Proffered papers

BMT and PSCT

1118 ORAL

AMIFOSTINE IMPROVES THE ANTILEUKEMIC THERAPEUTIC INDEX OF MAFOSFAMIDE: IMPLICATIONS FOR BONE MARROW PURGING

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To test the potential use of amifostine (Ami) to protect normal bone marrow (N1 BM) progenitor cells during ex vivo purging of leukemia, the dose response of mafosfamide (Mfs) ± Ami on N1 BM progenitor cells was determined and the LD_{95} was calculated. Ami pretreatment resulted in a statistically significant protection of CFU-GM and erythroid blast-forming units (BFU-E) from Mfs toxicity. The mean ± SEM μg/ml LD_{95} concentrations were: CFU-GM, Mfs alone 54 ± 13 vs Ami-Mfs 66 ± 14, p .005, BFU-E, Mfs alone 48 ± 14, vs Ami-Mfs 61 ± 11, p .005. In contrast, Ami pretreatment sensitized CFU-L to Mfs toxicity: LD_{95} for Mfs alone 33 ± 4 vs Ami-Mfs 27 ± 3, p .003. At the LD_{95} for CFU-GM and BFU-E, Mfs alone resulted in a ≈4 log cell-kill for L-CFU. Ami protection of N1 BM resulting in a higher Mfs LD_{95} concentration, coupled with the Ami-sensitization of the leukemia, provided an estimated additional 6+ log leukemia cell-kill. This enhanced selective leukemia cell-kill from Mfs during ex vivo purging using the LD_{95} concentration of Mfs for normal marrow progenitors offers the potential for lowering the incidence of leukemic relapse while preserving a greater number of normal progenitor cells for engraftment following autologous transplantation.

1119 ORAL

GLYCYL-GLUTAMINE SUPPLEMENTION AND HIGH DOSE THERAPY

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The amino acid, l-glutamine is the major energy substrate of the intestinal epithelium. Dietary supplementation reduces GI toxicity after RT and CT in animal models. The maximal insult to the gut occurs during high dose conditioning therapy and in this study glycyl-l-glutamine (GLG) supplementation is commenced one day before high dose therapy starts. *In vitro* testing showed minimal shifts in chemo or radiosensitivity with glutamine supplementation. This double blind randomised trial compares 50 g/day GLG iv supplementation versus an isonitrogenous mixture of aminoacids. Serum glutamine concs were doubled from a mean of 398 at baseline to 812 μmolar at end of infusion.

	GLG (19)	Placebo (12)
Median days to 0.5 neutrophils	14	16
Median days to 50 platelets	18	21
Median hospital stay post graft	19 (12–44)	22 (14–48)
Mucositis score (nurse)	3.1	7.5

These results suggest a beneficial effect of GLG supplementation on gastrointestinal toxicity and haematological recovery with reduction in hospital stay and warrant further study.

1120 ORAL

FACTORS THAT INFLUENCE PERIPHERAL BLOOD STEM CELL HARVEST AFTER HIGH-DOSE CYCLOPHOSPHAMIDE AND CARBOPLATIN FOLLOWED BY GM-CSF INFUSION

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The peripheral blood stem cell (PBSC) mobilization capacity of carboplatin (CBDCA, 800 mg/m^2) followed by GM-CSF infusion (5 μg/kg) is being compared with that of cyclophosphamide (CTX, 7 g/m^2) followed by the same dose of GM-CSF. So far, 18 patients, 5 MM, 9 LG-NHL, 4 HD, have been entered in the study. PBSC were not collected after CBDCA in 4 cases, one due to early discharge, one because of suspected, but unconfirmed, allergy to GM-CSF, one because the CBDCA dose was reduced to 400 mg/m^2, one because G-CSF was substituted for GM-CSF due to hypotension and dyspnea, which, however reappeared 3 times while patient was off treatment. 53 stemophereses were analyzed in the other 14 patients after CTX and 43 after CBDCA for a mean of 6.8 /patient. Mean CFU-GM × 10^6/l recovered were 0.34 ± 0.2 after CBDCA and 0.58 ± 0.78 after CTX (P = NS). Mean CD34+ × 10^6/l were 35.9 ± 118 after CBDCA and 24 ± 34.4 after CTX (P = .00034). Multifactorial analysis performed to identify the variables that influence CFU-GM × 106/l and CD34+ × 106/l recovery revealed that the relevant factors for CFU-GM were: the CFU-GM/ml, the percentage and absolute values of CD34+ /ml in the peripheral blood the day stemopheresis was effected, the type of disease, the number of bone marrow CFU-GM before starting therapy (bone-marrow proliferations). For CD34+ they were: the WBC/l, the percentage and absolute values of CD34+/ml present on the day of stemopheresis, the type of disease and the bone-marrow proliferation before starting therapy.

1121 ORAL

DNA SYNTHESIS OF PROLIFERATING SUBPOPULATIONS OF HUMAN BONE MARROW INCLUDING CD34+ CELLS ALONG THE CIRCADIAN TIME SCALE

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We have extended earlier flow cytometric circadian studies of total bone marrow (BM) cells to also include proliferating BM subpopulations (i.e., myeloid lineage, erythroid lineage, CD34+ cells) with the intent to further optimize cancer chromotherapy with chemotherapeutics or cytokines, taking into account temporal susceptibility rhythms of critical BM cell populations. BM was aspirated at 5 hour intervals from the sternum and iliac crests from 5 healthy men, aged 23–26 years, altogether 5 times during a 24 hour time span. To separate the myeloid, erythroid and lymphoid subpopulations indirect immunostaining was performed with the common leukocyte antigen CD45, and the myelomonocytic marker CDw65 (VIM2). The most proliferating myelomonocytic cells (VIM prol.) could further be separated from the rest of the myelomonocytic cells. Isolation of CD34+ cells was performed by a technique using immunomagnetic beads coated with the anti CD34 monoclonal antibody BI-3C5. Subsequent DNA staining was performed with a hypotonic propidium iodide solution. The circadian variation in S-phase for total proliferative BM cells was found in 4 of 5 subjects to be the same as earlier reported (i.e., high S-phase during day and low during evening or night; Blood 77: 2603–11, 1991). The most proliferating myelomonocytic cells also demonstrated higher S-phase during day as compared to night (P = 0.0198; Mann-Whitney U) with a mean S-phase of 14.2% ± 3.5.% (S.D.). The circadian variation of the CD34+ S-phase cells corresponded to the circadian pattern of the VIM prol. cells in 3 of 5 subjects;