(EE), and those with no nausea were evaluated. Adverse events (AEs) were collected to assess safety.
Results: A total of 58 patients were included in the study; almost 80% (45/58) were women. Breast cancer was the predominant tumor type, followed by colorectal cancer and lymphoma. Approximately half of patients were chemotherapy-naive at study entry. All patients received a variety of moderately to highly emetic regimens on Day 1. Twenty-four of the 58 patients enrolled (41.4%) received anthracycline/cyclophosphamide combination chemotherapy.

PALO+APREP+DEX (n = 58)	Acute (0–24 hr)	Delayed (24–120 hr)	Overall (0–120 hr)
Patients with CR	88%	78%	78%
Patients with no EE	93%	93%	91%
Patients with no nausea	71%	53%	52%

The most common treatment-emergent AEs (incidence ⩾10%), regardless of causality, were constipation, diarrhea, fatigue, insomnia and thrombocytopenia.
Conclusion: Results from this study demonstrate that the combination of a single dose of PALO 0.25 mg with a 3-day regimen of APREP and DEX offers remarkable 5-day protection from nausea and vomiting in patients receiving emetogenic chemotherapy. The triplet combination was shown to be safe, with an expected safety profile for patients under these regimens. This combination of antiemetic agents seems to offer a very effective treatment option to reduce incidence of acute and delayed CINV.

1288 POSTER

Results of a cross-over study on injection-site pain comparing subcutaneous epoetin beta and darbepoetin alfa in healthy volunteers

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Background: In anaemic patients with cancer, erythropoietic proteins are normally administered by subcutaneous (SC) injection. Whether therapy is administered in the clinic or self-administered by the patient, pain at the injection site may contribute to a lack of compliance in patients receiving erythropoietic proteins for cancer-related anaemia. The aim of this study was to ascertain whether differences exist in local pain at injection site between epoetin beta (NeoRecormon®) and darbepoetin alfa (Aranesp®).
Methods: This was a single-blind, randomised, cross-over study. After receiving placebo (0.9% saline SC injection [0.3 ml]), subjects were randomised to receive identical volumes (0.3 ml) and equivalent doses of either epoetin beta (6000 IU) or darbepoetin alfa (30 μg). Following a one-week washout period, subjects received the other study drug. To assess pain on injection a 10 cm ungraduated visual analogue scale (VAS) (0 = no pain, 10 = maximal pain) and a six-item verbal pain scale (VPS) (no pain = 0, very painful = 5) were used. Pain was assessed immediately after injection (T_0) and at 1-hour post-injection (T_{1h}).

Table 1

	Epoetin beta, overall (n = 37)	Darbepoetin alfa, overall (n = 37)
Median VAS score (T_0)	1.2	2.9
Interquartile range, Q1; Q3	0.0;1.5	1.3;3.9
95% CI	0.7–2.0	2.1–4.0
Median VAS score (T_{1h})	0.0	0.0
Interquartile range, Q1; Q3	0.0; 0.1	0.0; 0.2

Results: of the 40 healthy volunteers included (mean age 28.9±10.5yrs; men 47.5%), 37 completed the study. Data from the per-protocol population were analysed. Overall median values for VAS revealed that subjects experienced significantly ($p < 0.05$) less pain immediately after injection with epoetin beta than those injected with darbepoetin alfa (Table 1). Compared with placebo, median value differences were −0.2 (95% CI: −0.7–0.2) and 1.4 (95% CI: 0.8–1.9) for epoetin beta and darbepoetin alfa, respectively. Similarly by VPS, subjects experienced less pain immediately after injection with epoetin beta (1.5 [95% CI: 1.0–2.0]) than those injected with darbepoetin alfa (2.5 [95% CI: 2.0–2.5]). A greater proportion of subjects injected with darbepoetin alfa (32.4%) and placebo (13.5%) reported injections as moderately-to-very painful immediately after injection compared with those who received epoetin beta (5.4%) ($p = 0.0005$ darbepoetin alfa vs epoetin beta). In subjects injected with epoetin beta, none reported that injections were very painful. No significant differences were observed for any of the injections one hour after administration (Table 1). SC injections of epoetin beta, darbepoetin alfa and placebo were generally well tolerated in the subjects completing the study.
Conclusions: Epoetin beta by SC injection provides minimum discomfort, is as pain free as placebo (physiological saline) and is significantly less painful than SC injection of darbepoetin alpha.

1289 POSTER

Ibandronate: an effective treatment for colorectal carcinoma patients with bone metastases

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Background: Metastatic bone disease occurs in a high number of patients with various primary cancers and carries a high risk of complications. Ibandronate is a single-nitrogen, non-cyclic bisphosphonate that effectively prevents skeletal complications in patients with metastatic breast cancer. This study reports efficacy data from colorectal carcinoma patients with bone metastases treated with intravenous ibandronate.
Materials and methods: A randomized, placebo-controlled trial was conducted to evaluate the efficacy and safety of intravenous ibandronate. Fifty-two patients with metastatic bone disease received intravenous ibandronate 6mg or placebo administered via 15-minute infusion every 4 weeks. The primary efficacy endpoint was the proportion of patients with skeletal-related events (defined as pathologic fracture, spinal cord compression, radiation therapy or surgery to bone, or change in antineoplastic therapy). Secondary endpoints included time to first skeletal event, skeletal morbidity rate (events/year) and bone lesion progression time.
Results: Intravenous ibandronate 6mg significantly reduced the proportion of colorectal carcinoma patients with skeletal events (37% versus 80% with placebo; $p = 0.018$) and prolonged the time to first event by at least 6 months (median >279 versus 93 days with placebo; $p = 0.007$). Ibandronate also significantly reduced the skeletal morbidity rate (mean 2.35 versus 3.15 with placebo; $p = 0.018$) and prolonged time to progression of bone lesions (214 days versus 81 days with placebo; $p = 0.018$). Ibandronate was well tolerated with a safety profile comparable to placebo. No clinically-relevant changes were observed in serum creatinine levels.
Conclusions: Intravenous ibandronate provided significant clinical benefits for patients with bone metastases secondary to colorectal carcinoma. This suggests that ibandronate may be effective for patients with bone metastases following primary cancers other than breast cancer. Larger studies are required in these patient groups.

1290 POSTER

Bisphosphonates and jaw osteonecrosis: experience with ibandronate

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Background: A causal association between bisphosphonates (BP) and osteonecrosis of the jaw (ONJ) was highlighted by the recent Publication onlyn of a case series. Most patients were being treated for oncology indications and had undergone dental work (Ruggiero SL, et al. J Oral Maxillofac Surg 2004;62:527–34). Documents published by the FDA this year describe 610 spontaneous reports in detail, for 374 patients who received intravenous (i.v.) zoledronate only (mean time to ONJ onset: 18 months), and 120 patients who received i.v. pamidronate only (mean time to onset: 72 months). The remainder received at least two BPs sequentially. Patients switching from pamidronate to zoledronate had a higher risk of ONJ than those who received pamidronate alone (*http://www.fda.gov/ohrms/dockets/ac/cder05.html#OncologicDrugs*).
The underlying pathological mechanism for ONJ is uncertain. We investigated the incidence of ONJ following treatment with i.v. and oral ibandronate, a single-nitrogen, non-cyclic bisphosphonate, for the treatment of bone metastases.
Methods: An electronic database search was conducted of all ONJ events reported cumulatively to Roche by 15 May 2005. Cases were included if ONJ or surgical intervention for osteomyelitis was documented.
Results: See Table 1.
Discussion: Both case reports with oral ibandronate were confounded by prior exposure with zoledronate. As with other BPs, the time to ONJ onset after ibandronate exposure varied from a few months to a few years. ONJ associated with ibandronate is a serious, though rare adverse reaction.

Table 1: Cases of ONJ with ibandronate

Case	Age (years)	Ibandronate dose	ONJ site	Dental extraction/ prosthesis	Time to onset	Outcome
1	83#	I.v. 4 mg monthly	Both jaws	No	3 years	Oral surgery and subsequent abscess drainage
2	76	I.v. 6 mg every 2 weeks	Dental prosthesis	Yes	11 months	Sequestrectomy and plastic surgery
3	57	I.v. 6 mg monthly	Mandible	No	3 months	Resolved with bone decortication
4	70+	I.v. 6 mg monthly	Maxilla	Yes	5 years	Resolved with alveolar process resection
5	76*	I.v. 6 mg monthly	Mandible	Yes	2 months	Resolved with antibiotics
6	58*	Oral 50 mg once daily	Maxilla	Yes	4 months	Event persisted
7	54*	Oral 50 mg once daily	Mandible	Yes	6 months	Not recorded

*Prior history of zoledronic acid treatment; #Prior history of clodronate treatment

1291 POSTER

Capecitabine (XEL)+Oxaliplatin (OX) in elderly people (EP) with Colorectal Cancer (CRC): Comparison of safety (S) and feasibility (F) of two different schedules. Preliminary findings

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Rationale: CRC incidence arise in older patients. Aging is associated with decreased functional reserve of multiple organ systems with worsening of behaviour of pharmacokinetics and pharmacodynamics of drugs. EP show enhanced susceptibility to cytotoxic therapy, especially for bone-marrow, mucosal, CNS and neuroperipheral (NPH) toxicity (TOX). Treatment of EP with CRC must take in account the prevention of these effects. Combination XEL+OX seems to be safe and feasible for this purpose especially if dose drugs adjustment will be performed.
Aims: To evaluate a flat dose schedule of XEL (1000 mg b.i.d.)+OX (130 mg/sqm) q3wks vs XEL (1000 mg/sqm b.i.d.)+OX (130 mg/sqm) q3wks.
Methods: a totally of 22 elderly PTS Dukes C stage CRC (m/age 70) were treated in our dept after written informed consent acquired. 11 pts (Group A) were treated as follows: XEL (1000 mg/sqm/os b.i.d.) d2−15+OX (130 mg/sqm/2 h/i.v.i.)(Schedule A). Another group of 11 pts (Group B) received XEL 1000 mg/b.i.d (flat dose)+OX (130 mg/sqm/2 h/i.v.i.)(Schedule B). We evaluated GFR of each patient and CHT was adjusted according with Kintzel&Dorr formula. All patients were evaluated for common treatment-related adverse events haematological, liver, mucosal, CNS&NPH TOX, N&V and HFS, according to the ECOG. All patients were also evaluated for ADL/IADL both with ECOG PS and number of comorbidities. Plasma VEGF's values was also evaluated.
Results: Both Group A & B were evaluated at the end of treatment. Group A PTS received about 80% of expected dose only; Group B received full expected dose; TOXs: Group A: haematological: 10 PTS = G1; 2 PTS = G2. Liver: 6 PTS = G1; 5 PTS = G2; 1 PTS = G3. HFS: 3 PTS = G2; 1 PTS = G3/4; CNS&NPH: 11 PTS = G1/2. Group B: haematological: 6 PTS = G1; Liver: 10 PTS = G1; CNS&NPH: 4 PTS = G1.
Conclusions: The study show that schedule B have more safe and feasible profile compared with schedule A. Further, XEL flat dose (according with Lokich, Canc. Invest., 2004) improves PTS compliance for oral delivery (no needs to different tablets for size and concentration to reach the expected dose). No delivery delay was necessary in schedule B PTS. Only slight general TOX was also noted in schedule B PTS vs schedule A. Author believe that XEL flat dose administration works as antiangiogenic control in CRC elderly PTS, with preservation of DI, even if a larger number of PTS will be necessary to permit statistical analysis. DFS and OS are still under evaluation.

Publication
Patient management (including cancer in the elderly, palliative care, symptom management, psychosocial aspects, quality of life management)

1292 PUBLICATION

Effectivness of recombinant human erythropoietin (epoetin beta, EPO) in improving hematological parameters and QOL in patients with chemotherapy-induced anemia. A double-blind, parallel-group, dose-finding study

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Aim: of this randomized, double-blind, parallel-group, dose-finding study is to evaluate the effectivness of recombinant human erythropoietin (epoetin beta, EPO) in improving hematologicals parameters and QOL.
Methods: Anemic patients (hemoglobin(Hb)) $\leqslant$11g/dl(undergoing chemotherapy for colorectal cancer or malignant lymphoma received EPO 20000 or 30000 IU subcutaneously once weekly for 12 weeks. Changes in QOL were assessed with the Functional Assessement of Cancer Therapy-Anemia(FACT-An) survey before (day 1 of chemotherapy), during (7−11 weeks) and at the end of EPO therapy.
Results: A total of 50 patients were enrolled in the study. The increase in Hb from baseline to the time of final evaluation (12 weeks) was dose-dependent(1.04$\pm$1.75, and 1.75$\pm$2.15 g/dl in the 20000 and 30000 IU groups, respectively), and the increase in the 30000 IU group was significant ($p = 0.008$). The proportions of patients with an Hb increase $\geqslant$2 g/dl were 66.7 and 78.3% in the 20000 and 30000 IU groups respectively. The FACT-Fatique subscale score (FSS) before EPO therapy was high in these two groups. Changes in FSS were not dose-dependent, but the increase in FSS was significantly correlated with the Hb increase($r = 0.434$ $p < 0.001$), and significantly greater in patients with an Hb increase $\geqslant$2g/dl, compared to the patients with one of <2 g/dl (2.2 vs. −3.2 $p = 0.011$). Multiple regression analysis showed that the FSS increase was significantly correlated with the Hb increase ($p < 0.001$) and FSS values at the onset of EPO therapy ($p < 0.001$). The transfusion rates after 4 weeks of therapy were 16,8% (20000 IU) and 0% (30000 IU). Dose-dependent adverse events were not observed.
Conclusions: Once-weekly EPO at a dose of 30000 IU increased Hb levels in patients with chemotherapy-induced anemia and QOL benefits were significantly correlated with the Hb increase.

1293 PUBLICATION

Cancer pain control in the Eastern mediterranean region: many steps behind

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The World Health Organization (WHO) Eastern Mediterranean Region (EMR) comprises 22 developing countries of varied economic development. These countries constitute about 8% of the world population and have increasing cancer incidence with associated mortality and morbidity. The WHO monitors morphine consumption as an index of improvement in pain management & since1984 the world morphine consumption has been increasing in response to the WHO recommendations, suggesting improvement in global cancer pain control.
Objective: To assess cancer pain control in the EMR.
Method: United Nations' mid-year population estimates and International Narcotics Control Board data regarding morphine consumption were used to calculate the morphine consumption per capita for the World and the EMR, from 1996 to 2003. Globocan 2002 database was used to calculate the estimated cancer mortality in EMR.
Results: Although the EMR countries contain 4% of global estimated cancer mortality, they consumed only 0.002% of the global morphine consumption in 2003. World morphine consumption/capita has increased by 54% from 2.88 mg/capita in 1996 to 4.43 mg/capita in 2003. On the other hand there was almost no change in morphine consumption/capita in the EMR from 1996 (0.09 mg/capita) to 2003 (0.1 mg/capita).
Conclusion: These results indicate that cancer pain control in the EMR is completely inadequate with almost no improvement over the last years when compared to global trends. More attention should be paid to cancer pain control in the EMR, both on national and international levels with special attention to the barriers that prevent access to opioids in this region.