.25 (n=8)	4.5 (n=7)	6.75 (n=6)	9.0 (n=8)
Cmax (ng/mL)	4.686±2.129	7.781±2.490	12.247±3.160	17.698±2.870	32.473±9.484
tmax (hr)	78.1±21.4	81.1±22.1	78.6±29.8	71.9±26.2	86.6±33.7
AUC (ng·hr/mL)	477±163	920±345	1408±395	3346±1352	5579±1678

1010P RANDOMIZED PHASEII STUDY OF WEEKLY ADMINISTRATION OF DARBEPOETIN ALFA (DA) IN ANEMIC PATIENTS WITH LUNG CANCER AND OVARIAN CANCER RECEIVING PLATINUM-BASED CHEMOTHERAPY

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Background: Platinum-based chemotherapy in cancer patients results in a high incidence of anemia, which often affects the quality of life (QOL). To evaluate the dose-response and the optimal dosage of Darbepoetin alfa (DA), we conducted a randomized, open-label, multicenter, phase II trial in anemic patients with lung cancer and ovarian cancer in Japan.

Methods: Anemic patients (haemoglobin (Hb) ≤ 11 g/dL) with lung cancer and ovarian cancer receiving platinum containing chemotherapy were randomized at a 1:1:1 ratio to receive DA 1.0, 2.25, or 4.5 μg/kg subcutaneously once a weak for up to 12 weeks. The primary endpoint was to determine the clinically effective dose (CED) of DA in this setting. CED was defined as the dose at which at least 50% of the subjects achieved a Hb response (≥ 2.0g/dl transfusion independent increase in Hb from baseline). Haematologic endpoint, safety evaluation, and assessment of a FACT-anemia questionnaire were evaluated for all patients randomized to receive one or more doses of the study drug.

Results: A total of 128 patients were enrolled in the study. Hb response was observed in 31.6%, 55.6%, and 70.3% of patients in the 1.0, 2.25, and 4.5 μg/kg groups, respectively. The 2.25 μg/kg and 4.5 μg/kg doses met the CED efficacy criterion of at least 50% of subjects achieving a Hb response, however there was no obvious reduction in the median time to Hb response at 4.5 μg/kg compared with 2.25 μg/kg (10 and 13 weeks, respectively). No dose-dependent adverse events were observed. Japanese versions of the FACT-Fatigue scale had a high internal consistency with Cronbach's alpha scores of 0.81 at baseline and 0.93 at the end of the treatment phase. The FACT-Fatigue score also correlated with Hb level and ECOG performance status scores.

Conclusion: DA alleviated anemia caused by platinum-based chemotherapy, and a DA dose of 2.25 μg/kg was the lowest dose that met the CED criteria when administered once weekly. FACT-anemia questionnaires were found to be feasible and reliable for the measurement of QOL in the Japanese cancer population, and cancer patients taking DA had higher Hb concentrations, which correlated with better FACT-Fatigue scores.

1011P IS ONCE WEEKLY DARBEPOETIN ALFA EQUALLY EFFECTIVE AS THREE WEEKLY EPOETIN FOR CHEMOTHERAPY INDUCED ANEMIA IN PATIENTS WITH NONHEMATOLOGICAL TUMOURS?

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Background: Once weekly (QW) Darbepoetin is nowadays used by many oncologists for chemotherapy induced anemia although published data from head to head comparison with thrice weekly (TIW) Epoetin is scanty.

Methods: We randomly treated 110 cancer patients with chemotherapy induced anemia (Hb ≤ 11gr%) with either TIW Epoetin, 10.000 U (20.000 U in nonresponders after 4 weeks, Group A) or QW Darbepoetin alfa, 150mcg (300 mcg as above, Group B). Evaluation was performed on week 4 and 8 including QoL assessment using FACT- An scale.

Results: An increase of Hb from 10.11±0.94 at baseline to 11.02 ± 1.39 at 4 weeks (p=.000) and to 12.09 ± 1.78 at 8 weeks (p=.000) was observed in group A. Hb also increased between week 4 and 8 (p=.000). In group B, Hb increased from 10.26 ± 0.81 at baseline to 10.91 ±1.89 at 4 weeks (p= .003) and to 11.66 ± 2.25 at 8 weeks (p=.000). It also increased between week 4 and 8 (p=.001). In the whole group of 110 patients, Hb increased from 10.2 ± 0.87 at baseline to 10.95 ± 1.71 at 4 weeks (p=.000) and to 11.82 ± 2.08 at 8 weeks (p=.000). It also increased between week 4 and 8 (p=.000). Epoetin dose had to be doubled in 15 of 27 (55.6%) responding patients of group A versus 18 of 39 (46.2%) in group B (P=.61). Blood transfusions were required in 3 patients in group A compared with 9 in group B (p=.35). On an intent to treat analysis, RRs, at 4 weeks, were 46.7% for Epoetin versus 40% for Darbepoetin (p=.56) and they were 55.6% and 56.9%, respectively (p=NS), at 8 weeks, QoL analysis showed that mean physical, social, functional and emotional well-being scores as well as mean fatigue and non-fatigue subscale scores were not significantly different between the two groups.

Conclusions: Once weekly Darbepoetin can be considered an equally effective and more convenient therapy than thrice weekly Epoetin.

1012P A RANDOMIZED, CONTROLLED, NONINFERIORITY STUDY TO ASSESS THE IMPACT OF ONCE PER CYCLE CORRECTION AND MAINTENANCE DOSING OF DARBEPOETIN ALFA (DA) IN PATIENTS (PTS) WITH NONMYELOID MALIGNANCIES WITH CHEMOTHERAPY-INDUCED ANEMIA (CIA)

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Introduction: CIA can occur in cancer pts receiving multicycle chemotherapy (CTX) and can be effectively treated with erythropoiesis-stimulating agents (ESAs) like DA. Once per CTX cycle dosing with ESAs could aid compliance without compromising outcomes.

Methods: This phase 2, 25-wk, open-label, multicenter trial is comparing SC DA either on an extended dosing schedule (EDS: every 2 or 3 wks [Q2W, Q3W,]) or on a weekly schedule (QW) to treat CIA. Eligible pts were ≥18 years, had anemia (hemoglobin [hb]<11.0g/dL) and nonmyeloid malignancies, and were scheduled to receive ≥8 additional wks of CTX on a QW, Q2W (including Q4W with visits every 2 wks), or Q3W schedule. Pts were randomized 1:1 (DA EDS or DA QW) with stratification by CTX cycle length (≤35% of randomized pts received QW CTX), screening Hb (<10 vs. ≥10g/dL), and tumor type (lung or gynecological vs. other nonmyeloid malignancies). The DA QW treatment arm receives 150 mcg every wk regardless of CTX treatment cycle length. The DA EDS treatment arm receives DA in 1 of 2 regimens (300 mcg Q2W when CTX was QW or Q2W; or 500 mcg Q3W). Approximately 750 pts and approximately 135 sites in the USA and Canada are participating in this study. Endpoints include comparing the impact of EDS vs. QW administration on efficacy (including change in Hb from baseline to wk 13 [primary]), patient reported outcomes (PRO), resource utilization, and safety. We will describe outcomes from a planned interim analysis based on accumulated data for pts who have ended the study or have completed at least 13 wks in the study.

Results: Below are the baseline demographics and disease characteristics for the first 386 enrolled pts as of February 17, 2006 (see table below).

	QWn=191	EDSn=194	Alln=386
Sex - Women - n (%)	122 (64%)	138 (71%)	261 (68%)
Race - White - n (%)	151 (79%)	154 (79%)	305 (79%)
Mean (SD) Age - yrs	61.3 (14.1)	61.6 (14.2)	61.4 (14.1)
Age ≥ 65 years old - n (%)	90 (47%)	84 (43%)	174 (45%)
Age ≥ 75 years old - n (%)	33 (17%)	41 (21%)	74 (19%)
Most common primary tumor types -%Breast /%Lung/ %Gastrointestinal	31%/21%/26%	35%/24%/18%	33%/23%/22%

Conclusions: Data from this study should help address whether DA can be administered using a once-per-cycle regimen, synchronous with chemotherapy.

1013P TITLE: WEEKLY FIXED DOSE OF DARBEPOETIN ALFA (DA) IS EFFICACIOUS AND IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH CHEMOTHERAPY INDUCED ANEMIA (CIA). ON BEHALF OF THE AMG-DAR-2002-01 STUDY GROUP

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Background: Anemia is frequently diagnosed in cancer patients(pts) treated with chemotherapy(CT) and appears to have a significant adverse impact on the pts health-related quality of life(HRQoL). We investigated the effect of DA, an erythropoiesis-stimulating protein that can be administered less frequently than rHuEPO, in HRQoL in a group of cancer pts treated with CT.

Methods: Prospective, single-arm, multicenter study performed in 30Spanish centers. Eligible pts were ≥ 18 yrs, anemic(hemoglobin [Hb]≤11g/dL), with non-myeloid malignancies, scheduled to receive≥12 weeks(wks) of CT. Pts were treated with a fixed dose of DA150 mcg QW; the dose was to be doubled to 300 mcg QW if Hb increased ≤ 1g/dL after 4wks. Primary endpoint: hematopoietic response (Hb increase ≥ 2g/dL or Hb12g/dL in the absence of transfusions in the previous 28 days). Secondary endpoints included changes in HRQoL measured by FACT-Fatigue scale score.

Results: A total of 293pts were enrolled: women(56.4%), median age 64.9yrs (range: 20.6–88.4), median weight: 67.0 Kg (range: 40.5–115.0), with lymphoproliferative malignancies (44.3%) and solid tumour (55.7%). Stage III/IV:75.6%. Most (83.7%) pts had baseline Hb between 9–11g/dL. DA was administered for a median of 15.0 wks (range: 1–16). At wk 5, 21% pts had dose doubled to 300mcgQW. Hematopoietic response: 63.8%(95%CI: 58.1;69.4). We found statistically significant increases in FACT-Fatigue score between baseline and wk 6,12 and 16:1.7 (SD:9.2, p=0.008), 2.0

(SD:9.8 p=0.008) and 3.7 (SD: 9.9, p<0.001) respectively. Both groups,solid tumours(t-Test, p=0.02) and lymphoproliferative malignancies (t-Test, p<0.001), displayed significant increases in FACT-Fatigue score from wk0 to wk16. At wk16, statistical significant differences (p=0.0009) in FACT-Fatigue score increase was observed among pts increasing Hb≥2g/dl from wk0 (5,3 points; SD: 8.9) compared to pts with no increase in Hb from wk0 (-4,7 points, SD: 12.0)

Conclusions: Weekly fixed dose DA is effective in the treatment of CIA and significantly improves HRQoL in this routine clinical practice setting.

1014P CLINICAL BENEFIT ASSOCIATED WITH EARLY ERYTHROPOIETIC INTERVENTION IN CHEMOTHERAPY INDUCED ANEMIA (CIA)

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Anemia occurs frequently in patients (pts) receiving chemotherapy (CT). Clinical practical guidelines for the management of CIA recommend the use of erythropoietin (EPO) when Hb≤10.5-11 g/dL. However, maximal incremental gain in Qol was observed for Hb≥12 g/dl, and so the target Hb concentration is 12-13 g/dL. We analyzed the possible advantage in early intervention with EPO in pts receiving CT.

Methods: Pts with Hb≤10.5 g/gL were excluded of the study. Before beginning the CT pts were classified as anemic or no anemic (WHO definition): Anemic pts (Hb in the range of 10.5 and 12 in women or 13 in men) received EPO when Hb decreases 1 g/dl (group A). No anemic pts (Hb>12 in women and >13 in men) were treated when they become anemics (group B). We assessed the level of Hb at the beginning, at 3, 6, and 9 weeks of EPO treatment, as well as number of weeks of treatment with EPO, number of pts than required increment of EPO, response to the treatment, number of pts who required transfusion and percentage of pts that reached Hb≥12.

Results: 588 pts where included, 177 pts (30%) in the group A. 408 pts required EPO: 140 pts (79%) in the group A and 268 pts (65%) in the group B. Mean Hb 0, 3, 6, and 9 weeks of treatment with Epo was showed in table 1. The number of weeks of treatment with EPO was no different between the two groups (7.5 vs 6.2 w), but more pts in the group A required increasing the dose of EPO (33 vs 21%, p=0.008). Response to EPO was greater in group B (56% vs 77%, *P*<0.000). The target Hb≥12 g/dl was reached in 52% vs 76% of the patients (*P*<0.000). 14% of pts in the group A required transfusion during the treatment with EPO and 5% of pts in the group B (*P*<0.000).

Conclusion: Early erythropoeitic intervention in CIA is associated with a greater number of pts with Hb≥12 g/dl (possibly with a major improvement in Qol) and a decreased number of transfusions. The number of weeks of EPO is not different between both approaches and so, no increment of the cost was associated with early treatment with EPO.

Mean Hb (g/dl)	At the beginning	Week 3	Week 6	Week 9
Group A	10.6	11.1	11.1	11.1
Group B	11.5	11.9	11.8	11.7

1015P DARBEPOETIN ALFA (DA) EVERY 3 WEEKS (Q3W) +/– PARENTERAL IRON IN PATIENTS (PTS) WITH CHEMOTHERAPY-INDUCED ANAEMIA (CIA)

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Background and aim: The effect of intravenous (IV) iron supplementation on response to erythropoietic therapy in pts with CIA is unclear. This randomized, open-label, multicentre study was designed to evaluate the safety and efficacy of IV iron vs standard practice in CIA pts receiving darbepoetin alfa.

Methods: Eligible pts had a non-myeloid malignancy and hemoglobin (Hb) < 11 g/dL. DA 500 µg Q3W was administered using the SureClick™ injection device in pts randomized 1:1 to IV iron 200 mcg (single dose Q3W at the same time as DA or in 2 doses of 100 mg within 3 wks) or standard practice (oral iron or no iron). Randomization was stratified by tumour type and baseline Hb category (< 10 or ≥ 10 g/dL). Pts who completed or withdrew from the 16-wk study by 06 Feb 2006 are included in this interim analysis. Missing Hb values and values within 28 days of transfusion were replaced by the last value carried forward.

Results: A total of 196 pts were randomized and received at least 1 dose of DA; of these, 99% were Caucasian and 63% were women; mean age was 61 (SD 11) years. In the standard practice arm, 28 pts (29%) received oral iron. Result are shown in the table.

Conclusions: The combination of DA Q3W and IV iron was well tolerated with no unexpected safety concerns based on the interim results. In the arm that received IV iron, more pts achieved the Hb target and fewer pts had transfusions, suggesting that IV iron supplementation may enhance the response to DA Q3W.

	IV iron	Standard Practice
Safety Analysis Set*, n	102	94
Pts with adverse events, n (%)	80 (78%)	80 (85%)
Pts with serious adverse events (SAE), n (%)	29 (28%)	32 (34%)
Pts with treatment-related SAEs, n (%)	5 (5%)	2 (2%)
Pts with embolic/thrombotic event, n (%)	6 (6%)	6 (6%)
Intent-to-treat (ITT) Set, n	100	96
Baseline HbMean (SD), g/dL	10.0 (0.8)	9.9 (0.9)
Change in Hb from baseline to EOTPMean (SD), g/dL	1.8 (1.9)	1.4 (2.0)
ITT pts on study until at least day 29, n	94	92
Achieved target Hb (≥ 11g/dL) from wk 5 to EOTPCrude% (95% CI)	80% (70, 87)	66% (56, 76)
Transfusion from wk 5 to EOTPCrude% (95% CI)	11% (5, 19)	23% (15, 33)

EOTP, end of treatment period; SD, standard deviation; CI, confidence interval
*Two pts in the standard practice arm were given IV iron and were analysed in the IV iron arm for safety and as randomized for efficacy.

1016P COST AND EFFECTIVENESS OF DARBEPOETIN ALFA ADMINISTERED EVERY 3 WEEKS (Q3W DA) COMPARED WITH WEEKLY EPOETIN ALFA (QW EA) OR EPOETIN BETA (QW EB) IN PATIENTS (PTS) WITH CHEMOTHERAPY-INDUCED ANEMIA (CIA): A RETROSPECTIVE STUDY

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Background and objective: Management of CIA with erythropoiesis-stimulating agents (ESAs) aims at increasing and/or preventing further decline in Hb concentrations and subsequently reducing the frequency of blood transfusions and improving quality of life. This retrospective study was designed to evaluate usage patterns, effectiveness, and associated costs of Q3W DA, QW EA, and QW EB in the clinical practice setting.

Methods: Eligible pts had a diagnosis of non-myeloid malignancy and CIA, and had received at least one dose of Q3W DA, QW EA, or QW EB. Data were collected from treatment initiation up to a maximum of 16 weeks or until treatment discontinuation. Pts with baseline Hb <11 g/dL and receiving ~500 µg Q3W DA, ~40,000 IU QW EA, or ~30,000 IU QW EB were included in the effectiveness analyses. Analyses of treatment (including drug and administration costs) and transfusion costs were performed using Spanish reference data.

Results: Data from 928 pts were collected from 55 centres in 7 countries in Europe. Baseline characteristics were similar between the 3 treatment groups. Overall, most pts (97%) were Caucasian and 59% were women. Mean (SD) age was 61.9 (12.7) years. Over half of the pts (52%) had stage IV disease at diagnosis. The most frequent tumours were breast (18%), non-Hodgkin's lymphoma (17%), and non-small cell lung cancer (14%). Reasons for initiation of ESAs were: anaemia prophylaxis (13%), treatment of asymptomatic anaemia (34%), or treatment of symptomatic anaemia (52%). Mean (SD) duration of treatment was 12.4 (5.0) wks for DA, 11.6 (4.8) wks for EA, and 12.3 (4.6) wks for EB. Q3W DA treatment was 5-10% less expensive than QW EA and QW EB.

Conclusions: Treatment of CIA with Q3W DA was effective and less costly than QW EA and EB.

ESA	N	Median Baseline Hb, g/dL	Proportion with Hb ≥11 g/dL*	Proportion with ≥1 transfusion*
~500 µg Q3W DA	n=325	9.9	82% (76, 88)	31% (26, 37)
~40,000 IU QW EA	n=125	9.8	78% (69, 87)	37% (27, 47)
~30,000 IU QW EB	n=336	9.8	72% (67, 78)	37% (31, 43)

*Kaplan-Meier proportion (95% CI) from wk 1 to end of treatment.

1017P A MULTICENTER PHASE III RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY OF EPOETIN BETA ADMINISTERED ONCE-WEEKLY FOR CHEMOTHERAPY-INDUCED ANEMIA (CIA) IN CANCER PATIENTS: JAPAN ERYTHROPOIETIN STUDY GROUP

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Background: At ESMO 2004 (#830) we reported a dose-finding study of once-weekly subcutaneous (s.c.) administration of epoetin beta, and 36,000 IU was the recommended dose for CIA patients. Since few double-blind placebo-controlled studies of once-weekly erythropoietin have been reported, we evaluated the study with epoetin beta 36,000 IU in view of hematological efficacy, quality of life (QOL) and safety for CIA patients.

Methods: Patients with lung cancer or malignant lymphoma undergoing chemotherapy and having hemoglobin concentration (Hb) of 8.0–11.0 g/dL were randomized to the epoetin beta 36,000 IU group (EPO) or placebo group (Placebo), administered s.c. weekly for 8 weeks. The primary endpoint was the mean change in Hb from baseline to the last evaluation. Hematological response and requirement for red blood cell (RBC) transfusion were also assessed. QOL was measured by FACT-An.

Results: Patients with lung cancer (n = 65) or malignant lymphoma (n = 57) were studied. The mean change in Hb was significantly higher in EPO than in Placebo (1.4 ± 1.9 g/dL vs. -0.8 ± 1.5 g/dL, $p < 0.001$), and the percentage achieving a change in Hb ≥ 2.0 g/dL was 43% (26/61) for EPO but only 2% (1/56) for Placebo ($p < 0.001$). After 4 weeks of administration, fewer RBC transfusion units were required for EPO (10 units, n = 5) than Placebo (26 units, n = 7), and the proportion requiring RBC transfusion or with Hb < 8.0 g/dL was significantly lower for EPO, compared with Placebo (16% vs. 32%, p = 0.046). Changes in the FACT-An total Fatigue Subscale Score (FSS) were less for EPO than Placebo (-0.5 ± 9.4 vs. -4.5 ± 10.0, p = 0.031). In subset analysis for EPO, mean changes in Hb did not differ between PD and non-PD patients (1.3 ± 1.7 g/dL vs. 1.4 ± 2.0 g/dL), but PD patients showed a severe decrease in FSS (-6.8 ± 9.4 vs. 0.19 ± 9.2, p=0.084). No significant differences in adverse events were observed between the EPO and Placebo, and no thrombovascular events related to EPO were observed.

Conclusion: Once-weekly administration of epoetin beta 36,000 IU significantly increased Hb and meliorated the decline of QOL in CIA patients over an 8-week administration period.

1018P ELYPSE 4: A PROSPECTIVE RANDOMIZED TRIAL COMPARING EPOA IN PRIMARY PROPHYLAXIS OF SEVERE ANEMIA REQUIRING RED CELLS TRANSFUSION IN HIGH RISK PATIENTS

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Cancer patients (pts) experience anemia as consequence of therapy or bone marrow invasion. EPO administration has been demonstrated to reduce the risk of transfusion. However, only a limited number of cancer pts receiving CT will experience anemia requiring transfusion. The identification of these pts would be useful in practice. Here we report a phase III trial comparing EPOα (arm1) versus no EPOα (arm 2) in primary prophylaxis of severe anemia in high risk pts (>30% RBC transfusion) according to our risk model (J Clin Oncol 1999).

Methods: Adult pts with solid or hematologic tumors requesting CT were randomized and stratified on Hb level <12g/dL, with one or two of the following criteria Ly count≤700/µL, and PS>1. EPOα was given in arm 1 at the dose of 10000UI/tiw by subcutaneous injection. Primary endpoint was the rate of transfusion; secondary endpoints: overall survival (OS), safety and QoL using QLQC30. The statistical hypothesis was a reduction of 15% of the risk of transfusion in arm1, with α=0.05 and β = 80%. 216 pts were scheduled to be recruited.

Results: 218 pts were included. The median age was 64 years (range 19-85). The most frequent tumors were: breast, sarcomas, lung and ovarian carcinoma respectively. 93% pts had PS>1, 35% pts had Ly counts ≤700/µL. Baseline Hb levels were 10.1g/dl (range 6.9–11.9). Patient's characteristics were well balanced between the 2 arms. 36% pts experience red cells transfusion in arm1 and 58% in arm 2, (p=0.0012). Median follow-up was 12.2 months (ms). Median OS was 7.5 ms (IC95% 5–12 ms) and 6 ms (IC95% 5–8 ms) in arm 1 and arm 2, respectively (p=0.16). Median OS were significantly worse for stratified pts with 3 prognostic factors (8.3 ms) compared to 2 factors (3.6 ms). No difference in adverse events observed between arms (47.3 vs 40.7% form arm1 and 2, respectively (p=0.34)). Number of thrombovascular events were similar in both arms (4.5 vs 3.7%).

Conclusion: The study confirms the significantly reduced transfusion risk by EPO in this high risk group of pts, where more than 50% of pts without prophylactic treatment were transfused. Overall survival was not decreased in the EPO group suggesting no promoting effect for tumor progression by EPOα.

1019P ONCE-WEEKLY 40,000 IU EPOETIN ALFA MIXED TUMOR STUDIES: META-ANALYSIS

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Background: Most chemotherapy (CT) patients (pts) develop anemia during treatment. To assess efficacy and safety across published once-weekly (qw) 40,000 IU epoetin alfa studies, a meta-analysis was needed.

Aims: This meta-analysis was designed to assess the efficacy, rate of adverse events, and potential sources of between-study variations.

Methods: Two independent surveyors extracted data from the 9 completed qw epoetin alfa studies identified by a Medline, Embase and Cochrane Library literature search to create a database. Quantitative analysis included: calculations of combined responses, appraisal of between-study homogeneity, analysis of publication bias, and assessment of the impact of qw epoetin alfa on hemoglobin (Hb) and quality of life (QOL). Analyses were categorized as mixed tumors or specific cancer; this abstract reports mixed tumor results.

Results: Data from n= 4,296 pts, in 6 studies with mixed tumor types, who received CT and qw 40,000 IU epoetin alfa for 16 weeks were pooled in this meta-analysis. The mean pt age was 62.5 years, 63.1% were female, and baseline Hb was 9.8 g/dL. QOL measures evaluated were Cancer Linear Analog Scales (CLAS): activity, energy and overall QOL. Baseline values were 43.4, 43.2, and 46.5 mm, respectively. Hb increase was significant at weeks 4, 8, 12 and end of study (1.0, 1.6, 2.1, and 2.1 g/dL). During study, 17.3% of pts were transfused. Most of the studies defined Hb response as an Hb ≥ 12 g/dL or increase of 1 or 2 g/dL; response rates for qw 40,000 IU epoetin alfa ranged from 45–74%. CLAS score (activity, energy, overall QOL) increases were significant, with increases of 28.8 mm (P=0.02), 23.8 mm (P=0.001) and 22.7 mm (P=0.007), respectively. There was a 7.8% reported incidence of thrombovascular events in the mixed tumor studies, comparable to the 5% epoetin alfa vs 3% placebo reported thrombovascular events in Witzig, JCO, 2005. Also, there was a significant (P<0.001) relationship between CLAS score increase and Hb increase.

Conclusions: Regardless of tumor type in anemic CT pts, qw 40,000 IU epoetin alfa is effective and well tolerated, with a significant Hb increase of 1 g/dL in 4 weeks and 2 g/dL in 12 weeks. QOL increase is associated with Hb increase, supporting the need for effective anemia management.

1020P ONCE WEEKLY EPOETIN BETA 30 000 IU: AN EFFECTIVE AND WELL-TOLERATED THERAPY FOR ANAEMIA IN CHEMOTHERAPY-TREATED PATIENTS WITH SOLID OR LYMPHOID MALIGNANCIES. NAUTICA STUDY INVESTIGATORS

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Introduction: Epoetin, an effective treatment of anaemia in patients with cancer, was traditionally administered via a three-times weekly schedule. However, a once-weekly (QW) regimen would be more convenient and may improve patient compliance.

Objective: We evaluated the efficacy and safety of epoetin beta (NeoRecormon®) 30 000 IU QW in patients with solid or lymphoid malignancies.

Methods: This open-label, single-arm, multicentre study enrolled adult patients with solid or lymphoid malignancies. Patients had anaemia (haemoglobin [Hb], 8–12 g/dl), a WHO performance status 0–2 and were scheduled to receive chemotherapy. Epoetin beta 30 000 IU QW was administered SC for up to 16 weeks. Primary efficacy parameter was change in Hb level. Hb response was defined according to Hb levels at baseline: in patients with Hb levels 11–12 g/dl, response was defined as achievement of Hb level of ≥13 g/dl; in patients with Hb levels <11 g/dl, response was defined as Hb increase of ≥2 g/dl or Hb level of ≥12 g/dl.

Results: In total, 691 patients were included, recruited between 31 Dec 2003 and 30 Aug 2005. Mean (SD) age was 62.6±13.1 years; 53% had solid tumours, 47% had lymphoid

malignancies. Median duration of epoetin beta therapy was 14 weeks. Mean baseline Hb level was 10.1±1.1 g/dl. At endpoint, mean Hb level increased to 12.0±2.2 g/dl. Hb response was comparable in patients with lymphoid malignancies (60%) or solid tumours (61%). Hb response was seen with all types of chemotherapy. Median time to response was 49 (range 10-130) days. For patients with Hb <11 g/dl at entry (n = 540), corresponding to the intervention level recommended by the EORTC, mean Hb increase after 3 weeks was 0.94 g/dl and after 6, 9 and 12 weeks was 1.42 g/dl, 2.03 g/dl and 2.45 g/dl, respectively. Epoetin beta treatment was well tolerated. Thromboembolic events occurred in 7% of patients, a rate consistent with information provided in the current label for epoetin beta.

Conclusion: Epoetin beta 30 000 IU QW is effective in anaemic patients with solid or lymphoid malignancies. QW treatment offers a convenient and well-tolerated therapy for anaemia, which may improve patient compliance.

1021P META-ANALYSIS OF ONCE-WEEKLY 40,000 IU EPOETIN ALFA STUDIES: BREAST CANCER

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Background: Anemia and diminished quality of life (QOL) commonly occur in breast cancer chemotherapy (CT) patients (pts). The number of recently published once-weekly (qw) 40,000 IU epoetin alfa studies prompted a meta-analysis to assess pooled results.

Aims: This meta-analysis was designed to assess the efficacy, rate of adverse events, and potential sources of between-study variations.

Methods: A Medline, Embase and Cochrane Library literature search identified 9 completed qw 40,000IU epoetin alfa studies; from the publications, data was extracted to form a database. Quantitative analysis included: calculations of combined responses, appraisal of between-study homogeneity, analysis of publication bias, and assessment of the impact of qw epoetin alfa on hemoglobin (Hb) and QOL. Analyses were categorized as breast cancer studies or mixed tumor types; this abstract reports the results of the breast cancer studies.

Results: Data from n=2,019 pts in 3 breast cancer studies in which pts received CT and qw 40,000 IU epoetin alfa were pooled for this meta-analysis; two studies were 12 weeks and one was 24 weeks. One study recruited anemic (Hb < 12 g/dL) breast cancer patients, and two had no Hb eligibility criteria. Overall the mean pt age was 52.2 years and baseline Hb was 12.1 g/dL. QOL measures evaluated were Cancer Linear Analog Scales (CLAS): activity, energy and overall QOL, with baseline values were 61.5 mm, 59.1 mm, and 65.3 mm. All pts were female. Objective of the breast cancer studies was to minimize the expected effect of CT on Hb (~2 g/dL Hb drop) and maintain Hb level. Hb change was significant at weeks 4, 8, and end of study (0.5, 0.8, and 1.1 g/dL). All 3 CLAS score increases (activity, energy, overall QOL) were statistically significant when pooled across the 3 breast cancer studies (P <0.001, 0.045 and .02). Pooled breast cancer study reported incidence of thrombovascular events was 6.7%, comparable to the 5% epoetin alfa vs 3% placebo reported thrombovascular events in Witzig, JCO, 2005.

Conclusions: The meta-analysis demonstrated that in breast cancer pts receiving CT, qw 40,000 IU epoetin alfa is effective and well tolerated, ameliorating the impact of CT on Hb level and improving QOL, thus stressing the benefits of good anemia management.

1022P PLATINUM-BASED CHEMOTHERAPY FOR PATIENTS (PT) WITH NON SMALL CELL LUNG CANCER (NSCLC) WITH ANEMIA TREATED WITH EUPOETIN BETA OR BLOOD TRANSFUSION, A PILOT STUDY

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Objective: Anemia is frequent after platinum-based chemotherapy of NSCLC. This study aimed to establish the role of eupoetin beta in management of this anemia.

Methods: Between January and October 2005, 48 Pts with NSCLC and anemia were involved in the study: Lot A (23 Pt) which received eupoetin beta (commercial: Neo Recormon® = NR), and Lot B (25 Pt) which did not receive NR.The doze of NR: 10 000IU, 3 times by week. Pts from Lot B were treated by blood transfusions, iron and vitamins. The chemotherapy administrated for the two groups was a platinum compound plus: gemcitabine or taxanes or eroposid. ''quality of life scores'' (QL) EHA-ASCO was used to evaluate the QL before and after treatment of anemia. The main symptoms evaluated were asthenia, dyspnea and dizziness by a scale of 3 degrees. Time to progression (TP) was established by means of Caplan Meier curves. Intensity of dose was assessed by the number of delayed cycles of chemotherapy.

Results: The main characteristics of patients in the two lots were similar: age mean 55, sex Lot A 2 women, 18 males, Lot B 4 women 21 males. Diagnostic: all Pts had histology documented for NSCLC; the stage was IIIB and IV in similar proportion in the two groups. The incidence of anemia for all Pts was 63.9% grade 1 and 36.1% grade 2. The incidence of main symptoms in the two lots were: dyspnea 56%, asthenia 38%, dizziness 29%. The mean number of cycles of chemotherapy was 4 in Lot A and 3 in Lot B. The score of QL (EHA-ASCO) was similar in Lot A compared with Lot B.

TP was similar in the two groups with a trend to be greater in Lot A.

Response rate to chemotherapy was: 35% for Lot A and (CI 95%: 20.5–45) and 30% for B (CI 95%, 18–39).

Conclusion: The treatment of induced anemia by platinum-based chemotherapy in NSCLC improves QL and allows the dose intensity of chemotherapy to be maintained.

1023P ONCE-WEEKLY EPOETIN BETA TREATMENT IS EFFECTIVE IN PATIENTS WITH SOLID TUMORS – RESULTS FROM THE GERMAN SURVEILLANCE STUDY

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Background: Efficacy and safety of epoetin beta (NeoRecormon®) administration three times a week (tiw) has been shown in all kinds of oncological patients. In patients with hematologic tumors also extended dosing (once weekly, qw) is proven and considered as standard practice but rare data are available in patients with solid tumors.

Methods: The german multicenter surveillance study analysed the changes in hemoglobin under subcutaneous tiw (3 × 10.000 IU) versus qw (1 × 30.000 IU) use of epoetin beta in 1458 cancer patients. Patients with hematologic or solid tumors were included from february 2003 until april 2005. Patients requiring transfusion during the study were excluded from the analysis (n=403).

Results: 24,1% of all patients were treated with platin based and 53% with non-platin based chemotherapy. There was no significant difference in the proportion of patients requiring transfusions independent of platin or non-platin chemotherapy, of tiw or qw dosing scheme and of type of tumor. In 754 (71,7%) patients target hemoglobin level (11 g/dl, consistent with the evidence-based practice guidelines) was achieved after a mean duration of 6 weeks. An increase of hemoglobin of 2 g/dl was reached in 437 (42,6%) patients on average after 8 weeks of epoetin therapy with no significant differences in patients with solid tumors or hematologic malignancies. There was also no difference in proportion of patients treated tiw or qw achieving the target hemoglobin level. 1087 (74,6%) patients had solid tumors. 73% of these patients were treated qw and only 20% were treated tiw. 63% of the tiw treated patients received 30.000 IU weekly and 24% received 10.000 IU weekly. There was no significant difference in hemoglobin increase achieved with qw or tiw application (increase of 1 g/dl: tiw 69,9% versus qw 72,1%; increase of 2 g/dl: tiw 41,1% versus qw 38,4%). Toxicities were similar in all groups. 0,6% (n=9) of all patients showed thromboembolic adverse events.

Conclusions: As proved in hematologic malignancies, once weekly dosing of 30.000 IU epoetin beta in patients with solid tumors is as effective and safe as the established three times weekly dosing scheme.

1024P COMPARING THE EFFICACY OF TWO FIXED DOSE OF EPOETIN ALFA, 40,000 IU ONCE-WEEKLY (QW) VERSUS 10,000 IU THREE-TIMES-WEEKLY (TIW), IN ANEMIC CANCER PATIENTS RECEIVING CHEMOTHERAPY (CT)

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Background: The purpose of this prospective, multicenter, open-label, nonrandomized controlled cohort study was to evaluate the efficacy of two fixed dose of epoetin alfa in anemic patients with solid tumors receiving CT.

Methods: A total of 409 patients (pts) were enrolled: a cohort of 205 pts received epo alfa 10,000 IU TIW and a second cohort of 204 pts received 40,000 IU QW. Epo alfa dose could be increased to 60,000 IU/w depending on Hb response. Efficacy parameters were hematopoietic response (defined as an increase in Hb ≥ 2 g/dL or achievement of a Hb level ≥ 12 g/dL at any time point during the study); changes in hematologic parameters; rate of pts who needed increase epo dose; duration of epo treatment and the rate of pts transfused.

Results: There were no significant differences in baseline clinical characteristics between the two cohorts. Hematopoietic response rate was 67.3% for tiw group versus 71.5% for qw group (p=0.361); mean Hb during epo treatment was 11.4 g/dL (95% CI 11.3–11.6) for TIW versus 11.6 g/dL (95% CI 11.4–11.8) for QW (p=0.176); the mean change in Hb was higher in qw cohort, (1.9 g/dL; 95% CI 1.3-2.1) than in tiw cohort (1.1 g/dL; 95% CI 1.0–1.3) (p=0.007); Hb level at the end of study was 11.3 g/dL (95% CI 11.1–11.6) for TIW versus 11.8 g/dL (95% CI 11.6–12.1) for QW (p=0.007); dose was increased in 36.1% of pts in tiw cohort versus 12.3% in qw cohort (p=0.0001); Mean number of weeks of epoetin treatment was 7.2 w (95% CI 6.6–7.8) for TIW versus 6.2 w (95% CI 5.8–6.7) for QW (p=0,016); mean weeks with escalating dose of epoetin was higher in tiw group (2.1 w; 95% CI 1.4–2.5) than in qw group (0.6 w; 95% CI 0.4–0.8) (p=0.0001). The rate of pts transfused was similar in both groups (13.7% for tiw vs 10.8% for qw; p=0.576).

Conclusion: 40.000 IU QW epoetin alfa seems to have more efficacy that 10.000 IU tiw in maintaining and increasing Hb levels, but with a shorter duration of epoetin treatment and lower need of escalating dose.

1025P THE DEVELOPMENT OF A NEW SCALE FOR ASSESSING PATIENT PERCEPTIONS OF CANCER-RELATED FATIGUE (CRF)

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Background: Instruments are available to measure the intensity, frequency, and duration of CRF and its impact on quality of life, though few include patient beliefs and attitudes regarding CRF. The aim of the present study was to develop an instrument for use in clinical practice which would measure both the intensity and impact of CRF on patients, as well as their attitutudes and beliefs regarding CRF and its treatment.

Methods: An initial item pool was obtained by integrating information from: (1) a literature review performed to identify related studies; (2) content analysis of two focus groups carried out with cancer patients; (3) two expert meetings with oncologists. Items generated in the first phase were administered to a sample of the target population in a multicentre cross-sectional study which would allow for reduction of items to a number suitable for administration in clinical practice. Item reduction was based on statistical analysis (clinimetric and psychometric approaches) and qualitative criteria (expert opinion). Preliminary reliability (internal consistency) was assessed by means of Cronbach's alpha (CA).

Results: The initial item pool of 75 items was administered to 238 cancer patients for item reduction: mean age 57 years, 56% women, 30% breast cancer, 64% with metastasis, mean (SD) Karnofsky score 72.3 (20.2), 46% with anemia, low-to-moderate CRF. 95% of the sample responded at least 85% of items. 50 items were eliminated in statistical analyses, and a further 13 through expert opinion. The final measure for validation consists of 12 items (CA=0.92), distributed in 3 dimensions: physical function (4 items, CA=0.78), activities of daily living (4 items, CA=0.85) and beliefs/attitudes (4 items, CA=0.81).

Conclusions: Results from the item reduction process have led to pre-validated version of the questionnaire with 12 items and 3 dimensions, all with satisfactory internal consistency. Validation of the questionnaire is currently underway.

1026P MONITORING SERUM LEVELS OF DIFFERENT AMINOGLYCOSIDES DURING FEBRILE NEUTROPENIA CAUSED BY NEPHROTOXIC THERAPY

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Background: Fever in cancer patients has been closely linked with infection, especially when the patient is granulocytopenic. Since fever can be the only sign of infection in neutropenic patients, its appearance commands a series of therapeutic measures to be taken empirically without the precise knowledge of the nature of the infection. It should be emphasized that the beneficial effect of aminoglycoside-containing combinations with broad spectrum beta-lactam has been used primarily in severely neutropenic patients. Beside the aminoglycosides marked therapeutic efficacy, their main drawback has been occurrence of nephrotoxicity and ototoxicity in a significant number of patients.

Purpose: The aim of this work was to investigate the possible existence of increased nephrotoxicity caused by once daily aminoglycosides in febrile neutropenic patients who were previously treated with nephrotoxic chemotherapy.

Patients and methods: Thirty one patients with metastatic tumors received standard chemotherapy and as a result, developed febrile neutropenia. Patients were randomized in regard to treatment with cisplatin chemotherapy (n=15) or chemotherapeutic regimen without cisplatin (n=16). Both groups received iv empiric treatment which included combinations of once daily aminoglycosides (amikacin 15 mg/kg or gentamicin 4 mg/kg) with beta-lactams (ceftriakson 2g).

Conclusions: An analysis of the cumulative nephrotoxicity of administrated aminoglycosides, between cisplatin and non-cisplatin patients, revealed a significantly greater occurrence of nephrotoxicity ($P< 0.05$) in those who received cisplatin chemotherapy regimen. An analysis of increased nephrotoxicity revealed a statisically significant difference between various aminoglycosides regimens ($P< 0.05$) manifesting as a greater occurrence of nephrotoxicity in the gentamicin compared with the amikacin groups, predominantly in the cisplatin chemotherapeutic regimen. These results have shown that a cisplatin chemotherapy regimen followed by a once-daily aminoglicosides regimen causes heightened renal toxicity, which is more pronounced in patients treated with gentamicin in relation to amikacin.

1027P 5 YEAR TRENDS IN POSITIVE MICROBIAL CULTURES IN PATIENTS WITH FEBRILE NEUTROPAENIA

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Background: Febrile neutropaenia causes considerable morbidity in patients on cytotoxic chemotherapy although a causative organism is not usually found. In recent years there has been a trend towards fewer Gram negative and more Gram positive infections. This has been combined with a growing level of antibiotic resistance, particularly in some countries. To assess these patterns, data from a supra-regional cancer centre in Ireland was reviewed.

Methods: A 5 year review of all positive microbial cultures in patients undergoing anticancer chemotherapy was carried out. Sources, patterns of infection, neutrophil count, pathogens and antimicrobial resistance were assessed.

Results: There were 2610 positive microbial results, of which, 381 positive cultures were in neutropaenic patients. Amongst neutropaenic patients pathogens were identified from 173 blood cultures. Gram positive organisms accounted for the majority of causes of blood stream infections (71%), with gram negative bacilli (27.8%) and fungal infections (1.2%) making up the remainder. 53.7% of Gram positive organisms were Staphylococci species. Of these, 69.9% were coagulase negative Staphylococci and 30.1% were Staphylococci aureus species. The majority (89.3%) of staphylococci aureus species were methicillin resistant staphylococcus aureus (MRSA). In consecutive years (2001–2005) MRSA was identified from 1,2,21,1 and 0 blood cultures in 1,1,5,1 and 0 patient with febrile neutropaenia. The annual number of patients colonised with MRSA was 9,18,21,20 and 26. The number colonised with vancomycin resistant enterococci (VRE) was 0,2,4,2 and 6. There were no cases of VRE blood stream infections in neutopaenic patients. Overall 22.8% of enterococci were resistant to vancomycin. Most isolates from urine were of Gram negative bacilli with Escherichia coli alone accounting for 40.8% in neutropaenic patients.

Conclusion: Amongst patients with cancer in Ireland who develop febrile neutropaenia there is a large proportion of gram positive infections. MRSA blood stream infection is an important cause of morbidity but absolute colonisation rates are low.

1028P RISK ASSESSMENT MODEL FOR FIRST-CYCLE CHEMOTHERAPY-INDUCED NEUTROPENIA (CIN) AMONG BREAST CANCER (BRCA) PATIENTS. ON BEHALF OF THE DELFOS STUDY GROUP

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Background: CIN is common in BrCa patients(pts) who receive myelosuppressive chemotherapy(CT) and contributes to therapy induced morbidity and mortality. Recent studies suggest that most breast cancer pts develop severe or febrile neutropenia particularly during the first cycle. Objective: to determine a predictive model for first-cycle CIN in BrCa pts.

Methods: Data were obtained from the Delfos Study, a multicentre non-interventional prospective-cohort study in Spain. This study has completed enrolment and data are available for this planned analysis. To obtain the predictive logistic regression model (LRM), the hierarchical principle was followed as a way to enable results replication. The model was implemented for CIN defined as neutropenia grade≥3 (with or without body temperature≥ 38 C°). A ROC Curve was used to determine the model's sensitivity and specificity.

Results: A total of 435 pts with BrCa (99% female; mean age: 54 yrs (SD: 12); 100% ECOG ≤ 2) were included in 77 Spanish oncology health centres. CT and G-CSF (G) use in first cycle were: 89 pts received taxane-based CT (72% with G), 64pts high-dose anthracycline-based CT (9% with G), 237pts low-dose anthracycline-based CT (10% with G) and 45pts CMF CT (4% with G). The LRM obtained predicted the CIN (pChi-sq<0.0005) containing the following statistically significant factors: ECOG status(p<0.0005;OR=9.72), age≥55yrs vs <55yrs (p=0.011;OR=9.99), baseline neutrophils count (BNC)≥1.5x109 vs <1.5x109 -(p=0.019;OR=0.04), treatment regimen-high-dose anthracycline-based vs taxane-based (p=0.031;OR=6.88), and the interaction between treatment regimen and age -category ≥55yrs and high-dose anthracycline-based vs <55yrs and taxane-based-(p=0.013;OR=0.047). Inherent sensitivity and specificity of the equation were, respectively, 57.1% and 75.5%.

Conclusion: A statistically significant risk prediction model for first-cycle CIN in patients with BrCa has been obtained. Four prediction factors were identified: age, ECOG status, BNC and treatment. Increased toxicity of anthracycline-based CT vs taxane-based CT is strongly dependent on the impact of G administration in first cycle.

1029P HEPATITIS B AND C SEROPREVALANCE IN CANCER PATIENTS: A CASE CONTROL STUDY

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Introduction: Patients who give blood and/or blood products or undergo invasive procedures, hemodialysis or hemophilia patients are all under increased risk for hepatitis B and C. The knowledge of hepatitis prevalence and a comparison with the normal population can help in better understanding the problem among cancer patients.
Material and Method: In 2005, 500 cancer patients who had been histologically diagnosed in the Ankara Oncology Hospital were entered into the study along with 500 non-cancer patients who had been admitted to the study by the Ankara University School of Medicine to serve as the control group. Median age was 51+/-14.5 and 60+/-11.8 years and the male/female ratio was 0.90 and 1.6, respectively. HBs Ag, Anti-HBs, Anti-HCV were evaluated by the enzyme-linked immunosorbent assay method (ELISA). Liver function tests (AST, ALT, GGT, ALP and bilirubin levels) and liver metastases were documented in cancer patients. Patient's characteristics are shown in the table below.
Results: Five hundreds cancer patients and 500 non-cancer patients were considered in the study. HBsAg or Anti-HCV positivily is significantly higher documented in cancer patients compared to non-cancer patients (7.6% and%2.4 respectively, p=0.00001). HBsAg is significantly higher (4.8% vs 1.2%, p=0.001) and Anti-HBs is significantly lower (14% vs 42.4%, p=0.00001) in cancer patients than in the control group but Anti-HCV did not show differences (%2.8 vs 1.4% respectively p=0.13). Anti-HBs among cancer patients and Anti-HCV among patients in the control group were found to be associated with age (R: 0.190, p=0.0001 and R: 0.129 p=0.004 respectively).
Conclusion: This report has shown that hepatitis prevalence is more frequent among cancer patients than non-cancer patients. Hepatitis markers should be evaluated before chemotherapy.

Cancer patients, according to primary tumor region

Primary tumor region	n	%
Breast	88	17,6
Lung	68	13,6
Colon	72	14,4
Gastric	53	10,6
Lymphoma	34	6,8
Head and neck	16	3,2
Gynecologic and genitourinary	38	7,6
Others	102	26.2
	500	100%

1030P HEPATITIS B REACTIVATION DURING ADJUVANT ANTHRACYCLINE BASED CHEMOTHERAPY IN PATIENTS WITH BREAST CANCER: SINGLE INSTITUTION EXPERIENCE

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Purpose: In Korea, about 5–8% of the population have chronic hepatitis B virus infection. We investigated the frequency of hepatitis and HBV reactivation for patients with chronic hepatitis B during breast adjuvant chemotherapies of AC, CAF or AC followed by paclitaxel chemotherapy.
Patients and methods: We studied the outcomes of 96 consecutive HBs Ag positive breast cancer patients who received adjuvant chemotherapy for breast cancer. Hepatitis was defined as ALT ≥ 3 X UNL or an absolute increase of ALT to more than 100U/L. Hepatitis attributable to HBV reactivation was defined as an increase in DNA levels of tenfold or more or an absolute increase of DNA level that exceeded 1X105 copies/ml.
Results: From Jan 2002 to Dec 2005, 2291 patients with breast cancer were received adjuvant chemotherapy. The median age was 46 years (range, 32–65). The median number of cycles that patients received was 4 (range 1–8). 63 patients (72.4%) administered AC, 10 patients (11.5%) received CAF chemotherapy. 36 (37.5%) of the 96 patients developed acute hepatitis, of which 19 (19.8%) was attributable to HBV reactivation. Disruption in chemotherapy occurred in 28 patients. 11 patients had premature termination of chemotherapy. There was no significant predictive markers on HBV reactivation in terms of patient's age, baseline ALT and bilirubin levels, the use of corticosteroid, and the abnormality on hepatic US in the HBV reactivation group. The 19 patients who developed HBV reactivation received lamivudine as a therapeutic measure at the time of HBV reactivation. Despite this, 13 had disruptions of chemotherapy, and 7 patients had premature termination of chemotherapy. In the HBV reactivation group, the AST/ALT prior to hepatitis B reactivation was almost increased when compared with the levels of previous cycle of chemotherapy although it remained within the normal range.
Conclusion: The results suggest that the physician must pay attention to the risk of HBV reactivation when there is small degree of AST/ALT elevation during adjuvant anthracycline-containing chemotherapy and consider to prescribe the prophylactic lamivudine in patients with positive HBs Ag.

1031P BURDEN OF ILLNESS AND ECONOMIC IMPACT OF MUCOSAL INJURY (MUI) IN SOLID TUMOR – A MULTINATIONAL PROSPECTIVE OBSERVATIONAL STUDY DESIGN

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Objective: There are few studies documenting the risk, severity, duration, and clinical & economic outcomes of mucosal injury (MUI) in patients receiving radiation therapy (RT) and chemotherapy (CT) for solid tumor cancers. Our objective is to report the design of a recently initiated burden of illness study by an international not-for-profit consortium of investigators created for the purpose of managing the investigation (Triad BOI, Inc.).
Methods: This is a prospective, multi-center, observational study of about 1600 patients with solid tumors at 48 sites across 10 countries. Anticipated recruitment by European participating countries is about 800 patients across 7 European countries. Patients being treated with 1 of 8 specific regimens for breast, colorectal, head and neck, non-small cell lung and ovarian cancers will be studied over the duration of RT, or for up to 4 cycles of CT. Patient-reported outcomes include the oral mucositis daily questionnaire (OMDQ) and health-related quality of life instruments using the weekly Functional Assessment of Cancer Therapy (FACT-E and FACT-Fatigue). Patient-reported MUI will be validated with clinician assessed oral mucositis for those patients in laryngeal, hypopharyngeal and NSCLC cohorts. Medical resource assessment will determine hospitalizations, ER visits, out-patient visits, hospital procedures and surgeries, medication, TPN and feeding tube placement for each study cohort. Cost of medical services will be derived by applying country-specific average reimbursements and/or unit country-specific costs to resources used. Mucositis-related RT treatment breaks and/or CT delays and dose-reductions also will be reported.
Results: We will report overall and country-specific estimates of the risk, severity, duration, clinical outcomes, medical resource use, and cost of mucosal injury.
Conclusion: The study will provide comprehensive estimates of the risk and economic and clinical outcomes of MUI in patients being treated for solid tumors. A comprehensive cost model for MUI and its outcomes will inform geographically specific decisions regarding reimbursement of new efficacious interventions for the treatment of MUI.

1032P ROLE OF ITRACONAZOLE FOR PROPHYLAXIS OF FUNGAL INFECTIONS IN BMT SETTING

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Introduction: Fungal infections pose a serious risk of morbidity and mortality in the setting of Hematopoetic Stem Cell transplantation (HSCT).Increasing resistance to drugs like fluconazole (due to widespread use of this drug in the community) makes selection of the ideal antifungal prophylaxis difficult. We studied the role of Itraconazole as prophylaxis in the recipients of autologous and allogenic HSCT.
Patients and methods: A total of 47 patients from August 2004 to February 2006 were offered Itraconazole as the prophylactic antifungal. 24 (51.1%) underwent auto and 23 allo HSCT. The majority 40 (85.1%) of patients were males. 5 patients were of pediatric age group (<15 years of age). The disease distribution was: AML-12, Hodgkin's disease-9, Multiple myeloma-7, CML-6 and others. 22 (46.8%) patients were not in complete remission before HSCT. The common Conditioning regimens used were TBI based-12,

BEAM-13, High dose melphalan-7, Busulfan based-9. All the patients received Itraconazole dose of 200 mg per day (41 oral, 6 i.v) from day -7 to day +100 in allo and upto day +30 in auto-HSCT patients. Pediatric patients recieved doses as per bodyweight.
Results: None of the patients required discontinuation of itraconazole due to toxicity. 7 patients had received antifungal drugs prior to HSCT. 30 patients (63.8%) needed antifungal treatment post HSCT in spite of Itraconazole prophylaxis. In the majority of these patients-26(86.6%) the antifungals were used empirically. The median number of days of antifungal use after failure of prophylaxis was 8 (range 4–60)with Amphotericin B being used in majority (27 out of 30 patients). Proven fungal infection was seen in 2 patients (4.2%) and probable in 2 (4.2%). Out of these four patients; three expired,at +26, +42, +80 days post HSCT (14,30,60 days after starting therapeutic dosages of ampho B; one with proven infection and two with probable infections). One patient with proven infection recovered with appropriate treatment given for 14 days. Three patients had nonfungal infection related mortality.
Conclusion: In our study in spite of having a population that was at a high risk; we were able to limit our morbidity and mortality due to fungal infections by using itraconazole as the prophylactic antifungal.

1033P PREVALENCE OF MALNUTRITION IN NON-SELECTED CANCER PATIENTS: A ONE-DAY SURVEY

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Rationale: Dewys et al. (Am J Med 1980; 69:491–7) have demonstrated a high prevalence of malnutrition in cancer patients. The aim of the present study was to re-evaluate, 25 yrs later, the prevalence of malnutrition in a non selected population of cancer patients and their nutritional support.
Methods: A prospective one-day prevalence survey was carried out in 154 wards of private or public hospitals in 24 cities in France. Height, actual and usual body weight were assessed in outpatients and inpatients were present that day. Malnutrition was defined as a BMI<18.5 or 21 in patients of 75 yrs or more and/or a loss of body weight > 10% from the beginning of the disease.
Results: 2,068 patients (1,189 men and 879 women) aged 60±13 yrs were evaluated and nutritional status was available in 1,903 patients. Cancer was local, locoregional, or metastatic in 25, 31 and 44% of patients, respectively. Previous therapy included chemotherapy (75.5%), surgery (47.5%), radiotherapy (42.6%). Performance status (PS) was 0 or 1 in 52.3% of patients, 2 in 25.3%, 3 or 4 in 22.4%. 38% of women and 40% of men were malnourished. Prevalence of malnutrition according to the different types of cancer was: head and neck (n=366): 49%, leukemia/lymphoma (n=377): 34%, lung (n=247): 45%, colon/rectum (n=191): 39%, stomach (n=41): 59%, oesophagus (n=41): 61%, pancreas (n=42): 67%, breast (n=229): 21%, ovarie/uterus (n=87): 45%, prostate (n=72): 14%. The prevalence of malnutrition was 22.7, 44.3 and 45.9% in patients with localized, loco-regional or metastatic cancer, respectively. The prevalence of malnutrition was 14.4%, 31.4%, 52.3%, 53.6%, and 65.3% in patients with a PS ranging from 0 to 4, respectively. Regarding the nutritional support, 71% of malnourished patients versus 46% of well nourished patients had at least one of the following nutritional support: dietetic advices, oral supplementation, enteral nutrition and/or parenteral nutrition.
Conclusions: Along with an improvement of cancer treatments, the prevalence of malnutrition is still very high in cancer patients. Systematic screening and care of malnutrition is mandatory in these patients.

1034P PATIENTS WITH CISPLATIN-INDUCED PERIPHERAL NEUROPATHY ARE CHARACTERIZED BY A LOW PLASMA LEVEL OF VITAMIN E

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Background: Peripheral neuropathy is one of the most frequent side effects of cisplatin-based chemotherapy. Cisplatin-based chemotherapy also induces a decrease of plasma vitamin E level. Vitamin E deficiency is often associated with symptoms of peripheral neuropathy.
Objective: We evaluated whether the development of peripheral neuropathy induced by cisplatin-based chemotherapy was associated with changes in basal vitamin E concentration.
Method: A one-group pre-post treatment study was performed on cancer patients in Dr. Sardjito Hospital, during April 2004 – December 2005. The inclusion criteria were as follows: histologically confirmed malignancies, chemo-naïve, planned to treat with cisplatin-based chemotherapy with total cumulative doses of ≥ 300 mg/m^2, no peripheral neuropathy and normal plasma level of vitamin E. The evaluation of nerve function was based on symptoms, clinical signs and electrophysiological findings. The vitamin E plasma level and neurotoxicological score were measured before and after total cumulative doses of cisplatin were ≥ 300 mg/m^2. Paired t-test and Wilcoxon signed rank test were used to determine whether the decrease in circulating vitamin E levels was associated with increased neurotoxicological score.
Results: Cisplatin-based chemotherapy was applied for 56 cancer patients who were eligible for evaluation. Thirty one patients completed therapy with mean cumulative doses of 310 mg/m^2 for cisplatin. Anova test showed a main effect of chemotherapy ($P < 0.05$). There were no differences between the vitamin E levels of 18 healthy subjects and the 56 cancer patients at the beginning of the therapy. In fact, post-hoc comparisons between the beginning and the end of anti-neoplastic therapy revealed a decrease in the vitamin E levels ($P < 0.05$). After completing chemotherapy, 23 patients (74.2%) with peripheral neuropathies were noted ($\chi^2 = 56.48$; $P < 0.01$). Significant association was found between the decrease in plasma level of vitamin E and the increase in neurotoxicological score in 31 patients who completed the study ($P < 0.01$).
Conclusion: Peripheral neuropathy induced by cisplatin-based chemotherapy is associated with a low plasma level of vitamin E.

1035P PREMEDICATION WITH MAGNESIUM (MG), CALCIUM (CA), AND REDUCED GLUTATHIONE (GSH) MAY REDUCE OXALIPLATIN INDUCED PERIPHERAL NEUROPATHY AND ALLOW PROLONGED CHEMOTHERAPY APPLICATION

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Background: Oxaliplatin (OX) may induce two distinct types of peripheral neuropathy (PNP) which both may be dose limiting: early neuropathy that is exacerbated by exposure to cold, and late neuropathy that is temperature independent and increases with higher cumulative OX doses. Recent work showed separately a reduction of early PNP by MgCa and of late PNP by GSH. We hypothesized that combined premedication with MgCaGSH reduces both types of PNP and prevents early termination of OX.
Methods: We conducted a phase II study with a planned sample size of 30 patients (pts), treated with chemotherapy (CT) regimen similar to 12 cycles of fortnightly FOLFOX4. Premedication consisted of $MgSO_4$ (5 mmol) and Ca glucobionate (1.375 g) in NaCl 0.9% 100 ml i.v./30 min followed by GSH (1500 mg/m^2) in NaCl 0.9% 100 ml i.v./15 min immediately before OX. Primary endpoints were number of CT cycles before dose limiting PNP and extent of PNP assessed by physical examination, pts history and questionnaire.
Results: 31 pts were included (cancers: 24 colon, 6 rectal, 1 gastric; adjuvant 13, palliative 18). CT was FOLFOX4 (26), FOLFOX4/bevacizumab (3), or XELOX (2). Premedication with MgCaGSH was well tolerated, no cardiovascular side effects occurred. Mg was discontinued in 1 patient after the 5th dose for skin reaction. Otherwise, premedication was given as scheduled. 22 pts received the full number of OX CT cycles. Dose reductions and delays occurred for hematotoxicity. PNP was never dose limiting (compared to 15-20% previously reported). Grade 3 PNP occurred in 1 patient. OX was discontinued in 9 pts: tumor progression (3), partial liver resection in PR (1), CNS disorders (2; 1 pt each with Lhermitte's sign and reversible demential syndrome), depression (1), allergy (1), lack of cooperation (1).
Conclusion: Premedication with Mg, Ca, and GSH preceeding OX is feasible, safe and may reduce early and late PNP. CNS disorders still occurred. Response rates to CT were in the expected range. A larger randomized study is warranted to determine the potential benefit of MgCaGSH in OX-treated patients.
This study was supported by Sanofi-Aventis (Switzerland).

1036P EVALUATION OF GABAPENTIN IN PATIENTS WITH CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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Background: The aim of this study was to determine if gabapentin, an anti-convulsant used for neuropathic pain, is effective in improving pain and symptoms due to chemotherapy-induced peripheral neuropathy.
Methods: 40 patients with chemotherapy-induced peripheral neuropathy (for ≥1 month, with average pain rating of ≥ 4/10 or ECOG sensory neuropathy ≥ l/3) were randomized in this double-blind, placebo-controlled trial to either: 1) gabapentin (target dose=900 mg TID) for 6 weeks then cross over to placebo for 6 weeks (n=19) or 2) treatment in the reverse order (n=21). A 2-week washout occurred between cross over treatments. The co-primary endpoints were the average daily pain numerical analogue intensity rating (0=no pain to 10=worst pain imaginable) and the ECOG toxicity rating for sensory neuropathy (0=none to 3=severe). The study provide 80% power to detect an average pain score difference

of 0,58 standard deviations (a moderate effect size) using a two-sided t-test with 0,05 Type I error rate.

Results: Gabapentin did not significantly improve the co-primary endpoints of pain intensity (-0,5 versus -1,0 change from baseline to week 6 for patients on gabapentin and placebo respectively, p=0,17) or the ECOG toxicity rating for sensory neuropathy (-0,2 versus -0,1 for gabapentin and placebo respectively, p=0.36). Patients on gabapentin reported significantly more nystagmus (p=0.007) and dizziness (p=0.01).

Conclusion: Gabapentin did not significantly improve the primary endpoints of pain intensity or sensory neuropathy due to chemotherapy-induced peripheral neuropathy in this study.

1037P OUR EXPERIENCE WITH TRANSDERMAL THERAPEUTIC SYSTEM FENTANYL IN THE PAIN MANAGEMENT OF HIGH DOSE CHEMOTHERAPY ASSOCIATED ORAL MUCOSITIS

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Background: oral mucositis is a frequent and significant side effect of both chemotherapy and radiation treatment; it is an especially severe problem in the setting of patients undergoing high dose chemotherapy (HDC) followed by peripheral blood progenitor cells (PBPCs) transplantation. The current study was performed to evaluate the effectiveness and safety of transdermal therapeutic system (TTS) fentanyl in the management of acute pain due to oral mucositis in patients receiving HDC and PBPCs transplantation.

Material and methods: A cohort of 68 consecutive cancer patients with painful oral mucositis were enrolled. All patients received HDC followed by PBPCs transplantation. Initially, 25 microg/h of TTS fentanyl was administered for the treatment of oral mucositis pain.

Results: sufficient analgesia was achieved with a dose of 25 microg/h in 40 patients with WHO grade I-II mucositis and with 50 microg/h in 28 patients with grade III-IV mucositis. Ten (14.7%), twelve (17.6%) and eight (11.8%) patients experienced headache, improved sleep and nausea-vomiting, respectively. The median duration of the treatment was 9 days (range 6–15 days).

Conclusions: our experience suggest that TTS fentanyl is reliable in pain management of HDC-associated oral mucositis.

1038P EFFECTIVE PALLIATION OF PAINFUL BONE METASTASES FOLLOWING MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND (MRGFUS) TREATMENT: PRELIMINARY RESULTS

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Background: Magnetic Resonance guided Focused Ultrasound Surgery (MRgFUS) is a non-invasive thermal ablation technique that has been shown to be clinically effective in the treatment of soft tissue tumors, such as uterine fibroids. Additional studies are investigating the use of this method for other indications of tumor ablation in the breast, liver, brain and other organs. In this study, the goal was to evaluate the safety and initial effectiveness of MRgFUS for the palliation of pain due to bone metastases in patients for whom other available treatments are considered either not effective or not feasible.

Methods: Seven patients suffering from symptomatic pelvic bone metastases underwent MRgFUS procedure using ExAblate® 2000 system (InSightec Ltd. Haifa, Israel). The patients were treated at Sheba Medical Center (Ramat Gan, Israel). Treatment safety was evaluated by recording and assessing the incidence and severity of device-related complications from the first visit through 3-months post-treatment. Effectiveness of pain palliation was evaluated using Visual Analog Scale (VAS) pain questionnaires and changes in dosage of patient medications.

Results: A total of eight treatments were performed, targeting eight lesions in seven patients. Patients were followed for a period of at least 3 months. Of the seven patients treated, one patient's general health deteriorated very quickly following treatment, thus no follow-up data was collected. Another was unable to tolerate treatment under conscious sedation, so treatment was prematurely terminated. No severe device related adverse events were recorded. All five patients, who received adequate treatment and were followed up, reported improvement in pain score (mean VAS score at days 0, 3, 14, 30, 90 were 5.5, 1.5, 1, 0.5 and 0.3 respectively). The patient who did not receive adequate treatment reported no improvement.

Conclusion: These preliminary results show promise that MRgFUS may provide a safe and effective non-invasive alternative for palliation of pain, caused by bone metastases.

1039P TRANSDERMAL FENTANYL (TDF) IN FRONT-LINE TREATMENT OF SEVERE CANCER PAIN. IS THE EVIDENCE OF SAFETY SO EVIDENT?

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Background: Oral morphine represents the opiate of choice in the treatment of severe cancer pain. Nevertheless, other opiates may be used as front line approach for their interesting safety profile. We report the results of a systematic review about safety and efficacy data of TDF when compared with sustained release oral morphine (SRM) in randomized clinical trials (RCT).

Methods: We performed a meta-analysis of RCT (1980–2005) comparing TDF and SRM in severe cancer pain. Overall safety, constipation, nausea/vomiting, and somnolence were the primary end points; overall gastrointestinal and neurological safety, laxatives use, patient preference, trial withdrawal for side effects and pain control were the secondary ones. Statistical analysis was performed using the fixed effect model of Mantel-Haenszel.

Results: Three RCT (373 patients) met the eligibility criteria and were included into the analysis. No significant heterogeneity was evidenced using the chi-square test. A significant reduction of the relative risk of constipation (pooled odds ratio=0.44, P=0.005) and use of laxatives (pooled odds ratio=0.46, P=0.007) were observed in patients treated with TDF, while no significant differences were observed either in overall, gastrointestinal, and neurological side effects or in trials withdrawal for side effects. A significant preference of the patients for TDF was documented in the three trials (pooled odds ratio=0.39, P<0.001). The differences in pain assessment in the three trials did not permit a pooled analysis of efficacy data.

Conclusions: Our data seems to confirm that TDF is safe and well accepted by the patients as front line treatment of severe cancer pain with opiates. Moreover, the reduction of the relative risk of constipation makes TDF an interesting option for patients with subocclusive status or chronic stipsis who need opiates for cancer pain, and are at risk for side gastrointestinal effects. Nevertheless, limited evidence exists about its superiority in a comprehensive safety assessment, making the differences between the two molecules not enough to prefer TDF in all the patients with severe cancer pain.

1040P TOTALLY IMPLANTABLE VENOUS ACCESS PORT SYSTEMS VIA FEMORAL VEIN FOR CANCER PATIENTS: RESULTS OF A MONOCENTRE SERIES OF 30 PATIENTS

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Purpose: To determine the safety of totally implantable venous access port systems via femoral vein for patients receiving chemotherapy for solid tumors.

Patients and methods: Between January 2004 and April 2006, 30 patients (21 female, 9 male) with an average age of 52 years (21–79 years) were placed subcutaneously implanted venous access systems via the femoral vein for long term chemotherapy. All patients were retrospectively reviewed.

Results: The reasons for the percutaneous femoral access with a totally implantable port reservoir located in the abdomen were as follows: History of complicated port systems via the internal jugular vein or subclavian vein in 5 patients, inaccessibility to subclavian or jugular veins in 7 patients, bilateral mastectomy in 3 patients, head and neck cancer in 3 patients, presence of cardiac pacemaker in 2 patients, radiodermitis in 1 patient, massive cutaneous metastases in 2 patients, breast prosthesis in 1 patient, and esthetical reasons in 6 patients. The retrospective analysis showed an average catheter life of 174 days. A total of 25 (83%) of the patients had no implant related complications. Five of 30 (17%) patients were associated with complications, including port pocket infection, port-related deep venous thrombosis of the lower extremity, and erosion of the overlying skin on the abdominal wall by the port (skin necrosis). All the complicated ports were explanted.

Conclusion: Totally implantable venous access port systems constitute a reliable and convenient access for patients who need long-term intravenous chemotherapy. Implantation of a port system via the femoral vein appears to be safe alternative for cancer patients who are not suitable for venous access port system via the internal jugular vein or subclavian vein.

1041P QUALITY OF LIFE (QOL) AND PSYCHOLOGICAL SUPPORT IN NON SMALL CELL LUNG CANCER (NSCLC) PATIENTS: RESULTS OF A RANDOMIZED TRIAL

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The impact of psychosocial support on QOL in NSCLC patients has been poorly defined in the literature. The Lung Expressive-Supportive Therapy (LEST) study is an RCT of structured supportive-expressive (SE) group therapy in NSCLC patients. Between 1998 and 2005, 112 NSCLC patients were randomized to participate in

a weekly, 90-minute, therapist-led support group that adhered to principles of SE therapy or to a control arm (no SE). All patients received educational material and any type of medical or psychosocial care deemed necessary. QOL data were prospectively collected using the EORTC QLQ-C30 questionnaire at 4 planned assessment times: baseline, 4, 8, and 12 months. Baseline characteristics at the time of first development of metastasis and at randomization were not significantly different between study arms. Survival was similar in the two arms. The primary QOL analyses were completed using a mixed model for repeated measures. QOL analyses were limited to eligible patients with appropriate baseline QOL information (n=102). The rate of missing items was minimal (0,9%). Overall question- naire completion rates at baseline, 4, 8, and 12 months were 100%, 60%, 46%, and 48% respectively (% received/alive at the time of assessment). Baseline EORTC scores were not different between the two groups (all p>0.04). Primary analysis of all subscales failed to show a significant influence of the intervention on QOL (p>0,04). There was a significant deterioration over time in a number of functional scales: global health status (p=0.02), physical (p=0.0003), role (p=0.02), and cognitive functioning (p=0.03) and symptom scales: dyspnea (p=0.006), appetite loss (p=0.03), and fatigue (p=0.004) but these time effects were independent of randomization group. Additional analyses of overall QOL using a variety of approaches to handling missing data (i.e. complete case, summary statistics and imputation methods) identified no significant effects of the intervention. In conclusion, group psychosocial therapy in NSCLC patients does not appear to affect QOL as measured by the EORTC QLQ-C30.

1042P RENAL SAFETY OF 70–80 MG/M^2/DAY CISPLATIN ADMINISTRATION ON AN OUTPATIENT BASIS

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Background: Nephrotoxicity is the major limitation to the clinical use of cisplatin (CP). Mild to severe renal failure occurs in about 25-40% of CP-treated patients. Hydration is a well-established mean of prevention, for which overnight-hospitalisation is still frequently recommended. No data are available concerning the safety of CP-administration on an outpatient basis.
Aim of the study: To assess renal safety of CP-administration in a one-day care unit.
Methods: We retrospectively studied data from 36 patients (126 cycles) with normal kidney function at baseline, treated with intravenous CP once every 3 or 4 weeks. All patients were treated with CP as outpatients, in our one-day care hemato-oncology unit. Two-thirds of the patients suffered from non-small cell lung cancer. Most frequently associated agent was gemcitabine (59%). Hydration was performed with 4 liters of dextrose 5% and NaCl 0.9%, in equal parts, and forced diuresis was obtained by the use of mannitol 15%. Kidney function was evaluated by creatinine clearance (Cl_{Cr}, Cockroft-Gault formula or MDRD2 equation) before and one to three weeks after each cycle of CP.
Results: For the whole population, a median of 3 cycles was given (range 1–8). As expected, Cl_{Cr} was significantly reduced by the treatment, from 107.2±40.9 ml/min to 77.7±27.5 ml/min (p<0.001). Kidney function was mildly (Cl_{Cr} 30-60 ml/min) or severily (Cl_{Cr} < 30 ml/min) altered at the end of the treatment in 22% and 6% of the patients, respectively. Six percent of all CP cycles were complicated by acute renal failure (defined as a an increase in serum creatinine > 0.5 mg/dl).
Conclusions: Administration of CP at the dose of 70 to 80 mg/m^2/day on an outpatient basis, with standard hydration, leads to an acceptable proportion of kidney dysfunction, similar to previously published data. These results may allow to consider it as a safe, less expensive and more convenient way than overnight-hospitalisation.

1043P EVALUATION OF FROZEN GLOVE USE IN THE PREVENTION OF DOCETAXEL INDUCED ONYCHOLYSIS AND CUTANEUS REACTION IN BREAST CANCER PATIENTS (BCP)

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Background: Onycholysis and skin toxicity occur in about 12% of breast cancer patients (BCP), treated with docetaxel (D). We investigated the efficacy and safety of an Elasto-Gel flexible frozen glove (FG) for the prevention of D-induced onycholysis and skin toxicity.
Methods: Breast cancer patients (BCP) receiving D at 75 mg/m2 (1 hour infusion q3w) alone or in combination chemotherapy were eligible for this matched case-control study. Each patient wore a FG for a total of 90 minutes (min) on the right hand (15 min before, during D administration, and 15 min after). The left hand was not protected by FG and acted the control. Onycholysis and skin toxicity were assessed at each cycle by NCI-CTC v.2 criteria and documented by photography. Wilcoxon matched-pairs ranks test was used to determine the magnitude of difference between two matched groups.
Results: Between Aug 2004 and Sept 2005; 32 breast cancer patients (BCP) with median age 63 years were evaluated. Onycholysis and skin toxicity (main criteria) was significantly lower in the FG protected hand compared with the control hand (p=0.0001, Wilcoxon test). Onycholysis was grade (G)0: 89% vs 49% and G1_2: 11% vs 51% in the FG-protected hand and the control hand, respectively. Skin toxicity was G0: 73% vs. 41% and G1_2: 27% vs. 59% in the FG-protected hand and the control hand, respectively. Median time to nail and skin toxicity occurrence was not significantly different between FG-protected and the control hand, respectively [106 days (5 cycles) vs. 58 days (2,7 cycles) for nail toxicity; 57 days vs. 58 days for skin toxicity]. 3 breast cancer patients (BCP) experienced discomfort due to cold intolerance of the FG protected hand.
Conclusions: Frozen glove significant reduces the nail and skin toxicity associated with docetaxel and provides a new tool in supportive care management for a better breast cancer patient's quality of life.

1044P FUNCTIONAL OUTCOME IN PATIENTS WITH SPINAL CORD COMPRESSION DEPENDS ON PROMPT DIAGNOSIS AND TREATMENT

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Background: Spinal cord compression is a medical emergency. Delays in treatment can result in irreversible paralysis. This study is undertaken to asses outcome with respect to the neurological state of the patient treated with urgent radiotherapy.
Methods: This retrospective analysis was conducted at the Oncology department UCHG, Ireland during Jan'01 to June'03. Clinical details were obtained from hospital notes comprising of patient's age, sex, diagnosis, signs & symptoms, radiological investigations, treatment and outcome.
Results: 31 patients were diagnosed as spinal cord compression on MRI. 83.8% patients were referred for urgent radiotherapy. 3.2% underwent spinal stabilization and 12.9% received no treatment due to critical clinical condition. 65% received radiotherapy within 24 hours of diagnosis. Radiotherapy was delayed beyond 24 hours in 29%. Lack of bed availability, delays in patient referral and acutely unwell patients on arrival were reasons for delay. The median range of delay from onset of symptoms to treatment was 4.6 days. 86% patients made neurological recovery as summarized in the table below.

Nuerological Status

At Diagnosis	Post RT
Ambulatory 45%	58%
Paraparesis 19%	16%
Paraplegic 19%	12%

Lack of information 16%.

Conclusion: Functional outcome in patients with suspected spinal cord compression depends on pre-treatment neurological state. Delays in diagnosis, referral and treatment can strongly influence outcome hence appropriate investigation and timing of radiotherapy is crucial in management.

1045P TO ASSESS THE EFFECT OF CHEMOTHERAPY ON REACTIVATION OF TUBERCULOSIS

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Background: Tuberculosis is a chronic infective disease. With modern drugs majority of tuberculosis patients can be cured. It has also been observed that significant proportion of patient with tuberculosis relapse or gets reactivated. Compliance, old age, alcoholism, immunosuppression has been implicated for these recurrence. Methotrexate when used in rheumatoid arthritis has known to reactivate tuberculosis. Effect of short term chemotherapy on reactivation is not known.
Material and methods: We retrospectively collected data from one of our lymphoma study. Patients with proven tuberculosis were included. All these patients should have received standard anti-tubercular treatment earlier. At the time of starting of chemotherapy they should not have any signs, symptoms and investigation finding attributes to achieve tuberculosis. They should have been followed up for at least 1 year after chemotherapy got over. Any patient with any sign and symptoms attributable to tuberculosis should have been investigated.
Results: There were 141 patients included in this study. 8 patients had history of tuberculosis. 7 patients had pulmonary tuberculosis and 1 patient had lymph node tuberculosis. Out of 8 patients 7 patients were male and one patient was female. They had received optimal treatment for tuberculosis and had no signs, symptoms or investigational finding suggestive of active tuberculosis. Only 2 patients X-ray showed fibro tic lesion seen in apical region. Patients were followed up at the time of treatment every 3 weekly. Post treatment they were followed every 3 monthly. 7 patients had adequate follow up, 1 patient who progressed on the treatment had lost to follow up after 3 months of treatment. Out of 8 patients none of them had recurrence or reactivation of tuberculosis.

Interpretation: Short term chemotherapy does not lead to reactivation or recurrence of tuberculosis. This also suggest that prophylactic ATT is not required for old treated tubercular disease as needed for old treated fungal Infection.

1046P INCIDENCE, INTERVAL FROM INSERTION AND RISK FACTORS FOR CATHETER RELATED SYMPTOMATIC THROMBOSIS IN ADULT CANCER PATIENTS ON CHEMOTHERAPY

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Background-aim: Uncertainty exists regarding the central venous catheter (CVC) related thromboembolic events in cancer patients (pts). We wanted to shed further light on the CVC related symptomatic thrombosis.

Patients and methods: We retrospectively reviewed notes of patients who had chemotherapy through a CVC within a two years period. We recorded patient demographic, site and stage of tumour, history of previous treatments, type of catheter used, site and side of insertion, type of anticoagulation if used before or after the insertion [pts with peripherally inserted central catheters (PICC) were on prophylactic 1 mg of Warfarin daily], type of current chemotherapy, presence of concurrent infection of the catheter and time of thrombotic event in relation to the insertion of the catheter. Statistical tests applied were student's t-test and chi-square techniques.

Results: 320 cases (269 pts, mean age 59) with a CVC (Hickman tunneled catheters, implanted ports or PICC) were reviewed. 42% were men and 58% women. 79 had breast, 50 colon, 38 rectal and 24 bladder carcinoma and the other 78 pts had other types of cancer. Hickman was used in 263 cases, ports in 15 and PICC in 42 cases. 11 cases (6 in women, 5 in men) with symptomatic thrombosis were identified (3.4%). Median time to thrombosis from the day of insertion was 30 days and mean time 40 days. Cancer sites with high frequency of thrombosis were rectum (4) and oesophagus (2). 6 had stage IV. PICC had the higher incidence of symptomatic thrombosis (7.1%) compared with ports and Hickman catheters (6.7% and 2.7% respectively) (p=0.2). Line infection was more common in cases with thrombosis (36.4% vs 15.3%, p: 0.06). Also, left sided CVC insertion was seen more often in cases with thrombosis rather than in cases without thrombosis(45.5% vs 35.7%). No pulmonary embolism or death was attributed to the thrombotic event. All pts with an event had anticoagulation and in 8 cases the catheter had been removed.

Conclusion: Symptomatic thrombosis in adult cancer patients is relatively low and it varies with the CVC used. It seems to occur early after the insertion of the catheter and this period (first 40 days) may be the one to be targeted for anticoagulation.

1047P INCIDENCE OF THROMBOEMBOLIC DISEASE IN KOREAN PATIENTS WITH PANCREATIC ADENOCARCINOMA

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Background: Venous thromboembolism (VTE) is a common complication of cancer, and pancreatic adenocarcinoma is one of the most frequently associated cancer with reported incidences of 17% to 57% in Western countries. Asian-Pacific islanders are known to have lower risk of VTE than Caucasians but studies on the incidence of VTE in pancreatic cancer patients in these regions are lacking.

Methods: Retrospective review of charts of all patients histologically diagnosed with advanced pancreatic adenocarcinoma and followed at a regional teaching hospital from Jun 2003 to Dec 2005.

Results: In total, 132 patients were diagnosed and 70 were available for evaluation (M:F=43:27, locally advanced: metastatic=22:48, median age: 65 years). Four patients (5.7%) with VTE were identified (bilateral calf vein and portal vein thrombosis in one, bilateral femoral vein in one, IVC in one and isolated portal vein thrombosis in one) during 8 months of follow up. Three of four patients had extensive metastatic diseases and two were receiving chemotherapy when VTE developed. Mean time from cancer diagnosis to detection of VTE was 5.3 months. There were no episodes of arterial thrombosis but four multiple cerebral infarctions occurred which was the cause of death in three patients. Median survival did not show statistically significant difference in patients with or without VTE (4.3 vs 8.0 months).

Conclusion: Unlike series from most Western countries, incidence of VTE in Korean patients with advanced pancreatic cancer was 5.7%, which suggests ethnic difference in the incidence of cancer-related VTE. Incidence of VTE, together with cerebral infarctions in cancer patients warrants further prospective investigation in different ethnicity before adopting primary prophylaxis.

1048P THROMBOSIS AND CANCER: CLINICAL, LABORATUARY AND GENETIC EVALUATION

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Introduction: Coagulation disorders are common in cancer patients. Activation of coagulation system in malignancies is considered to play a role in the progression and dissemination of the tumor. In this study we aimed to investigate clinical and genetic features which may be associated with thrombosis in patients who had the diagnosis of cancer.

Patients and method: The study was conducted between June 2003 and March 2006. Patients with thrombosis and the solid malign tumors were enrolled to the study.

Results: Forty three men and 40 women were included in the study. Median age was 56 (range 21–78). Gastrointestinal (GI) malignancies, lung cancer, lymphomas, breast cancer, and gynecological malignancies were observed in 26,12,10,8 and 6 patients respectively. Median time from the initial diagnosis to the development of thrombosis was 8 months (0-62 months). Seventy three venous, 9 arterial and 1 atrial thrombosis was observed. Venous thrombosis was mainly located in the lower extremities and most commonly in the deep calf veins (42/73, 58%). Thrombocytosis in 7, thrombocytopenia in 12, protein C deficiency in 10, protein S deficiency in 8 patients and resistance to activated protein C in 13 patients were observed. Thirty three patients had positive lupus anticoagulant analysis and one of them also had anticardiolipin antibodies. Genetic analysis was available in 43 patients and revealed heterozygous polymorphism for MTHFR enzyme (C677T) in 21 patients and homozygous polymorphism in 5. One patient in each group had also gene mutations for FV Leiden (G6191A) and prothrombin (G202101). Acquired factors playing role in thrombosis development were chemotherapy, previous surgery, interventions for obtaining biopsy specimens, radiotherapy, central venous catheters, and hormonal therapy.

Conclusion: Patients with GI tumors seem to have highest risk for developing thrombosis. Deep vein thrombosis was far more frequent. Thrombocytopenia, protein C and S deficiencies, resistance to APC and presence of the lupus anticoagulant were the main abnormalities observed in coagulation pathway. Polymorphism for MTHFR was observed in 60% of the patients and seemed relevant with thrombosis.

1049P EVALUATING THE COST EFFICIENT POSITION OF PALONOSETRON WITHIN ROUTINE CHEMOTHERAPY PRACTICE

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Introduction: The longer acting 5HT3 antagonist palonosetron (Aloxi®) has been shown to improve chemotherapy induced nausea and vomiting over ondansetron1. However, it is more expensive than other 5HT3 agonists and may not be required in most patients. This study, within a single community day case oncology unit, aimed to evaluate the cost efficient position of palonosetron for its introduction into routine chemotherapy practice.

Method: The complete records of 220 non-platinum based chemotherapy cycles were retrospectively analysed from consecutive patients attending the unit from October 2005 to March 2006. Patients with breast cancer had 68 cycles of FEC, 12 of AC, 37 of Epirubicin, 34 of CMF, 32 of Taxotere and 16 of Vinorelbine. The remaining patients with lymphoma received 21 cycles of CHOP chemotherapy. The antiemetic drugs and dosage, initially prescribed (1st cycle adhering to network guidelines), added to rescue nausea or subsequently modified for remaining cycles, were all costed. Antiemetic tariffs were taken from the British National Formulary (BNF).

Results: The antiemetic drug cost per cycle ranged from £1.68 (€2.5) – £149.5 (€223.2) with an average cost of £24.3 (€36.3). The 51% cycles costing less than £20 (€36.3) required no additions or modifications from the initial schedule. A further 18% required minor additional oral 5HT3 antagonists but on average still cost less than £40 (€59.7). 21% of cycles (6% between £40 (€59) to £55 (€82), and 15% over £55 (€82), required substantial additional antiemetics including prolongation of oral 5HT3, additional per rectal administration and addition of other drugs. In this group the average antiemetics cost was £78 (€116), 30% higher than the equivalent cost of palonosetron (£55, €82).

Conclusion: It is clear from this evaluation that a group of just over 20% require a level of antiemetics that is significantly higher than the cost of palonosetron. Notwithstanding the convenience of a single IV administration, these data suggest it would be cost efficient to use palonosetron in subsequent cycles rather than increase the standard antiemetics drugs. A prospective cost effectiveness study is underway to confirm this conclusion.

References

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1050P

IMPACT OF GENDER ON THE EFFICACY OF THE NEUROKININ-1 ANTAGONIST CASOPITANT MESYLATE IN CINV WITH MODERATELY EMETOGENIC CHEMOTHERAPY (MEC): SUBGROUP ANALYSIS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE II TRIAL

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Introduction: Casopitant mesylate (C) added to ondansetron/dexamethasone (OND/dex) increased the rate of control of chemotherapy-induced nausea and vomiting (CINV) following MEC in patients (pts) with solid tumors (NKV101983, Proc ASCO 2006). This analysis examines its efficacy by gender.

Methods: The regimens classified as MEC have been previously described (Proc ASCO 2006, Abstract #8512). Pts received OND 8 mg BID D1-3 + dex 8 mg IV D1 with either placebo, C 50 mg, C 100 mg, or C 150 mg daily D1-3. An exploratory arm evaluated C 150 mg D1 only (+ OND/dex). Primary endpoints were complete response (CR) rate (no vomiting, retching, rescue medications or premature withdrawals) and rate of significant nausea (SN, ≥25 mm on visual analogue scale) during the first 120 hours after MEC. Results: CR rates were significantly improved with C in both primary analysis and female pts. (Table). Rates of no SN at 120 hrs were similar in all groups in the primary analysis. Rates of no SN were higher for men (56-70%) than for women (45-53%); casopitant did not significantly alter the rates in either group. All C doses were generally well tolerated. Most common adverse events in women were nausea (18%), fatigue (15%), and neutropenia (13%); in men, fatigue (14%), constipation (12%), and nausea (11%).

	Control	C50	C100	C150	C150 D1
N (ITT)	120	120	121	119	119
120-hr CR rate,%ITT †(N=719)	70	81	79	85	80
Female (N=434)‡	68	79	73	86	77
Male (N=285)±	72	83	88	83	83

ITT: intent-to-treat.
*exploratory arms, not included in primary analysis.
†p=.012, Cochran-Armitage (CA) trend test.
‡p=.04, CA trend test.
±p > .05 for males, CA trend test.

Conclusion: Although female gender is a negative prognostic factor for CINV control, the improvement in CR offered by the addition of casopitant to OND/dex was clearly demonstrated in women treated with chemotherapy.

1051P

EFFICACY OF THE NEUROKININ-1 ANTAGONIST CASOPITANT MESYLATE IN CINV WITH TAXANE- AND NON-TAXANE-BASED, MODERATELY EMETOGENIC CHEMOTHERAPY (MEC): SUBGROUP ANALYSIS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE II TRIAL

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Introduction: Casopitant (C) added to ondansetron/dexamethasone (OND/dex) significantly increased the rate of control of chemotherapy-induced nausea and vomiting (CINV) following MEC in patients (pts) with solid tumors (NKV101983, Proc ASCO 2006). Taxane-treated pts may have less CINV than other pts due to the use of steroid premedication. This analysis examines the efficacy of casopitant by taxane- vs non-taxane-containing regimen. Methods: MEC regimens have been previously described (Proc ASCO 2006, Abstract # 8512). Pts received OND 8 mg BID D1-3 + dex 8mg IV D1 with placebo, C 50 mg, C 100 mg, or C 150 mg daily, D1-3. An exploratory arm evaluated C 150 mg D1 only (+ OND/dex). Primary endpoints were complete response (CR) rate (no vomiting, retching, rescue medications or premature withdrawals) and rate of significant nausea (SN; ≥25 mm on visual analogue scale) during the first 120 hours after MEC. Results: C produced a significant improvement in CR rates in the primary analysis and non-taxane group (Table). Rates of no SN at 120 hrs were similar in all groups in all analyses. The most frequently reported adverse events in the taxane groups were fatigue (17%), constipation (15%), and alopecia (14%); in the non-taxane group, nausea, anemia, and fatigue (6% each).

120-hr CR rate,%	Control (N=120)	C50 (N=120)	C100 (N=121)	C150 (N=119)	C150 D1* (N=119)
ITT (N=719)†	70	81	79	85	80
Non-taxane (N=473)±	68	78	78	85	79
Taxane (N=246)‡	73	85	80	85	80

ITT: intent-to-treat.
*exploratory arm, not included in primary analysis.
†p=.012, Cochran-Armitage (CA) trend test.
‡ p >.05, CA trend test.
±p=.02, CA trend test.

Conclusion: The addition of casopitant to standard antiemetic therapy significantly improves the rate of control of CINV following MEC in non-taxane treated pts. Improvement in the taxane group was also seen but did not reach significance perhaps due to sample size.

1052P

PHASE II TRIAL OF THE NEUROKININ-1 ANTAGONIST CASOPITANT MESYLATE FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA/VOMITING (CINV) IN CANCER PATIENTS (PTS) RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY (HEC): SUBGROUP ANALYSIS BY CISPLATIN DOSE

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Introduction: Casopitant (C) added to ondansetron/dexamethasone (OND/dex) significantly reduced CINV rates over a 5-day period in pts receiving HEC in a randomized, double-blind, placebo-controlled phase II trial (NKV20001, Proc ASCO 2006). This analysis examines the safety and efficacy of C by cisplatin dose (< 70, 70-90, and >90 mg/m^2).

Methods: Pts receiving HEC regimens including cisplatin ≥70 mg/m^2 IV over 1-4 hours day 1 (D1) received OND 32mg IV D1 and dex PO D1-4 with either placebo control, C50mg, C100mg, or C150mg, each QD D1-3. Exploratory arms evaluated C 150 mg D1 only and aprepitant 125 mg D1, 80 mg D2-3 + OND/dex. Primary endpoint was complete response (CR) rate (no vomiting, retching, rescue medications or premature withdrawals) during the first 120 h following initiation of HEC.

Results: The results for the intent-to-treat group are reported in the table below. The overall rates of adverse events (AEs) did not differ among groups by cisplatin strata, with neutropenia, nausea, and hiccups most commonly reported.

	Control	Casopitant				Aprepitant† D1-3
		50 mg D1-3	100 mg D1-3	150 mg D1-3	150 mg D1†	
N (Intent-to-Treat)	84	82	81	81	83	82
120-h CR rate,%*	60	76	86	77	75	72
		p=0.0198	p<0.0001	p=0.0033	p=0.0295‡	
Cisplatin < 70 mg/m^2 (n=44),%	56	64	100	87	75	89
Cisplatin 70-90 mg/m^2 (n=237),%	62	75	89	75	74	72
Cisplatin > 90 mg/m^2 (n=44),%	45	100	79	70	83	67

*p-values for ordinal contrasts after Cochran-Armitage trend tested detected a dose-response.
†exploratory arms not included in primary analysis.
‡ p value calculated using Chi-Square test.

Conclusions: Casopitant mesylate when added to OND/dex for the prevention of CINV seemed to demonstrate improvement in CR across a range of cisplatin doses.

1053P

A PHASE II DOSE-RESPONSE STUDY OF PALONOSETRON (PALO) IN JAPANESE PATIENTS RECEIVING MODERATELY EMETOGENIC CHEMOTHERAPY (MEC) – PALO JAPANESE COOPERATIVE STUDY GROUP

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5-HT_3 receptor antagonists ($5HT_3$ RAs) represent the standard of care for patients receiving emetogenic chemotherapy and are recommended in combination with dexamethasone (DEX) for prevention of chemotherapy-induced nausea and vomiting (CINV). In MEC, PALO is the first $5HT_3$ RA used for the prevention of acute and delayed CINV following a single intravenous (IV) injection. In this dose-ranging, randomized, double-blind, multi-center study the efficacy and safety of PALO were evaluated in Japanese patients. Patients receiving MEC (as per NCCN 2004 guidelines) were assigned to one of 3 dose groups of PALO. PALO was administered as a 30-sec IV injection, 30-min prior to MEC. DEX 8 mg was infused within 45 minutes before PALO. DEX 24 mg was infused before administration of paclitaxel according to Japanese prescribing information of this agent. The primary endpoint was Complete Response (CR; no emetic episodes, no rescue medication) in acute phase (Day 1). The safety assessment was according to Common Terminology Criteria for Adverse Events (CTCAE ver.3.0). A total of 204 patients (88 men, 116 women) were included in the intent-to-treat population. Ninety-six (47.1%) patients received paclitaxel and 80 (39.2%) a combination of anthracyclines and cyclophosphamide (AC/EC).

CR rates (% of patients)

Chemo	Time Priods (hrs)	0.075 mg	0.25 mg	0.75 mg
All		N=67	N=68	N=69
	0–24 (Acute)	85.1	82.4	92.8
	24–120 (Delayed)	62.7	66.2	71.0
	0–120 (Overall)	59.7	64.7	69.6
AC/EC		N=26	N=27	N=27
	0–24 (Acute)	61.5	63.0	85.2
	24–120 (Delayed)	38.5	48.1	63.0
	0–120 (Overall)	30.8	44.4	59.3

Apparent dose-response of PALO for efficacy was not clearly observed in the overall population. Conversely, CR rates for delayed and overall phases increased in a dose-dependent manner in patients receiving AC/EC. The most commonly reported adverse events related to PALO were constipation and headache, commonly to other agents of the $5HT_3$ RA class. In summary, some differences in CR rates may exist between doses in the whole population. Furthermore, dose response relationship has been observed in the delayed and overall phases in patients receiving AC/EC, a regimen currently considered to be more than moderately emetogenic.

1054P A PHASE II DOSE-RESPONSE STUDY OF PALONOSETRON (PALO) IN JAPANESE PATIENTS RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY (HEC) - PALO JAPANESE COOPERATIVE STUDY GROUP

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Chemotherapy-induced nausea and vomiting (CINV) is among the greatest fears of patients with cancer. PALO is a novel, highly selective 5-HT_3 receptor antagonist ($5HT_3$ RA) used in EU and US for the prevention of nausea and vomiting due to emetogenic chemotherapy.

This dose-ranging, randomized, double-blind, multi-center study assessed the dose-response relationship among single intravenous (IV) doses of PALO 0.075 mg, 0.25 mg and 0.75 mg for prevention of acute and delayed CINV due to HEC in Japanese patients. Patients receiving HEC (as per 2004 NCCN guidelines), assigned to one of 3 dose groups, were administered a 30-sec IV injection of PALO, 30-min prior to HEC. Dexamethasone (DEX) 12-16 mg was infused within 45 minutes before PALO, plus 8 mg at 24-26 hours and 4-8 mg at 48-50 hours following HEC as per several guideline recommendations. The primary endpoint was Complete Response (CR; no emetic episodes, no rescue medication) in the acute phase (Day 1). The safety assessment was according to Common Terminology Criteria for Adverse Events (CTCAE ver.3.0). In a proportion of patients (n=24), samples for a 7-day assessment of the PK profile of PALO were taken. A total of 231 patients (169 men, 62 women) were included in the intent-to-treat population. All patients were administered cisplatin >=50mg/m^2 as HEC.

CR rates (% of patients)

Time Period (hrs)	0.07 5mg (N=76)	0.25 mg (N=77)	0.75 mg (N=78)
0–24 (Acute)	77.6	81.8	79.5
24–48	68.4	71.4	75.6
48–72	65.8	77.9	78.2
72–96	59.2	67.5	71.8
96–120	61.8	72.7	74.4
24–120 (Delayed)	40.8	53.2	56.4
0–120 (Overall)	38.2	49.4	56.4

Apparent dose response was not observed in acute phase, while a clear dose-response relationship (p=0.048) was observed in the daily evaluations during the whole study period. The most commonly reported adverse events related to PALO include constipation and headache, confirming the class safety profile. PK analysis confirmed an elimination half-life of approx. 40 hours, with dose-proportional exposure among the 3 tested doses.

The results of this study indicate that the dose-response relationship among the tested doses of PALO seems to be due mainly to differences observed in the delayed phase.

1055 PERCUTANEOUS BALLOON PERICARDIOTOMY (PBP) FOR TREATMENT OF CARDIAC TAMPONADE AND LARGE PERICARDIAL EFFUSIONS

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Pericardial effusion due to malignant invasion of pericardium is an oncologic medical emergency and in contrast to pleural or peritoneal effusion is relatively rare. Between 1995 and 2004, 17 percutaneous balloon pericardiotomy were performed in 14 patients with symptomatic pericardial effusion. Median age of patients was 52 years (range 34–82). There were 11 males and 3 females. Ten patients had lung cancer, 3 breast cancer and one patient had pleural malignant mesothelioma. PBP was performed in 8/17 cases as front line therapy due to cardiac tamponade and in 9/17 procedures it was performed after relapse of a pericardiocentesis procedure or PBP (3/17). The success rate of the procedure was 100% for either resolution of clinical symptoms or presence of residual pericardial fluid. Median drawn volume was 920 cc. (range 450–2000 cc.). Hematic fluid was obtained in 10 cases (59%) and serohematic in the rest. Malignant etiology by citology was confirmed in all of the cases except for a pleural malignant mesothelioma. Death rate at the moment is 12/14 (85%) and one patient was loss to follow-up. Median survival was 7 months for the entire group. Relapse rate of pericardial effusion was 21%. No complication by the procedure was observed. In conclusion, our data confirm prior data of other series published related to the feasibility and effectiveness of the procedure.

1056 DARBEPOETIN ALFA IN CHEMOTHERAPY-INDUCED ANEMIA TREATMENT

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Background: Darbepoetin alfa is often used to treat patients with chemotherapy-induced anemia using weekly, every-2-weeks or every-3-weeks administration schedules. The every-3-weeks schedule can be synchronized with many chemotherapy regimens, resulting in fewer visits and reduced burden to patients. This study was conducted in order to assess the efficacy and safety of this regimen and its benefits in the clinical practice.

Methods: Observational, non-comparative study in anemic patients with non-myeloid cancer under chemotherapy. Included patients had chemotherapy-induced anemia (hemoglobin (Hb) > 8 and ≤ 11 g/dL) and received darbepoetin alfa 500 μg every-3-weeks. After inclusion, laboratory values (Hb, hematocrit, ferritin and iron) were

registered. Study primary efficacy parameter, the percentage of patients who achieved Hb ≥ 11g/dL or with an Hb increase of 1.5 g/dL in the absence of RBC transfusions in the preceding 28 days, was measured.

Results: Twenty-nine patients were included, 55% females, mean age 65.7 ± 9.7 years. Colorectal carcinoma (31.0%), NSCLC (17.2%) and gastric cancer (13.8%) were the most common cancer types. Forty-one percent were on stage IV and 38% on stage III. Fifty-nine percent of the included patients were under platinum-based chemotherapy. All patients included started the study with darbepoetin alfa 500 μg every-3-weeks. At week 12 one patient changed darbepoetin alfa dose to 300 μg every-3-weeks and other changed 500 μg administration schedules from every-3-weeks to a 4-weeks regimen. Until week 12 none of the patients received RBC transfusion. The mean basal Hb value was 9.8 g/dL (range between 8.1 and 11.0 g/dL) and at the final evaluation Hb value was 11.3 g/dL (range between 8.5 and 13.5 g/dL). The mean change in Hb level was 1.05 g/dL between week 1 and week 12, and 1.49 g/dL between week 1 and final evaluation. The percentage of patients with Hb ≥ 11 g/dL or with an increase of 1.5 g/dL or more was 68.8%. No adverse events related with darbepoetin alfa administration were reported.

Conclusions: Patients with chemotherapy-induced anemia can be treated effectively and safely with 500 μg of darbepoetin alfa every-3-weeks, with the benefit of synchronizing anemia treatment with chemotherapy treatment.

1057 MORTALITY FIGURES IN A HEMATOLOGY-ONCOLOGY DEPARTMENT

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Objective: To assess the main characteristics of death occurring in Hematology-Oncology department at Hotel Dieu de France University Hospital, Lebanon.

Methods: Data were retrospectively collected from patients hospital files for patients (pts) admitted between June 2005 and January 2006.

Results: Among 685 different pts admitted, 77 died. Sex Ratio is 1. Mean age is 61.7 years (range 23–90). There are 56 (73%) solid cancer (SC) mortalities and 21 (27%) hematologic malignancy (HM) mortalities distributed as following: 14 lung cancer, 11 breast cancer, 6 colon cancer, 5 ovary cancer, 4 stomach cancer, 5 lymphomas, 4 AML, 3 CLL, 3 multiple myeloma and 24 others. Mean previous disease duration is 29.7 mo (range, 5 days – 162 mo). Mean previous SC disease duration is 27.9 mo (range, 1 – 162). Mean previous HM disease duration is 34.5 mo (5 days - 110 mo). Mean duration of the last hospital stay is 18 days (range, 1 – 92). Only 2 pts have been admitted for the first time. The most probably immediate causes of death are: septic shock in 25 cases (32.4%), respiratory failure in 22 cases (28.6%), liver failure in 9 cases (11.7%), hemorrhages in 8 cases (10%), bowel obstruction in 4 cases (5%), renal failure in 3 cases (4%), pulmonary embolism in 2 cases (2.6%) and others (5.7%). Septic shock is the main cause of mortality in HM pts (71%). Eleven HM pts died in the ICU unit (52%) while only 4 pts (7%) died in the latter section. The frequencies of the evaluated clinical complaints are: pain necessitating opiates (38%), infection- or disease- related fever (74%), dyspnea (76%), hemorrhage (22%), CNS disturbances (28%). In this end stage situation, pts were still receiving: antibiotics (87%), steroids (81%), anti-coagulation (62%), diuretics (52%), transfusions (51%), benzodiazepines (42%), chemotherapy (40%) and analgesics (38%).

Conclusion: HM pts died mainly from septic shock in the ICU, while the majority of SC pts died from the progression of the disease in the department. We report that many drugs were used excessively during the end-stage period in our department. A prospective analysis is expected to be done and will concentrate on the importance of supportive care, when needed, in collaboration with the patient's family which can replace progressively the actual aggressive strategy.

1058 AN OPEN-LABEL STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF EPOETIN BETA 30,000 IU ONCE WEEKLY IN ANAEMIC PATIENTS WITH METASTATIC BREAST CANCER

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Introduction: Patients with metastatic breast cancer often experience anaemia as a consequence of myelosuppressive chemotherapy or their underlying disease. The purpose of this study was to assess the impact of a new once-weekly regimen of epoetin beta (NeoRecormon®) on haemoglobin (Hb) levels in anaemic patients with metastatic breast cancer.

Patients and methods: Adult patients with metastatic breast cancer, Hb levels <11.0 g/dl and ECOG performance status 0-2 were entered into this open-label, one-arm, single-centre study. Patients received epoetin beta 30,000 IU once weekly subcutaneously for up to 16 weeks. Hb assessments were made at 4-weekly intervals. Blood transfusion requirements and adverse events were monitored throughout.

Results: Thirteen patients were enrolled into the study; two patients withdrew their consent and, therefore, 11 were available for analysis. Median age was 55.5 years (range 29.6-73.6). Patients received concomitant hormonal therapy, a taxane-based regimen or supportive care only. Mean (±SD) baseline Hb level was 9.95±0.70 g/dl. There were significant increases in mean Hb level at week 4 (10.81±1.44 g/dl; p=0.024) and at week 16 (12.31±2.04 g/dl; p=0.008). In the eight patients who completed the 16-week study, the mean increase in Hb level was 2.36±1.82 g/dl. Only one patient (12.5%) completing the study received a red blood cell transfusion. Epoetin beta was well tolerated. Three patients were withdrawn before week 16. Reasons for premature withdrawal were: death from thromboembolic complications after breast surgery (one patient); disease progression (one patient); inadequate response to epoetin beta (one patient).

Conclusions: Our experience shows that treatment with epoetin beta 30,000 IU once weekly is effective in anaemic patients with metastatic breast cancer, resulting in significant increases in Hb levels. The once weekly regimen of epoetin beta is well tolerated and offers a convenient treatment for anaemia.

1059 PEGINFO: CLINICAL REGISTRY ON PEGFILGRASTIM PATIENTS UNDER CHEMOTHERAPY

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Background: Chemotherapy-induced neutropenia (CIN) is a frequent complication in cancer patients receiving myelosupressive chemotherapy, and can result in febrile neutropenia and potentially life-threatening infections requiring hospitalization and intravenous antibiotic therapy. Antineoplastic drugs may be reduced or delayed as a result of CIN, which can negatively impact treatment outcomes. The aim of this study was to evaluate the efficacy of a single dose of pegfilgrastim per cycle of chemotherapy compared with multiple daily doses of G-CSF, in patients receiving myelosupressive chemotherapy.

Methods: An observational cross-sectional study involving 8 centers was performed. Patients under myelosupressive chemotherapy were included. Demographic and clinical data (diagnosis, therapeutics, changes in chemotherapy schedules/doses, pegfilgrastim usage and adverse events) were registered.

Results: Thirty-seven patients were included, 57% of those were male, with a mean age of 51,1 years. Most frequent diagnosis was colon cancer (15,8%), Hodgkin's lymphoma (15,8%) and breast cancer (13,2%). Overall, 52.9% of patients had received prior treatments. Pegfilgrastim was administered in 67 cycles, 57 of those immediately after the chemotherapy cycle. G-CSF was administered in 45 cycles, with a mean number of days of 4,7±2. Pegfilgrastim was administered as primary and secondary prophylaxis in 42% and 43% of the cases, respectively. G-CSF was used as treatment for chemotherapy-induced neutropenia in 56% of the cases. Chemotherapy was delayed in 22 cycles and the dose was reduced in 9. Planned dose on time was achieved in 90% of the patients receiving pegfilgrastim versus 67% of those receiving daily G-CSF. In total, 37 cases of neutropenia were observed, being 8 of those febrile neutropenia. A lower incidence of neutropenia was observed in pegfilgrastim cycles when compared to G-CSF.

Conclusions: The current study showed that a single dose of pegfilgrastim provides similar or higher support to cancer patients than multiple daily doses of G-CSF. Additionally, a fixed dose of pegfilgrastim provides all the clinical benefits of G-CSF with the advantages of planned dose on time superior achievement and once-per-cycle dosing.

1060 AN INNOVATIVE TREATMENT APPROACH FOR CANCER-RELATED ANOREXIA/CACHEXIA (CACS) AND OXIDATIVE STRESS (OS). A PHASE III RANDOMISED CLINICAL TRIAL

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Based on our results published in Cancer Epidemiol Biomarkers Prev 2006 in press, showing that an integrated treatment approach was effective in 22 out of 39 cachectic cancer patients, we are currently conducting a Phase III randomized study which aims to demonstrate which is the safest and most effective among the following treatments for CACS/OS. All patients enrolled receive as basic treatment poliphenols (300 mg/day) + antioxidants agents alpha lipoic acid 400 mg/day, carbocysteine 2.7 g/day, Vitamin E 400 mg/day, Vitamin A 30000 IU and Vitamin C 500 mg/day, all orally. Patients are randomised to one of the following treatment arms:

Arm 1. MPA 500 mg/day;
Arm 2. Pharmaco-nutritional support containing eicosapentaenoic acid + DHA, 2 briks/day;
Arm 3. L-carnitine 4 g/day;
Arm 4. Thalidomide 200 mg/day;
Arm 5. MPA + Pharmaco-nutritional support + L-carnitine + Thalidomide

Treatment duration: 16 weeks. Eligibility criteria: advanced stage tumor of any site, loss of at least 5% of ideal or pre-illness body weight in the previous 3 months, and/or abnormal values of laboratory parameters predictive of the onset of CACS; concomitant antineoplastic therapy or supportive care or off-treatment; life expectancy ≥ 4 months. Hypothesizing a difference between arms of 20%, considering an alpha and beta type error of 0.05 and 0.20, 95 patients will be enrolled for each arm (475 patients). The efficacy of each arm versus the others will be tested by ANOVA test for the following key variables: lean body mass; grip strength, resting and total daily energy expenditure; proinflammatory cytokines IL-6 and TNF-alpha; fatigue symptoms by MFSI-SF. Survival (overall survival and progression free survival) will be evaluated from study entry by Kaplan-Meier analysis. The trial has started the accrual in March 2005 and at April 2006 70 patients have been enrolled. An optimal compliance was achieved and no significant side effects were observed. The preliminary results will be presented.

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1061 EVALUATION OF PAIN CONTROL AMONG HOSPITALISED PATIENTS

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The aim of this project was to evaluate the prevalence of pain among hospitalized patients; to increase perception of the professional caregivers for pain and to decrease the prevalence of pain by a standardized evaluation and treatment approach. In the departments of internal medicine, oncology and pneumology, the physicians were trained to measure pain with a visual analogue scale (VAS); then a clinical pathway to treat pain was introduced and the physicians and nurses of the departments were given an information session on pain and pain treatment. Pain was evaluated before and after the introduction of the clinical pathway for 3 weeks. Pain was absent (VAS = 0) in 48% and 60%; low (VAS 1-3) in 33% and 14%; mild (VAS 4-7) in 17% and 19% and severe (VAS 8-10) in 1% and 7% of 59 oncological and 42 non-oncological patients, respectively. After the intervention pain was absent in 56% and 63%; low in 18% and 16%; mild in 17% and severe pain in19% and 9% and 2% in 47 oncological and 41 non-oncological patients, respectively. Oncological patients experienced significant less pain than non-oncological patients, while 26% of these last patients had mild or severe pain. The intervention seemed not to result in a decrease of the pain scores. When the physicians were asked, they agreed that the VAS was an easy way to measure pain but 33% experienced problems to explain it to the patients. Pain is an important problem oncological and non-oncological patients. VAS is an easy method to evaluate pain and should be integrated into the patient file. Physicians should be even more sensitized to the problem of pain.

1062 PLEURODESIS IN MALIGNANT PLEURAL EFFUSIONS. REPORT FROM A SINGLE INSTITUTION

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Introduction: Malignant pleural effusion is a common complication of cancer, most frequently associated with advanced disease. Pleurodesis is considered the best palliation in recurrent pleural effusion. We report and analyse the pleurodesis for malignant pleural effusion performed in our hospital in the last five years.

Methods: Clinical records from 25 patients (p) diagnosed with malignancy who underwent pleurodesis were reviewed. There were14 females and 11 males, median age 58 years (32–78) The primary malignancy was lung cancer in 5p, breast cancer in 13. The rest consisted of 2 cases of non-Hodgkin lymphoma, 2 gastric cancer,1 mesothelioma, 1 multiple mieloma and 1 ovarian cancer. Most p presented with dyspnea. Biochemical analysis of the pleural effusion showed pH under 7,30 in 2 p, and glucose under 60 mg/dl in the same 2 p. Cytopathology study was positive for malignant cells in 9p, in 5 was negative and not-available in the rest. Pleurodesis were performed as an inpatient procedure under sedation and using a 24 F intercostal tube. The agent used was always talc slurry (dose 3 to 9 grams), infused as soon as the lung was expanded in chest radiography and preceded by intrapleurally administration of lignocaine.

Results: immediate symptomatic benefits after the procedure was achieved in 19 cases (76%). Side effects were minor and consisted in pain (20%) and fever (5%). No episodes of talc-induced acute respiratory distress syndrome were observed. Complete control of the pleural effusion until death occurred in 68% of cases. Reaccumulation of fluid was reported in 2 p at 8 and 10 months of the initial procedure. Median survival time was 5,5 months. In all documented cases, death was related to progressive malignancy

Conclusion: Talc pleurodesis is a safe and effective method to control malignant pleural effusions, obtaining lasting pleural symphysis.

1063 OSTEOMYELITIS COMPLICATING LONG-TERM CENTRAL VENOUS CATHETER PLACEMENT IN PATIENTS RECEIVING INFUSED CHEMOTHERAPY

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Introduction: Indwelling central venous catheters (CVCs) are used for the administration of infused chemotherapy. We describe 4 patients with osteomyelitis secondary to chronic CVC use, highlight diagnostic delays and report the potentially serious outcome.

Methods: 4 patients with osteomyelitis as a complication of CVCs were retrieved from a database of all cancer patients receiving chemotherapy with indwelling CVCs in 3 NHS trusts (University College London, North Middlesex and Princess Alexandra, Harlow) in the UK between 2001 and 2006. 2 further patients will be presented on the poster.

Results: see table below.

See abstract 1063

Patient No:	1	2	3	4
Type of CVC	PICC	Hickman line Portacath	PICC	Hickman line
Presenting symptom	R shoulder pain, sepsis	R shoulder pain	R shoulder & neck pain, sepsis	Back pain and sepsis
Diagnostic investigations	Bone scan CT Bone biopsy	Bone scan MR	Bone scan MR Bone biopsy	Bone scanMR
Time delay from presenting symptoms to diagnosis (days)	540	125	69	31
Site of infection (MR defined)	T9/10	R sterno -clavicular joint, sternum & clavicle	C6-7	T7/8, T8/9
Causative organism	Pseudomonas Aeruginosa (Blood, Bone biopsy) Staph epidermidis (Line)	Pseudomonas Aeruginosa (Portacath) Stenotrophomonas maltophilia (Blood)	Pseudomonas Aeruginosa (PICC and Bone Biopsy)	Escherichia Coli (Blood)
Treatment	IV antibiotics	IV antibiotics	IV antibiotics Orthopaedic stabilisation	IV antibiotics
Duration of infused chemotherapy	8 weeks	20 weeks	8 weeks	24 weeks
Grade of worst neutropaenia	4 (0.5)	0 (1.8)	0 (3.1)	0 (1.8)
Outcome	Recovery Orthopaedic stabilisation	Recovery	Recovery Orthopaedic stabilisation	Death

Conclusion: Approximately 1500 CVCs were placed in the study period, and therefore the estimated incidence is 0.4%. Although this is low there is a significant morbidity and mortality which may be in part be attributed to delayed diagnosis The incidence of gram negative aerobic gastrointestinal tract organisms is significantly higher than that which we would expect either in the general population or immunocompromised patients with malignancy suggesting that CVC's are colonised by bowel flora leading to chronic bacteraemia and bone sepsis. Osteomyelitis adds to the known toxicities of CVCs and should be considered when discussing the relative benefits of oral versus infused fluoropyrimidine.

1064 COMPARISON OF THE SENSES OF INTERNS WORKED IN HOSPICE CENTER AND GENERAL WARD

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Background: As the education on palliative & end-of-life care for physicians and the opportunity of clinical practice to treat terminally ill cancer patients is very insufficient.

Methods: From March to December, 2004, questionnaire was performed to interns worked in Kangnam St. Mary's hospital hospice center. Moreover, questionnaire of the same contents was also performed to interns working in general ward except hospice center of the same hospital.

Results: *Demographics* Twenty interns worked in hospice center(HC) and twenty eight interns worked in general ward(GW) answered. It was found that interns worked in HC participated in the treatment of advance cancer patients more than those worked in GW only(HC vs GW: 66% vs 13%, respectively). *Collaboration with Supportive/ Palliative care team* Compared to interns worked in GW only, those worked in HC maintained constant relation with palliative care medical specialist (57% vs 12%), palliative care nurse specialist (50% vs 4%), inpatient hospice (50% vs 7%) and social worker (28% vs 4%), thereby performing cooperative management. *Direct participation in Supportive and Palliative care of patients with Advanced Cancer* The experience of managing patients in HC was able to actively control the physical and psychological symptoms usually seen from advance cancer patients. Furthermore, the interns worked in HC execute discussing end-of-life care preference with patients and directly administer end-of-life care to dying cancer patients in higher frequency. (Refer to table)

	Hospice center	General ward
cancer pain	66%	32%
dyspnea	53%	16%
fatigue	50%	20%
nausea, vomiting	60%	28%
complication of chemotherapy	56%	50%
depression and anxiety	26%	4%
delirium	20%	0%
discussing end-of-life care preference with patients	33%	4%
directly administering end-of-life care to dying cancer patients	20%	8%

Conclusion: The experience of interns that directly taking care of patients in HC motivated them to actively participate in the treatment of terminally ill cancer patient and to control their the physical and psychological symptom. The interns worked in HC could collaborate with palliative care team and have an affirmative concept on palliative care.

1065 CHANGES ON PATTERNS OF IMPACT ON QUALITY OF LIFE (QOL) FOR CANCER PATIENTS (PTS) ON CHEMOTHERAPY (CT) IN A PUBLIC HEALTH SERVICE (PHS) IN SOROCABA (SP), BRAZIL

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Background: New drugs and procedures for symptom control for pts with chemo maybe have modified the spectrum of pts necessities. In Brazil there is massive attention on public health services, and this knowledge could be important orient specific strategies.

Methods: It was observed 60 pts (solid tumors and lymphomas) receiving up to 3 cycles (one evaluation for each pt) with moderate to high emetogenic drugs, in an out-patient service of PHS in Sorocaba (SP)-Brazil. Thirty males and 30 females, 31 to 60 years of age, 90% with PS (ECOG)=0-1, and 60% on stages III or IV. All pts received 5HT3 antagonists, steroids and hydration. A list with 44 physical symptoms and 26 psycho-social symptoms were self-applied after 15-21 days of CT cycle, and noted frequency and importance of symptom due to patient point-of-view. Palliative CT in 55,2%, adjuvant in 34,5%, and neo-adjuvant or salvage in 10,4%. Forty-eight (80%) pts lived with a partner, not alone.

Results: Grouping symptoms and ordering them by frequency and impact for quality of life for pts (Table). Only 14% of pts complained for being treated on a PHS. There were no significant relationships between physical and psycho-social symptoms, except for a marginal result (p=0.06) for nausea and anxiety.

Conclusions: In the studied conditions, physical symptoms continues to be important for brazilian PHS CT pts. Beyond those classics psycho-social symptoms (anxiety and depression), those related to personal relationships (sexual and social variables) had impressive frequency. We can observe a potential better change in pts behavior for being treated on a PHS.

Physical symptoms	percent	Psycho-social symptoms	percent
Alopecia	92,9%	Treatment affect family	53,9%
Nausea	60,0%	Antecipatory anxiety	50,8%
Disgeusia	55,9%	Anxiety status	45,8%
Fatigue	44,1%	Treatment affecting working	42,4%
Vomiting	43,3%	Depression status	35,0%
Weight loss and anorexia (each one)	41,7%	Inconvenience due to duration of chemotherapy	38,8%
Myalgias/arthralgias	35,6%	Lost of sexual pleasure	28,1%
Obstipation	32,1%	All others evaluable symptoms	< 20%
Xerodermia	30,0%		

1066 A CASE-CONTROL STUDY IN CANCER PATIENTS (PTS): THE ARACHIDONIC ACID/EICOSAPENTAENOIC ACID (AA/EPA) RATIO AS A BIOMARKER

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Omega3 (O3) are important molecules for membrane order and function; they can also modify gene-expression, inflammation-inducible cytokines production, regulation of eicosanoid production, plasma TAG level, blood pressure, and ion flux in cardiac cells. O3 have been hypothesized to influence colorectal carcinogenesis through many mechanisms (e.g. inhibiting COX2, increasing apoptosis, reducing angiogenesis). Low dose of docosahexaenoic acid (DHA) synergistically interacts with arachidonic acid, suggesting that dietary supplementation of DHA might achieve therapeutic gain. In breast cancer supplementation with DHA synergistically enhances taxane cytotoxicity, down regulate HER-2/neu (c-erbB-2) oncogene expression, modifies the production of the heparansulfate syndecan-1, suggesting a gene-nutrient interaction of critical importance for mammary carcinogenesis and supporting the hypothesis that O3 can be used as modulators of cancer cell chemo-sensitivity. Aim of the study was to evaluate the potential value of tumor risk assessment in colon and breast cancer pts by determining the ratio between arachidonic and eicosapentaenoic acids (AA/EPA) in plasma in a case-control study against healthy pts; secondary endpoint was to assess a difference within the cancer pts group correlated to stage, histology, steroids administration, O3 dietary intake.

We enrolled 46 cancer pts (colon 38, breast 8) with a median age 70 (range 53–81) and 77 (range 44–86) respectively; because from our previous studies we demonstrated that the AA/EPA ratio is age dependent, we used a control arm with the same median age.

The AA/EPA ratio was 22.232+1.852 in pts with colon cancer and 21.029+2.584 in pts with breast cancer; in healthy subjects with the same median age the AA/EPA ratio was 14.25+1.083 and 12.10+1.414 respectively. This difference was statistically significant ($p<0.01$).

These data suggest that AA/EPA ratio in plasma is strongly correlated with cancer disease. Previous data showed that supplementation of cancer pts with O3 reduces the AA/EPA ratio. These data may suggest a nutraceutical role of Omega 3 as adjuvant in cancer therapy that must be investigated in controlled trials.

1067 OTOTOXICITY OF PLATINUM-DERIVES AND TAXANES

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The purpose of this cohort study is to detect the incidence and time of the ototoxicity using a therapy with taxanes and platinum-compounds. We have monitored the hearing performance of 12 patients treated with cisplatin (4 patients), oxaliplatin (4), carboplatin (1) and docetaxel (3). In Literature we only have ototoxicity data from cisplatin therapy, with sensorineural hearing loss at the high frequences ranging from

10% to 90%. Our patients, with a mean age of 62 years, were affected by a metastatic cancer, all with a PS <2 and no one with a radiotherapy to the temporal bone before. Hearing tests were performed at the beginning of the chemotherapy, after the 1st cycle and the 5th one. The hearing loss was defined as a change of 10 or more dB at one or more frequences. We have also performed a vocal hearing test as monitoring of the patient's disability and to confirm the one pulse-tone hearing test.

Results: Four (2 with cisplatin treatment and 2 with oxaliplatin) of the twelve patients (33%) have expressed a hearing loss at the high frequences of the test. At 8000 Hz the average loss for all the patients was 18.75 dB; at 4000 Hz was 13.33 dB for 3 patients and at 3000 Hz was 10 dB for only 1 patient. The hearing loss was generally detected after the 5th cycle of therapy.

Conclusions: No case of ototoxicity was observed in carboplatin or docetaxel treatment. No variation in the decodification of the vocal hearing test was detected in the patients with a hearing loss at the tone test (50% of the ones treated with cisplatin and oxaliplatin). So we can observe that we have not a negative impact on the quality of life by the chemo-ototoxicity. No tinnitus we have observed. In the cases which have shown a hearing loss, the dose intensity was not different from the other ones, so that some individual factor could play an important role. It could be a key-item the individual DNA-mitocondria mutations which could facilitate the ototoxicity by chemo-agents.

1068 NAIL CHANGES AFTER TREATMENT WITH DOCETAXEL: A PROSPECTIVE ANALYSIS IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

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Purpose: To reduce severe myelosuppression, a well-known and sometimes fatal complication of docetaxel, alternative docetaxel schedules with weekly administration are actively investigated. However, with weekly docetaxel cumulative toxicities including skin and nail changes are prominent. To define the incidence of nail change as well as its association with specific risk factors, we analyzed prospectively data of patients enrolled in a randomized clinical trial.

Methods: Patients with chemotherapy-naïve, advanced or recurrent non-small cell lung cancer were randomly treated with either 3-weekly (75 mg/m^2 on day 1 every 3 weeks) or weekly (35 mg/m^2 on day 1, 8 and 15 every 4 weeks) docetaxel, plus cisplatin 75 mg/m^2 on day 1. Treatment was repeated for a maximum of 6 cycles, assuming no unacceptable toxicities or evidence of disease progression were seen. Toxicities were evaluated according to the National Cancer Institute criteria (NCI-CTCAE) v3.

Results: Of a total of 86 patients accrued, 41 patients were treated with 3-weekly docetaxel plus cisplatin, whereas 43 with weekly regimen. Twenty-two patients (26%) were diagnosed with nail changes during treatment: 13 patients had grade 1/2 and 9 had grade 3 nail changes. In patients with grade 3 nail changes, treatment with antibiotics resulted in transient improvement, but only one patient showed sustained improvement of nail changes after a week of antibiotic treatment. Most occurrences of nail changes were diagnosed in patients who were treated with weekly docetaxel regimen (p=0.02). A multivariate analysis of factors associated with the development of nail changes identified the following to have independent adverse significance: weekly docetaxel administration (odds ratio, 0.084; 95% CI, 0.014–0.510; p=0.01) and the number of chemotherapy cycles (odds ratio, 0.232; 95% CI, 0.067-0.805; p=0.02).

Conclusion: Nail toxicity is a complication that is correlated with frequent and prolonged use of docetaxel. Caution is required for prolonged use of weekly docetaxel.

1069 INTERSTITIAL PNEUMONITIS ASSOCIATED WITH DOCETAXEL ADMINISTRATION

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Introduction: Docetaxel is frequently used in breast cancer patients. Although, docetaxel induced interstitial pneumonitis has been reported many times while using for lung cancer, only one case report has been presented when used in breast cancer. In this study; we aimed to present 6 cases of breast cancer patients who developed rarely encountered interstitial pneumonitis after administering docetaxel.

Methods and results: The mean age of patients was 41±14.5 (20–65).The number of the patients having stage IV, stage III, and stage II cancer were 3, 2, and 1 respectively. Lung metastases were already recorded in one patient. All the patients were presented with cough and dyspnea. Computed tomography of the chest revealed diffuse bilateral infiltration. Four patients were given radiation therapy for breast cancer. The mean time duration between radiation therapy and presentation with interstitial pneumonitis was 6±5.2 (1.5–13) months. The mean radiation dose was 4525±1684 cGy (2100–6000). Docetaxel was administered intravenously over a 60-minute period at 75 mg/m^2,every 3 weeks,with premedication. The symptoms were observed 15.3±5.9 (5–20) days after the last docetaxel administration.Two patients presented with symptoms after 3 cycles, 2 patients after 4 cycles, 1 patient after 6 cycles and 1 patient after 8 cycles of chemotherapy. Bronchoscopy was done in 4 patients. Bronchoalveolar lavage examination and transbronchial biopsy (performed in 3 patients) were negative for malignancy, tuberculosis, and any microorganism. Methylprednisolon was prescribed to all patients. Although, 5 patients responded to the methyl prednisolon treatment well, 1 patient died from respiratory failure.

Conclusions: Docetaxel induced interstitial pneumonitis is a rare but potentially fatal complication. The possibility of an interstitial pneumonitis must be taken into account when a patient receiving docetaxel presents with respiratory symptoms and /or pulmonary infiltrates. Our patient population was relatively younger breast cancer patient, and most of them received radiotherapy. Thus, it might be speculated that radiotherapy may increase the possibility of docetaxel induced interstitial pneuomonitis in this group of patients.

1070 THE PROBLEM OF CANCER PATIENTS STIGMATIZING

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The modern oncology acquires growing social importance for the sickness rate throughout the world. though Russia has gained significant success in diagnostics and therapy of cancer the mortality rate caused by it is still growing and the share of patients with neglected forms remains very high. Patients with II and IV stages formed 60% of all with primary diagnosed in 2004. Prevailing public approach to cancer is one of main causes of the situation. Russians don't use to speak openly about cancer. ''Cancer'' for the majority of people coincides with a fear of inevitable death. Society as a whole percepts cancer patients as doomed and inferior persons. the problem of stigmatizing and isolation of cancer patients instead of adequate attitude towards them exists. Stigma (eg cancer patients) is a lable, specific feature, which sociery as a whole used to consider a disceditation mark, which converts the individual bearing it into the izgoy. The sense of stigma hinders the individual to ask for medical care in time. It compels the individual to avoid personal communications, creates problems with hiring as well as everyday living with other people. As a result the cancer disease has broad and deep social and economic consequences. Srigma creates sense of horror and doom, it destroys trust to medical treatment, and both factors determine the attitude of patients to preventive measures and treatment. To work out efficient methods of cancer treatment means to take into consideration that a patient is an indivisual who lives in family and society. The problem of destigmatizing of cancer patients demands to carry out interdisciplinary medical and social research.