242 POSTER

PREVENTIVE VERSUS THERAPEUTIC USE OF G-CSF FOLLOWING HIGH DOSE CYCLOPHOSPHAMIDE (H.D.CTX)

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The preventive vs therapeutic administration schedules of G-CSF is under study in this trial. Thirty-eight patients with advanced malignancies received CTX 4.5 gr/m^2 and equal dose of Mesna divided in two days. The pts were randomized to receive G-CSF 5 μg/kg/d s.c. on five schedules: (1) Control group without G-CSF, (2) Group A: 24 h after the end of H.D.CTX, (3) Group B: 48 h, (4) Group C: 72 h, (5) Group D: 96 h, (6) Group E: when WBC < 1000/μl. To date 38 pts and 67 cycles were evaluable. The median age was 52 years, 28 were women and 10 men ECOG PS 0–3 and all patients had received prior chemotherapy

	Control	A (24h)	B (48h)	C (72h)	D (96h)	E (WBC < 1000)
No of courses	**10**	**12**	**11**	**12**	**12**	**10**
Median duration of neutropenia < 500/μl	10	4	4	5	5	5.5
Median neutrophil nadir	100	200	150	100	180	100
Median duration of lebrile days with neutropenia	4	0	0	0	2	4
Incidence of neutropenia with fever > 38°C (% of courses)	10%	16%	27.5%	27.5%	66%	80%
Onset of neutropenia	8	8	7	9	8	8
Duration of G-CSF administration	-	12	11	10	8	8.5

(1) There is no significant difference among the groups in onset, in duration of neutropenia and neutrophil nadir. (2) Pts of 24, 48, 72 h had statistically less febrile days with neutropenia when compared with controls, 96 h and of WBC < 1000 μl. These data suggest that the timing of G-CSF administration does not affect the duration of neutropenia and neutrophil nadir. Although the cost of G-CSF administration decreases significantly when administered therapeutically, preventive administration up to 72 h is indicated.

243 POSTER

A PHASE II STUDY OF THE RECOMBINANT HUMAN INTERLEUKIN 3 (IL-3) FOLLOWING CARBOPLATIN (CBDCA) AND ETOPOSIDE (VP-16) CHEMOTHERAPY IN PATIENTS WITH SMALL CELL LUNG CANCER (SCLC)

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To evaluate the safety and the efficacy of IL-3 (Sandoz), SCLC patients (pts) received a subcutaneous infusion of IL-3 for consecutive 10 days. The chemotherapy was consisted of CBDCA (400 mg/m^2 for previously untreated pts or 350 mg/m^2 for previously treated pts on day 1) and VP-16 (100 mg^2 on days 1–3) every four weeks. If the nadir of platelet counts was < 75 × 10^3/ml in the observation cycle of chemotherapy, pts were randomly assigned for the next cycle to either 5 or 10 μg/kg/day of IL-3, administered on days 4–13 (28 pts, median age 67 years). The nadir of platelet counts were 42 × 10^3/ml in the observation and 62 × 10^3/ml in the IL-3 cycle ($P < 0.001$). Recovery of platelet counts > 100 × 10^3/ml was faster in the IL-3 cycle (17 days) than the observation cycle (21 days: $P < 0.001$). Grade I/II fever was most frequently observed (79%). There were no grade III/IV IL-3 related adverse events. **In conclusion,** the IL-3 infusion following the CBDCA and VP-16 chemotherapy appears to reduce chemotherapy induced-thrombocytopenia with an acceptable toxicity.

244 POSTER

GM-CSF INDUCED ACTIVATION OF T-LYMPHOCYTES AND MACROPHAGES

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The effect of GM-CSF infused after 7 g/m^2 cyclophosphamide (CTX) and 800 mg/m^2 carboplatinum (CBDCA) was evaluated in 16 (LG-NHL, MM, HD) patients. Serum concentrations of soluble CD8 (sCD8) and soluble IL-2 receptor (sIL-2R) as well as circulating levels of IL-2, IFN-γ, neopterin, IL-1α, IL1-β, TNF-α and IL-6 were determined on day 0 and days +4, +10 and +16 post-GM-CSF and intracellular IL-2, IFN-γ, IL-1α, IL-1β, TNF-α and IL-6 on days 0 and +16. sIL-2 R rose from day +4 to day +16 and reached twice basal values at 10 and 16 days after both CTX (2266 ± 904, 2292 ± 873 vs 1189 ± 608) and CBDCA (2225 ± 965, 2313 ± 1055 vs 1151 ± 518). Neopterin also rose and was maximum on day +16 (1.7 post-CTX, 1.6 post-CBDCA vs basal). Serum IL-1α concentrations varied little after CTX, but increased two-fold over basal values after CBDCA (39.3 ± 34.6 vs 15.8 ± 40.5). Serum IL-1β increased 1.3 on the 16th post-GM-CSF day after CTX and 1.8 after CBDCA. Serum TNF-α rose to 1.8 basal values on day +10 and to 3.5 on day +16 following CBDCA, but not after CTX. Changes in the other serum and intracellular indices studied were negligible. These results suggest that GM-CSF activates T-lymphocytes and macrophages, but that their activation partially depends on the therapy that precedes administration of the growth factor.

245 POSTER

AMIFOSTINE STIMULATES HEMATOPOIETIC PROGENITORS FROM HUMAN NORMAL AND MYELODYSPLASTIC (MDS) BONE MARROWS

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Studies have demonstrated the trilineage hemoprotective effects of amifostine (Ami). Recent studies suggested direct stimulation of hematopoiesis. *In vitro* growth of CFU-GEMM, BFU-E and CFU-GM from normal and MDS bone marrows was evaluated after 15 min preincubation with Ami or its active metabolite, WR-1065, glutathione (GSH), or recombinant growth factors. Concentrations of Ami and WR-1065 at 0.1–1000 μM stimulated growth of CFU-GEMM and BFU-E from normal marrow mononuclear cells; >10 μM GSH was toxic. Ami was the most potent stimulant yielding up to 9-fold greater BFU-E, 4× CFU-GEMM and 3× CFU-GM over controls. Compared to kit ligand, IL-1 and IL-3 (200 U/ml), Ami was a more potent hemopoietin yielding up to 3× greater CFU-GEMM and BFU-E recovery. Despite deficient colony growth in MDS controls, Ami preincubation with clinically achievable concentrations (100–500 μM) stimulated growth of CFU-GEMM and BFU-E 2–7-fold and improved colony/cluster ratio in 7 of 8 pts studied. The data indicate that Ami is a potent stimulant of primitive progenitor growth that exceeds that of recombinant cytokines. The profound simulation observed in MDS suggests that Ami may improve hematopoiesis in patients with MDS and warrants testing in clinical trials.

246 POSTER

COMPARISON OF TWO STEM CELL MOBILIZATION AND HARVESTING REGIMENS FOR PERIPHERAL BLOOD STEM CELL (PBSC) TRANSPLANTATION IN MULTIPLE MYELOMA (MM)

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We have investigated two regimens for the mobilisation of stem cells prior to PBSC transplantation in MM. Regiman A: 125 μg/m^2 GCSF b.d. for 7 days with harvest of stem cells days 5–8. Regimen B: 12–16 μg/kg for 4 days with harvest days 4 and 5. For each regimen the median total cell count, CFU-GM and CD34 + counts and days to engraftment as measured by time to attainment of neutrophil count 500 were calculated and compared by the Mann-Whitney non-parametric test.