

ent progenitor-derived CFU-GM to recovery. Pts were treated in remission from multiple myeloma (9), breast cancer (10), lymphoma (8) and teratoma (3). Harvests were analysed for CD34+ cell count by flow cytometry. Apheresis products on the first day were tested in CFU-GM and a delta assay (PΔ) performed with progeny from the plastic-adherent fraction of  $10^7$  mononuclear cells incubated for 7 days and enumerated by CFU-GM assay.

**Results:** A median  $3.69 \times 10^6$  CD34+ cells/kg were reinfused (range 0.25–51.9),  $6.1 \times 10^4$  CFU-GM/kg (range 0.10–79.0) and  $10.4 \times 10^4$  pΔ CFU-GM/kg (range 0.27–603.8). Median time to platelet count of  $50 \times 10^9/l$  was 14 days (range 9–gt; 80) and to neutrophil count of  $0.5 \times 10^9/l$  was 13 days (range 9–27). Inverse correlation was seen between CD34+ count and time to recovery of platelets ( $p = 0.002$ ) and neutrophils ( $p = 0.005$ ). Correlation was also seen between CFU-GM and platelet recovery ( $p = 0.031$ ). There was positive correlation between CD34+ count and PΔ CFU-GM numbers ( $p = 0.037$ ) but no correlation between PΔ CFU-GM count and engraftment time.

**Conclusion:** The delta assay of plastic adherent progenitor cells is capable of quantitating a primitive population in PBPC harvests but the CD34+ cell count remains superior as a means of predicting engraftment, suggesting that committed progenitors are more influential in the early phase of recovery.

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POSTER

### High-dose chemotherapy (HDC) and autologous peripheral blood stem cell support (PBSC) in patients with metastatic breast cancer (MBC)

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**Purpose:** The aim of this phase I/II study was to determine therapeutic efficacy and toxicity of a tandem (T)- or triple (TR)-HDC with PBSC in 38 patients with MBC as first line chemotherapy.

**Patients and Methods:** From 9/92 to 12/95 25 patients with MBC were enrolled onto the study with a tandem HDC-regimen and since 1/96 13 patients to the study with a triple HDC-regimen. Conventional chemotherapy (CC) consisted of two cycles epirubicin (120 mg/m<sup>2</sup>) and ifosfamide (7.5 g/m<sup>2</sup>) in case of (T)-HDC and one cycle Taxol (135 mg/m<sup>2</sup>), epirubicin (90 mg/m<sup>2</sup>) and ifosfamide (6 g/m<sup>2</sup>) in case of (TR)-HDC. Following (T)-HDC was composed of 2 cycles epirubicin (180 mg/m<sup>2</sup>), ifosfamide (12 g/m<sup>2</sup>) and carboplatin (900 mg/m<sup>2</sup>). In case of (TR)-HDC Taxol (180 mg/m<sup>2</sup>), etoposide (1.5 g/m<sup>2</sup>) and thiotepa (600 mg/m<sup>2</sup>) was added as third cycle. Only patients with CR or PR during CC were admitted to HDC ( $n = 21$  in case of (T)-HDC).

**Results:** Patients with (T)-HDC were evaluable for both response and toxicity and patients with (TR)-HDC only for toxicity in case of short-term follow up. With a median follow up of 37 months the probability of the progression free survival amounts 20% and of the overall survival 30% in patients with (T)-HDC. Severe non hematologic toxicities were not observed in both regimens. Patients with (TR)-HDC showed prolonged thrombocytopenia following HDC. Improved response rates were observed in patients with few metastatic sides.

**Conclusion:** Both HDC-regimens were well tolerated. Only a selected group of patients may have a benefit of HDC

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POSTER

### Cyclosporin A in the treatment of myelodysplastic syndromes (MDS)

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**Purpose:** Enhanced apoptosis is considered one of the main causes of cytopenia in MDS. Since Cyclosporin A (CyA) is known as an inhibitor of the apoptosis some authors used CyA for treatment of MDS patients (pts) with certain success. The aim of this study was to evaluate the efficiency of the CyA in the MDS treatment.

**Methods:** 8 pts with MDS (3 RA, 3 RAEB, 1 RAEBt and 1 CMML) in age from 16 to 67 years (median age – 50) received oral CyA in following doses: 10 mg/kg for the first 10 days, then 5 mg/kg for all period of the treatment (1–9 months). During the treatment the CyA level in blood was not more than 340 ng/ml

**Results:** A positive effect was achieved in 7 pts: in 6 cases PLT count increased, RBC-transfusion requirements decreased in 3 of 6 transfusion-dependent pts, WBC count increased in 3 of 6 pts with leukopenia. In one case there was a reductions of blast cells in bone marrow from 11% to 5%.

The duration of positive effect was no longer than 6 months. Two pts (one with RAEB and one with RAEBt) developed progressive disease to frank AML.

**Conclusion:** The treatment of MDS pts with CyA can be successful but improvement is transient.

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PUBLICATION

### Persistent lymphopenia six months after intensification with peripheral blood progenitor cells (PBPC)

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**Purpose:** Long term follow-up of hematological recovery after PBPC.

**Methods:** 31 consecutive breast cancer patients aged 28–50 years were treated by autografting with PBPC. All were given 3 g/m<sup>2</sup> cyclophosphamide as priming followed by daily 5 µg/kg of G-CSF. PBPC were harvested with a Fresenius AS 104 apheresis machine. A minimum of  $1 \times 10^6$  CD-34+ cells/kg of the patient were given after myeloablative treatment. The 31 breast cancer patients had the same treatment being cyclophosphamide 5 g/m<sup>2</sup>, melphalan 50 mg/m<sup>2</sup> and carboplatin 900 mg/m<sup>2</sup>. The non-cryopreserved PBPC were returned to the patient within 36 h of the harvest. Thereafter G-CSF is given at a dose of 5 µg/kg.

**Results:** All patients recovered reaching  $>1000$  neutrophils/mm<sup>3</sup> and  $>50.000$  platelets/mm<sup>3</sup> after a median time of 14 days. Blood counts were checked before priming and at 6 months on 28 patients. On the average the platelet count was decreased from 272.000 u<sup>3</sup> to 202.000 u<sup>3</sup>, the neutrophil count from 3.333 u<sup>3</sup> to 3.229 u<sup>3</sup> and the lymphocyte count from 1.070 u<sup>3</sup> to 788 u<sup>3</sup>. Only 3 patients had  $>1.000$  total lymphocytes count at six months post-PBPC.

**Conclusions:** Mostly T-lymphocytes were decreased. The 4 patients (15%) with the lowest B-lymphocyte count ( $<200$  u<sup>3</sup>) have persistent hypogammaglobulinemia. The results were independent from age, previous therapy and stage of disease. Measurements of HLA-DR and Thy-1 markers may allow better cell count prediction.

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PUBLICATION

### Economic costs of high-dose chemotherapy with peripheral blood stem cell rescue

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**Purpose:** When compared to bone marrow (BM) rescue, infusion of autologous peripheral blood stem cells (PBSCs) after high-dose chemotherapy (HD-CHT) allows faster hematologic recovery, less extrahematologic complications, shorter admission and lower mortality. This might result into lower cost. However, the increasing use of expensive drugs, p.e. colony-stimulating factors (CSFs) makes cost estimations based solely on the duration of admission unreliable.

**Methods:** The cost of PBSC mobilization and admission for HD-CHT (including both direct (wages, pharmacy, diagnostic tests) and indirect (overhead) costs of hospital stay) was evaluated in 27 consecutive pts treated at our institution (1995–6).

**Results:** Tumor types: breast cancer (15 pts), non-Hodgkin's lymphoma (6 pts) and other solid tumors (6 pts). Median hospital stay was 21 days (range 15–40). Mean cost was 3.5 million pesetas (ptas) (= 21959 ECU = 27665 US dollars). Median cost was 3.1 million ptas (range 1.9–6.7). Distribution of expenses: wages 37%, pharmacy 35%, PBSC mobilization 7%, blood bank 7%, fixed hospital costs 5%, diagnostic tests 3%, Hickman catheter 2%. Drugs causing the highest expense: paclitaxel (28% of all pharmacy expenses), carboplatin (11%), mesna (9%), imipenem (7%), fluconazole (6%), telicoplanin (5%), parenteral nutrition (5%), G-CSF (4%), granisetron (4%) and GM-CSF (2%).

**Conclusions:** The cost of HD-CHT+PBSC rescue found in this direct cost evaluation is similar to that reported in other European centers, and lower than for HD-CHT + BM rescue. Wages and pharmacy expenses represent 72% of the total cost. Since CSFs are not the drugs generating the highest expense, measures to limit the pharmacy cost should not focus exclusively on them.