1459 ORAL

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

A.A. Fauser. *on behalf of the European Dolasetron study group, Department of Hematology/Oncology, BMT Center Idar-Oberstein, Germany*

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.

1460 ORAL

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

A. Lipton[1], J. Berenson[2], R. Knight[3], Grace Hu[3], E. Levy[3]. *[1]Hershey Med Ctr, Hershey, PA; [2]UCLA & DVA, West LA, CA; [3]Novartis Pharmaceuticals Corp., East Hanover, NJ, United States*

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.

1461 ORAL

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

L. Fallowfield[1], D. Gagnon[2], M. Zagari[2], B. Bresnahan[2], E. Vercammen[3], T.J. Littlewood[4], P. McNulty[2]. *[1]University College London Medical School, London, United Kingdom; [2]Johnson & Johnson, ICOM Health Economics, Raritan, NJ, United States; [3]R.W. Johnson Pharmaceutical Research Institute, Basserdorf, Switzerland; [4]John Radcliffe Hospital, Oxford, United Kingdom*

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.

1462 ORAL

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

R. Garcia-Carbonero[1], J. Mayordomo[2], M. Tornamira[1], M. Lopez-Brea[3], A. Rueda[4], V. Guillem[5], A. Yubero[2], F. Rivera[3], H. Cortes-Funes[1], L. Paz-Ares[1]. *[1]Hospital Doce de Octubre, Medical Oncology, Madrid; [2]Hospital Clinico, Medical Oncology, Zaragoza; [3]Hospital M. Valdecilla, Medical Oncology, Santander; [4]Hospital Clinico, Medical Oncology, Malaga; [5]Instituto Valenciano de Oncologia, Medical Oncology, Valencia, Spain*

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

and microbiologically documented infection was similar between groups. Mortality rates were also not significantly different between the two groups.

Conclusions: Adding G-CSF to antibiotic therapy is cost-effective since it shortens the duration of neutropenia, and reduces the duration of antibiotic therapy and hospitalization in pts with high-risk febrile neutropenia.

1463 ORAL

Patients with hematological malignancies experience a higher rate of documented infections than patients with solid tumors after high-dose chemotherapy with autologous peripheral stem cell transplantation

O. Sezer[1], E. Späth-Schwalbe[1], H. Fuss[2], J. Eucker[1], C. Bauhuis[1], U. Kobert[2], W. Heinzel[2], R. Arnold[1], W. Schultze[2], K. Possinger[1].
[1]Department of Oncology/Hematology, Universitätsklinikum Charité, Humboldt-Universität, Berlin; [2]Humaine Klinikum Bad Saarow, Germany

There are only few reports on infectious complications in different subgroups of patients treated with high-dose chemotherapy (HDCT) and autologous peripheral blood stem cell transplantation (PBSCT). In a retrospective study, we analyzed the data of patients with hematological malignancies (group A, n = 143) or solid tumors (group B, n = 83) treated with HDCT in two german centers. Although febrile neutropenia occurred with the same frequency in both groups (81%), clinically or microbiologically documented infections occurred more frequently in group A (in 40% of patients with febrile neutropenia) than in group B (18%, $p < 0.005$). 74% of all isolated microorganisms were gram-positive. Severe organ infections were rare. There was one infection-related death.

Conclusions: Underlying disease is a determinant of the rate of microbiologically or clinically documented infections after HDCT with autologous PBSCT.

1464 ORAL

A randomized trial comparing the toxicity and the treatment costs of HD-VIC plus PBSC transplantation with or without amifostine (AMI) in patients with solid tumors

J. Hartmann, A. von Vangerow, S. Knop, W. Brugger, L. Fels[1], H. Stolte[1], L. Kanz, C. Bokemeyer. *Eberhard-Karls U Medical Center, Tuebingen; [1]Dept. Nephrology, U Hanover, Germany*

Purpose: Cytoprotection with AMI has demonstrated a reduction of nephro-, neuro- and myelotoxicity. The two-armed study evaluates the toxicity and the costs of HD-VIC ± AMI-treatment.

Methods: 40 pts with different solid tumors were randomized to receive HD-VIC (day $_{1-3}$ Carbo 1500 mg/m^2, Eto 1500 mg/m^2 and Ifo 12 g/m^2 ± AMI 1.5 g per day prior to the application of C and I). Pts were monitored for nephrotoxicity including early urinary marker excretion, mucositis, hematopoetic recovery and frequency of fever and infections. Pts with AMI (n = 19 evaluable; arm A) had a median decrease of creatinine clearance after HD-VIC by 12% compared to 34% to arm B (n = 20 evaluable) ($p = 0.06$). Mucositis III/IV° was 21% in arm B vs. 0% in the AMI-group ($p < 0.001$). Whereas the median no. of days to granulocytes >500/μl was equally in both arms (9.1 vs. 9.8), thrombocyte counts (>20.000/μl) recovered significantly earlier in arm A (10.1 vs. 12.4; $p = 0.02$), resulting in a lower no. of days of thrombocyte transfusions (2.5 vs. 3.5). In addition, the median no. of days with fever >38°C (2.1 vs. 3.9; $p = 0.008$) and days spent in hospital were in favour of pts receiving AMI. A pharmacoeconomic analysis revealed a reduction in costs for supportive care for pts receiving HD-VIC + AMI compared to those treated with HD-VIC alone. This has to be balanced against the drug costs.

Conclusion: This analysis demonstrates that both organ- and hematotoxicity of HD-VIC ctx may be ameliorated by the use of AMI resulting in less mucositis, fever episodes, thrombocyte transfusions and shorter hospital stays.

1465 POSTER

The effect of systematic rHu-erythropoietin (Epoietin alpha) treatment before and during radiotherapy (radio-chemotherapy) in unselected anemic cancer patients: Results of an Austrian multicenter observation study

R. Hawliczek, R. Oismüller. *Dpt. of Radiooncology, Donauspital, Vienna, Austria*

Anemia is a common situation in cancer patients, reducing quality of life, tolerance to treatment and likely treatment outcome. Erythropoietin (Epo) is a nontoxic and effective drug for treatment of anemia.

Purpose: The feasibility of systematic administration of Epo before and during radiation (radio-chemotherapy) and it's effect on Hb and quality of life.

Method and Material: One hundred fourty three anemic cancer patients were included in the study of the Austrian Society of Radiation Oncology by 11 centers. Patients recieved three times 300 IU/kg BW per week (Hb < 10 g/dl) subcutanously or 150 IU/kg BW (Hb 10 to 12 g/dl). Start of Epo treatment about 10 days prior to radiation.

Results: Eightyfour percent of patients responded. The median increase of Hb was 0.37 g/dl per week. Thirtyseven percent reached a Hb-level of >14 g/dl. Quality of life was measured at start of EPO treatment and end of radiation according to WHO-criteria. Patients improved in 20.3%, 50.4% remained stable and 27.3% decreased during radiation (+/−chemotherapy). Self assesment resulted in an increase in 19.6%, stability in 32.2% and 44.8% reduction. No relevant adverse reactions to Epo were reported.

Conclusion: The use of EPO under radiation (+/−chemotherapy) is feasible, save and effective. Overall condition may be improved in a significant number of patients, despite aggressive treatment. It's influence on tumor hypoxia and consequently tumor control is an important topic of future research.

1466 POSTER

Non neutropenic infections associated with docetaxel containing chemotherapy in patients with solid tumors

J. Souglakos, A. Kostakis, E. Sarra, S. Kakolyris, Ch. Kouroussis, S. Agelaki, N. Vardakis, K. Kalbakis, V. Georgoulias, G. Samonis.
[1]University General Hospital of Heraklion, Dpt of Medical Oncology, Heraklion, Crete, Greece

Purpose: Docetaxel is a potent agent as first line chemotherapy for the treatment of several neoplasias. However, the drug has severe side effects. Lymphopenia, which has been studied only in animals, is one of them. A plethora of infections has been observed recently in lymphopenic, but not neutropenic, patients treated with docetaxel.

Patients and Methods: To detect these of infections all patients receiving the drug during a two-year period were examined prospectively and all non-neutropenic infections were studied. A total of 680 patients, participating in 23 therapeutic protocols, suffering from different neoplasias (breast, non-small cell lung, gastric, pancreatic, uterine cancer cholangrocarcinomas and sarcomas), who had received 2.867 cycles of docetaxel containing regimens were examined.

Results: Fifty three non neutropenic infections were identified and included pneumonias (24), interstitial pneumonias of the pneumocystis carinii type (5), lung abscess (1), bacteremias (2), candida infections (11), herpetic (4), cellulitis (3), cytomegalovirus infection (1) perirectal abscess (1), and urinary tract infection (1). The majority (70%) of the patients was lymphopenic (less than 900/mm3), while all of them had low CD4 (less than 500/mm3), and CD8 (less than 400/mm3) cell counts. The incidence of non neutropenic infections in patients treated with paclitaxel containing regimens and in patients treated with non taxane compounds, during the study period, were calculated for comparison. Paclitaxel had been given in 157 patients with 752 cycles of chemotherapy. They developed 6 non-neutropenic infections ($p = 0.042$), while non-taxane containing chemotherapy had been given in 410 patients by 2.174 cycles and they developed 12 non-neutropenic infections ($p = 0.001$).

Conclusions: The majority of the patients of the two latter groups were non-lymphopenic. In conclusion, the use of docetaxel is associated with increased incidence of non-neutopenic infections. Lymphopenia and low CD4 and CD8 cell counts seem to be the main predisposing factor.

1467 POSTER

Treatment of febrile neutropenia with ceftriaxone monotherapy – Analysis of risk-factors

M. Karthaus[1], G. Egerer[2], T. Südhoff[3], D. Kämpfe[4], G. Heil[1], H. Jürgens[5].
[1]Hannover Med. School Dept. Hematology; [2]Med. Univ. Klinik Heidelberg; [3]Med. Univ. Klinik Düsseldorf; [4]KKH Lüdenscheid; [5]Univ. Münster, Dept. Pediat. Hematology, Germany

Purpose: There are no exactly defined recommendations for single-agent antibiotic treatment because a clear definition of low risk febrile neutropenia is lacking. We analyzed safety and efficacy of ceftriaxone monotherapy in febrile neutropenia (FN).