(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.