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Control of nausea and vomiting in patients with fractionated cisplatin chemotherapy: A double-blind randomised study comparing intravenous dolasetron alone and dolasetron plus dexamethasone

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Dolasetron has been proven to be effective in controlling acute emesis related to cisplatin and cisplatin containing chemotherapy regimens. We investigated the safety and efficacy of dolasetron alone or dolasetron plus dexamethasone in controlling nausea and vomiting related to cisplatin chemotherapy over a study period of up to 5 consecutive days. 192 cancer patients were randomised to receive 100 mg IV dolasetron alone or 100 mg IV dolasetron and 20 mg dexamethasone before chemotherapy primarily with cisplatin (15–50 mg/m^2) administered over a period of 4 hours for at least 2 but not more than 5 consecutive days. The safety and efficacy was measured at hour 24 of each study day using the following criteria: complete response, i.e. no vomiting and no rescue medication, and maximum nausea severity, self-assessed by patients using a 100 mm visual analogue scale. The overall complete response rates were significantly higher in the dolasetron plus dexamethasone group (72.9%) compared to the dolasetron only group (40.8%) ($p < 0.0001$). In addition, the complete response rates on each study day were also significantly higher with dolasetron plus dexamethasone. Day 1 revealed a response rate of (Dol/Dex vs. Dol) 91% vs. 78% ($p < 0.029$), respectively. The duration of chemotherapy and treatment exerted the only statistically significant subgroup effects on complete response ($p < 0.0001$). Dolasetron in combination with dexamethasone significantly increases the effectiveness in preventing nausea and vomiting related to fractionated cisplatin chemotherapy.

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Phase 2 trial of Zoledronate vs Pamidronate in multiple myeloma and breast cancer

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Purpose: To compare Zoledronate (CGP42446) (Z), a new potent 3rd generation bisphosphonate, with Pamidronate (P) in patients with osteolytic metastases.

Methods: Two hundred and eighty patients (172 breast cancer & 108 multiple myeloma) with osteolytic metastases were randomized in a double-blind design to receive 9 monthly infusions of either 0.4, 2.0, or 4.0 mg of Z as a 5-minute I.V. infusion or 90 mg of P as a 2-hour infusion. Evaluation period = 10 months in duration.

Results:

	0.4 mg Z (N = 68)	2.0 mg Z (N = 72)	4.0 mg Z (N = 67)	90 mg P (N = 73)
RT to bone	24%	19%	21%	18%
SRE (+HCM)	46%	35%	33%	30%*
Fracture	26%	22%	21%	21%
SMR (Events/yr) (+HCM)	2.27	1.59	1.45	1.13*
Bone lesion response (PR + S)	56%	55%	60%	44%
Bone mineral density (Mean)	+6%	+9%*	+10%*	+9%*
Ca/creatinine (Median)	−31%	−43%	−58%*	−32%
N-telopeptides (Median)	−37%	−59%*	−61%*	−58%*

* Statistically superior to 0.4 mg Zoledronate

The time to first skeletal related event (SRE +/− HCM) was significantly longer for P than for 0.4 Z. The safety profile for Z at all doses was similar to that of P.

Conclusion: A 5-min infusion of 4 mg of Z is at least as effective as 90 mg of P in preventing the skeletal complications of osteolytic disease. A dose response for Z is evident in this osteolytic bone metastases patient population. The optimal efficacy of Z may not have been reached, since Phase I bone marker studies suggest that higher doses (>4 mg) of Z may be more effective. Doses of 4 and 8 mg of Z are being compared with 90 mg of P in large Phase III bone metastases studies.

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Positive epoetin alfa effect on quality of life in anemic cancer patients receiving chemotherapy: Results from a randomized placebo-controlled trial

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Purpose: Debilitating fatigue and exhaustion are common in cancer patients receiving chemotherapy. The effect of epoetin alfa on quality of life (QOL) was assessed in patients with anemia in a multinational trial of 375 patients receiving chemotherapy for various malignancies. Epoetin alfa was hypothesized to affect QOL via improvement in hemoglobin (Hb) levels.

Methods: Patients were enrolled with Hb 10.5 g/dL or less or a decline in Hb of 1.5 g/dL or greater in a chemotherapy cycle. Study duration was variable across subjects, based upon the expected number of chemotherapy cycles per subject. QOL was assessed prior to treatment, at 4 and 16 weeks, and at study completion. Five cancer-specific QOL scales (FACT-G, FACT-An Fatigue, CLAS Energy, CLAS Activities, and CLAS Overall QOL), chosen from the Functional Assessment of Cancer Therapy-Anemia (FACT-An) and the Cancer Linear Analogue Scales (CLAS), were analyzed for an epoetin alfa treatment effect and for correlation with changes in Hb. Epoetin alfa treatment effects were tested using multiple linear regressions on QOL change scores from baseline to last assessment, accounting for the effect of disease progression and other patient characteristics, such as demographic variables, baseline Hb level, baseline endogenous erythropoietin level, and pre-study transfusion dependence.

Results: In multiple linear regression models adjusting for disease progression and other patient characteristics, epoetin alfa patients had significant improvements in FACT-G, FACT-An Fatigue, CLAS Energy, CLAS Activities, and CLAS Overall QOL (all p-values < 0.05). These scales were significantly correlated with improvements in Hb (correlation coefficients ranged from 0.27 to 0.33, all p-values < 0.0003).

Conclusions: Patients treated with epoetin alfa experienced significant improvements in health-related QOL, consistent with a mechanism of action mediated by an increase in Hb levels. Disease progression and Hb levels are independent contributors to patient QOL.

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Randomized comparison of broad spectrum antibiotics with or without filgrastim in the treatment of patients with high-risk fever and grade IV neutropenia

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Purpose: to evaluate in a prospective multicenter randomized clinical trial the efficacy of filgrastim in the treatment of patients with solid tumors and high-risk febrile neutropenia.

Methods: every patient with a solid tumor treated with conventional dose chemotherapy that presented with fever and grade IV neutropenia was considered eligible for the trial if they met at least one of the high risk criteria. High risk criteria were defined as follows: profound neutropenia (ANC below 100/mm3), short time elapsed from previous chemotherapy cycle (less than 10 days), sepsis or clinically documented infection at presentation, serious independent comorbidity, ECOG 3–4, prior inpatient status, and failure of ambulatory management of low risk febrile neutropenia (modified from Talcott et al., JCO 1992; 10: 316). Eligible patients were randomized to recieve broad spectrum antibiotics with or without granulocyte colony-stimulating factor (G-CSF, filgrastim 5 mcg/kg/day). From I/97 210 patients from 5 spanish university centers were included in the study. Treatment with filgrastim was continued untill ANCs rose above 1000/mm3, and antibiotics were continued for at least 5 days or untill 2 days after fever subsided and ANCs rose above 1000/mm3.

Results: patients randomized to G-CSF had a significantly shorter duration of grade IV neutropenia (2 versus 3 days, $p < 0.005$), antibiotic therapy (5 versus 6 days, $p < 0.005$) and hospital stay (5 versus 7 days, $p < 0.005$), compared to patients in the control arm. The proportion of pts with clinically