dose of 5 mcgr/kg/day, for 7 days each. The 48 patients received a total of 96 cycles of HDCT.

Results: Toxicity: grade IV leukopenia and thrombocytopenia were observed in all patients. Twenty episodes of febrile neutropenia were observed. Transfusions: platelet to 13 patients, red blood cells to 14 patients. No treatment related death occurred. Complete response in 17 patients (35.4%), partial response in 13 patients (27.1%), for an overall response rate of 62.5% (95% confidence interval 47.3%-76.01%). Stable disease was observed in 6 patients (12.5%) and progressive disease in 12 patients (25%). Median TTP was 9 months (range 1-91). Median survival was 15.1 months (range 3-91). 1 and 3-year survival rate were 58% and 30%, respectively, after a median follow-up of 35 months.

Conclusions: These data indicate that dose intensified CT may be delivered safely without bone marrow or peripheral stem cell support.

350 POSTER

IL2 effect on T lymphocyte phenotype of PBPC from healthy donors and patients

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Interleukin 2 (IL2) can increase the anti-tumoral activity of peripheral blood progenitor cells (PBPC) used in autologous haematopoetic transplantation. The aim of this work was to evaluate the in vitro activation of T lymphocytes (lymps) from PBPC of healthy donors (HD) (n=6) and patients (n=4) following IL2 incubation. The patient diagnosis were Non Hodgkin Lymphoma (2), Acute Myeloid Leukemia (1) and Hodgkin's Disease (1). PBPC were incubated for 24hrs with 1000 U/ml IL2 and the cells immunophenotypes, pre and post incubation, were evaluated by flow cytometry, using 4-colour staining.

In this study, PBPC from HD were used as controls and when gated on CD3+ lymps the % of positive cells (median values) were: CD2bright 51; CD4 51; CD7 bright 48; CD8 39; CD16 0.6; CD25 17; CD28 84; CD56 6; CD57 13; CD69 5; CD94 5; HLA-DR 16; Granzyme B 15; NKb1 1 and the CD4/CD8 ratio was 1.4. When gated on CD8+ lymps the % of CD25+ and CD122+ cells were 5 and 7 respectively. Following the IL-2 incubation we observed a significant increase ($p<0.05$) in the % of cells expressing the following antigens (pre-post IL2 incubation): CD69+ 5-33; CD69+ CD56-CD16- 3-32; CD8+ 39-44 and CD8+CD28+ 29-36. We also detected a reduction in the % of cells which were: CD4+ 51-45; CD8+CD122+CD25-6-0.4. There was also a decrease in the CD4/CD8 ratio 1.4-1. So far, no significant changes in the % of cells expressing other antigens were observed.

In comparison with HD, patients T lymps showed increased % of cells expressing CD57, HLA-DR, Granzyme B and CD8+ cells with an inverted CD4/CD8 ratio. After IL2 stimulation patients T lymps showed an increase in the % of CD69+ cells, in particular in the same population as the HD (CD3+ CD56- CD16-). For the other antigens studied we did not observe any other variation trend.

In summary, our preliminary results show that IL2 incubation leads to some changes in T lymphocyte phenotype in particular a significant increase in %CD69+ cells both in HD and patients. Our results are in agreement with previous reports showing that CD69 is expressed shortly after T cell activation. Since, CD69 has been associated with an increase in T cell cytotoxicity, it seems that the IL2 incubation of PBPC will rise the cytotoxic potential of the graft.

Bone marrow and stem cell supported therapies

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A phase I study of high-dose paclitaxel for stem cell mobilization in patients with metastatic breast cancer

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Background: Infusion of large numbers of peripheral blood stem cells to support high-dose chemotherapy has been correlated with milder toxicity. Patients with prior exposure to multiple courses of chemotherapy have difficulties to mobilize stem cells. There is a need for better stem cell mobilization strategies that reliably yield sufficient numbers of stem cells even in heavily chemotherapy-pretreated patients. Paclitaxel (PTX) at a dose of 200 mg/m2 in combination with cyclophosphamide is an effective mobilization inducer. However, there is a lack of data on the mobilizing effect of different doses of PTX alone, and the optimal mobilizingdose remains to be established.

Methods: Twelve patients (pts) with metastatic breast cancer and a median number of 9 prior courses of chemotherapy (6 adjuvant + 3 for metastases) were enrolled in an ongoing phase I trial of tandem high-dose chemotherapy consisting of: A) 1 course of high-dose PTX (400-650 mg/m2) delivered by 24-hour infusion (day 1) with G-CSF: 10 mcg/kg/day s.c. on days 3-12 (and ciprofloxacin 750 mg BID po on days 3-12), with stem cell apheresis beginning on day 11; followed by B) 1 course of high-dose chemotherapy (CTCb) with stem cell support. Patients were discharged as soon as the PTX infusion was completed.

Results: Median numbers of cell harvested for pts treated with each of the four dose levels of PTX tested were as follows:

PTX dose mg/m2	Total MNC/kg	Total CD34+/kg	Days of apheresis 1st apheresis	MNC/kg in 1st apheresis	CD34+/kg in
400: 3pts	11.4	10.1	2	6.4	6.2
500: 3pts	7.2	14.6	1	7.2	14.6
600: 3pts	6.6	17	1	6.6	17
650: 3pts	7	3.8	3	3	1.4

The study is still ongoing since maximun tolerated dose of PTX has not been reached yet. Only 1 pt treated with 650 mg/m2 had to be admited for neutropenic fever.

Conclusion: the optimal dose of paclitaxel for mobilization of maximum numbers of peripheral blood stem cells in pts with metastatic breast cancer is 500-600mg/m2.

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Increased renal toxic effect of total body irradiation in combination with radioimmunotherapy

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Purpose: Renal toxicity of total body irradiation (TBI) alone and with radioimmunotherapy (RIT) in conditioning regimes for bone marrow transplantation (BMT) was examined retrospectively. Since 3/98 we have performed additional RIT with Re-188-labeled anti-CD66 monoclonal antibody for high-risk leukemia patients. Dosimetry showed an uptake of labeled 188Re-Mab not only in the bone marrow but also in the kidneys.

Methods: From 10/97-11/99 58 adults underwent TBI for BMT and survived at least 9 months posttransplant. We performed TBI alone in 35 patients (15 female, 20 male, median age 40.5 y (17 - 60 y)). 23 patients with high risk-leukemia (8 female, 15 male, median age 47 y (16 - 58 y)) received additional RIT. All patients had normal serum creatinine values (female <96 micromol/l, male <110 micromol/l) before conditioning. We evaluated serum creatinine levels 6, 9 and 12 months after transplantation and their association with the application of nephrotoxins and the delivered dose to the kidney.

Results: The mean kidney dose due to the radiolabeled antibody was 8.3 Gy (2.3 - 11.6 Gy). The additive dose of TBI was reduced using renal shielding to 6 Gy. Patients who underwent TBI alone received 12 Gy to the kidney (2 x 2 Gy daily). 4/35 patients with TBI and 16/23 patients with TBI and RIT subsequentely had increased serum creatinine levels. Before transplantation and after 6, 9 and 12 months the median creatinine was 77.14 mmol/l (11.01), 85.66 mmol/l (20.58), 85.00 mmol/l (17.95), 89.39 mmol/l (20.18) for TBI alone and 78.22 mmol/l (12.63), 119.33 mmol/l (35.72), 126.95 mmol/l (32.78), 149.47 mmol/l (69.30) for TBI and RIT. Foscavir, Gancyclovir or Cidofovir were given to 12/35 patients with TBI over a median period of 2.83 months and to 12/24 patients with TBI and RIT over a median period of 4.08 months. 8 patients with TBI and 3 patients with TBI and RIT received amphotericin. Median delivered dose to the kidney by RIT in patients with pathologic serum creatinine was 7.25 Gy (2.3 - 11.5 Gy) and in patients with normal serum creatinine 9.4 Gy (5.2 - 11.6 Gy).

Conclusion: The incidence of severe bone marrow transplantation nephropathy is low, when TBI is performed with a dose of 12 Gy, fractionated 2 x 2 Gy daily. Intensifying the conditioning regime by RIT for high-risk patients, exposed to several nephrotoxins increases the risk of renal damage.