1126 POSTER

HIGH DOSE TREATMENT WITH ICE REGIMEN FOLLOWED BY AUTOLOGOUS HEMATOPOIETIC RESCUE IN CANCER PATIENTS

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Fourteen patients diagnosed with neoplastic disease (5 breast cancers, 9 lymphomas) were treated with Ifosphamide 12 g/sqm, Carboplatin 1500 mg/sqm and VP-16 1800 mg/sqm, followed by either PBSC (n = 9) or Bm (n = 5) rescue. In 8 PBSC infused pts, the cells were collected after a 4 days G-CSF course (15 mcg/kg), without any mobilization chemotherapy. The pts infused with BM received G-CSF (5 mcg/kg) starting on +6. All patients were able to complete the regimen: major toxicity was represented by vomiting and mucositis (grade 1–3); 7 required TPN. Transitory increase of hepatic enzymes was also observed. All pts achieved complete hematopoietic reconstitution, with an advantage of PBSC in platelets recovery. Median hospitalization time after the infusion was 14 days (range 11–22).

1127 POSTER

INTENSIFICATION CHEMOTHERAPY (IQ) WITH AUTOLOGOUS PERIPHERAL BLOOD PROGENITOR CELL (PBPC) SUPPORT IN PATIENTS WITH BREAST CANCER: RESULTS OF THE TRANSPLANTATION PROCEDURE

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The use of high-dose chemotherapy supported by PBPC in patients (p.) with solid tumours is increasing. From Dic. 93 to Feb. 95, 14 p. with breast cancer were included in our program of I.Q. with autologous PBPC support. *Methods:* On day 14 after a course of CAF chemotherapy, priming was given with G-CSF 10 μg/kg/day × 7 for mobilization, with planned leukopheresis on days 5, 6, & 7, following the surgical implantation of a double lumen central vein catheter, performed with the use of one of two cont. flow blood cell separators (Baxter CS 3000 & Cobe spectra), until number of 7×10^8/kg MNC were reached. The product was reconstituted with DMSO & autologous plasma, and cryopreserved using controlled rate freezing. I.Q. was given as an outpatient procedure with Carboplatin 800 mg/m^2, Mitoxantrone 25 mg/m^2 and Thiotepa 600 mg/m^2 on days −5 to −3; P. were admitted to individual rooms with double barrier nursing on day −1 and each bag of PBPC infused in less than 15 min. under cardiovascular control. Antiemetic was given with Granisetron & Dexamethasone. Infection prophylaxis was made by Cotrimoxazole, Acyclovir, Fluconazole, and after day +2. GCSF 5 μg/kg until ANC > $1.0 \times 10^9 \times 2$ days. Pentoxiphylline was added from day 0 for 2 months). *Transplantation Results:* Age (median): 42 (26–52); *Stages:* 11B:7; IIIA:1; IIB:3; IV:3; Apheresis: (median) 2.2; Hospitalization days: 12 (11–16). *Product of cells infused:* (median) Nucleated Cells (MNC) 7.47×10^6/kg, CFU-GM: 33.23 (in 10 p.), CD34+: 7.46×10^6. Viability (Trypan blue): 90.32%. *Hematologic recovery:* days with ANC < 0.5×10^9/l:7 (5–9); platelets >20×10^9/l: 4 (1–7). *Toxicities:* Hypertension (post-infusion) >30 mmHg: 10 p; Mucositis GII: 4 p. GIII: 1 p; Vomiting GIII: 4 GII: 10 p; Diarhea: GIII: 3 p, GII: 2 p.; Hepatotoxicity: GII 1 p; Flebitis >5 days: 2 p; Low Back pain during G-CSF priming: 10 p. *Complications:* Fever >38.5°C: 9 p; Days with empiric antibiotics: 3.6 (0–9);. Peritransplantation mortality. O; *Conclusions:* Autologous PBPC support of this I.Q. therapy was associated with low morbidity and the phases of mobilization, apheresis and intensification could be given in an outpatient setting, reducing thus the cost of the procedure.

1128 POSTER

TOTAL BODY IRRADIATION (TBI) BEFORE BONE MARROW GRAFTING (BMG): ANALYSIS OF LATE SIDE EFFECTS

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Side effects after TBI and BMG indicated for various diseases (acute lymphoid leukemia -ALL, acute myeloïd leukemia -AML, chronic myeloïd leukemia -AML, lymphoma, multiple myeloma, neuroblastoma) were retrospectively analyzed for 52 patients (pts) treated from 10/88 to 12/93 (36 adults, mean age: 36.7 years (y), and 16 children, mean age: 7.4 y). All pts were irradiated with a single fractionated per-day schedule (8 Gy by 4 f in 4 d), or in a bifractionnated per-day schedule (12 Gy by 6 f in 3 d or 14 Gy by 7 f in 3.5 d). No patient had received previously any cranial irradiation. Global survival of pts after BMG (Kaplan Meier method) was 49% at 45 ms. Veino-occlusive disease (VOD) occurred in 3/36 adults and 1/16 children; 3 of these pts were in relapse disease and had received a massive chemotherapy and an irradiated dose of 14 Gy during TBI. Cumulative rate of clinical interstitial pneumopathy (IP) or spirometric abnormalities only according to IP was 28.3% (9 pts) at 66 ms. IP was noted in 2/20 pts (11.3%) who received a maximal dose of 9.5 Gy in the lungs (1st group) and in 7/32 pts (45.2%) who received more than 9.5 Gy (maximal prescribed dose of 10 Gy) (2nd group). Due to the lack of population studied, no statistical conclusion can be drawn. Moreover, the relapse rate in the 1st, group was 51.2% versus 21.8% in the 2nd group one can be noted in the 1st group of pts the more severe prognosis of the disease treated, like multiple myeloma or stage IV neuroblastoma. There was no correlation between the incidence of IP and the severity of the graft versus host disease (GVHD). Five pts (1/36 adults and 4/16 children) suffered of thyroïd function impairment. Cumulative rate of peripheral gonadal insufficiency was 36.7% at 66 ms (women 5/16, men 2/20); all puberal children at present time of this study have had gonadal insufficiency. All children (8/16) alive beyond one year after BMG have had a delayed development in height and weight: the underheighting was significant for children alive more than 2 y after BMG.

The results of these series are similar to those reported in the literature, apart a slight increase of IP incidence. From end 1993, we are systematically limiting the radiation dose in the lungs at 9.5 Gy for all pts.

1129 POSTER

LONG-TERM FOLLOW-UP OF ALLOGENEIC MARROW TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA AFTER CYCLOPHOSPHAMIDE-TOTAL BODY IRRADIATION AND CYCLOSPORINE

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Eighty-five patients (44 female, 41 male; 2–48 years, median 27) with acute myeloid leukemia (AML) in first complete remission underwent allogeneic bone marrow transplantation (BMT) from HLA-identical siblings. The conditioning regimen comprised cyclophosphamide (120 mg/kg) and single-fraction total-body irradiation (950 cGy, n = 48; 1050 cGy, n = 30; 1150 cGy, n = 7). Cyclosporine was used for the prophylaxis of graft-versus-host disease as a single agent. 25 patients (29%) died of transplant-related complications at 20 days-104 months (median 3 months) post-transplant, and 1 at 10 years of unrelated causes (coronary heart disease). Only 1 transplant-related death occurred beyond 2 years (chronic GVHD and aspergillosis). 19 patients (22%) relapsed at 3–45 months (median 6.5 months), and died of disease or complications of further therapy. 3 relapses occurred beyond 2 years. 40 (47%) patients were alive and well at the last follow-up 66–186 months (median 145 months) after BMT; 7 with limited chronic GVHD requiring therapy. We conclude that allografted patients who are alive and well 2 years post-transplant have excellent prospects of long-term survival with only a small chance of relapse or complications.

1130 POSTER

ALLOGENEIC BONE MARROW TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA AFTER MELPHALAN AND TOTAL BODY IRRADIATION

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Between 11/88 and 1/95, 44 patients (3–51 years, median 32) with AML in first remission underwent BMT from HLA-identical siblings after 110 mg/m^2 melphalan and 950 cGy (n = 6) or 1050 cGy (n = 38) single-fraction TBI. Cyclosporine and methotrexate were used for GVHD prophylaxis. Myeloid engraftment was achieved in all patients. Acute GVHD was seen in 34 patients (77%), and chronic GVHD in 12 of 29 (41%) of patients at risk. 14 (32%) patients died of toxicity 21–300 days (median 72) post-transplant; all had received 1050 cGy TBI ($P = .072$). 3 patients relapsed; 1 died of leukemia, and the other 2 are alive in CR with

chronic GVHD after immunotherapy with donor cells ± interferon-α. 25 patients are alive in continuous remission at 2–52 months (median 20); 6 with chronic GVHD requiting therapy. The overall survival is 66% (29/44). We conclude that melphalan-TBI is an active conditioning regimen for AML and permits consistent alloengraftment. Although the toxicity is considerable, the risk of relapse is low. Decreasing the TBI to 950 cGy appears to have controlled the toxicity, but the experience is still limited and longer follow-up is required to see if relapse rates increase.

1131 POSTER

EFFECTIVE RECOVERY OF GRANULOPOIESIS AFTER BONE MARROW TRANSPLANTATION BY CONTINUOUS INFUSION OF LENOGRASTIM (RHUG-CSF)

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Randomized study of continuous iv infusion (A) vs 30 min-infusion (B) of G-CSF (5 μg/kg/day) after BMT was conducted in 101 cases with aplastic anemia, acute lymphoblastic leukemia or malignant lymphoma. Both groups had the same distribution of age, disease, stage of BMT and marrow donor. The analysis of 82 allogeneic BMT cases showed that stable recovery (> 500/μl) of peripheral granulocyte was found at 15.59 ± 5.41 days in group A and 19.30 ± 9.36 in group B ($p = 0.05$) after BMT. Multivariate analysis also demonstrated that method of administration (A vs B) was a significant independent factor for granulocyte recovery by multivariate analysis. The median day of platelet recovery to >100,000/μl was day 28 in group A and day 33 in group B. These results indicate that continuous iv infusion is preferred to 30 min-infusion for the administration of G-CSF in BMT cases.

1132 POSTER

G-CSF MOBILIZATION EFFECT ON PSC IN PEDIATRIC MALIGNANCY

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The aim of our multi-center study was to evaluate the mobilization effect of recombinant human granulocyte colony-stimulating factor(rhG-CSF; lenograstim) on peripheral blood stem cells (PSC). Dynamic movements of CD34 positive cells after 6 types of myelosuppressive chemotherapy followed by intravenous administration of rhG-CSF that started from the day at less than 500 per micro-liter of granulocyte and continued 14 days were analyzed in 59 patients with pediatric malignancy (18 of non-Hodgkin's lymphoma, 17 of neuroblastoma, 10 of acute lymphoblastic leukemia and 14 of other solid tumors). The dosage of rhG-CSF was escalated from 2 to 12.5 microgram per kg and following results were obtained; the number of CD34 positive cells was correlated with that of colony forming unit-granulocyte/macrophage ($r = 0.616$) but not with the dosage of rhG-CSF. The type of chemotherapy and duration of granulocyte recovery affected the maximum CD34 positive cell number.

1133 POSTER

COMPARISON BETWEEN CD34+ CELLS AND CFU-GM GROWTH IN LEUKAPHERETIC PRODUCTS OF PATIENTS UNDERGOING CPC TRANSPLANT

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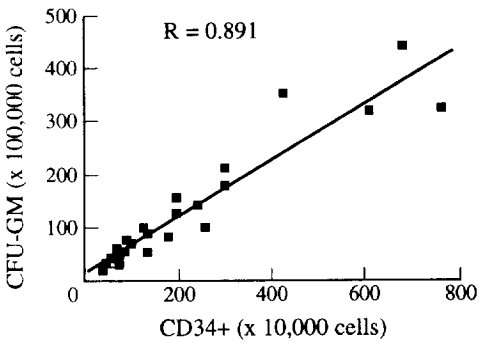
An extremely rapid and complete hematopoietic reconstitution occurs in patients receiving high dose chemotherapy when circulating progenitor cells (CPC), collected by leukapheresis, rather than marrow-derived cells, are reinfused. The amount of progenitor cells collected, which correlates with the speed of bone marrow reconstitution, is usually evaluated by the number of CD34+ cells and/or the number of clonogenic cells (CFU-GM). Since not all investigators agree with the correlation between these two parameters, we have compared CFU-GM growth and CD34+ cells in 27 leukapheresis from patients with solid tumors undergoing CPC transplantation. In our study a clear correlation between the two assays was shown (see fig. below) and we conclude that there is no need to perform both of them. Since CD34+ assay is simpler, less time-consuming and can be completed in a few hours versus weeks, we now perform only immunophenotypic analysis for clinical decision making.



1134 POSTER

IMMUNOTHERAPY FOR ACUTE LEUKEMIA RELAPSING AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION

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8 patients (20–50 years, median 36) relapsing 2–27 months (median 5) after BMT from HLA-matched sibling (n = 3) or unrelated (n = 3), or HLA-mismatched sibling (n = 2) donors were treated with interferon-α (IFN) ± donor cells ± IL-2. The plan was to administer IFN alone first. 100% lymphoid cells and 0–90% myeloid cells were of donor origin at relapse. The diagnoses at BMT were: secondary AML (n = 2), primary refractory AML (n = 3; one relapsing after a previous allograft), AML in first remission (n = 2), and ALL in refractory relapse (n = 1). Marrow from mismatched donors (n = 2) was depleted of T-cells. Response to immunotherapy was not evaluable in 2 patients who died of treatment-related toxicity. Of 6 responders, 2 relapsed and died of toxicity of further therapy, and 1 died of acute hepatic GVHD but with improvement in the clinical signs of the disease. Two other patients developed acute skin GVHD which resolved. 3 patients are alive in remission 2, 8 and 18 months after therapy; all with evidence of chronic GVHD. We conclude that remission can be attained after immunotherapy in acute leukemia relapsing post-allograft, and long-term survival may be achieved. IFN alone may have significant activity, especially with patient-donor HLA disparity (unrelated or mismatch).

1135 POSTER

ABSENCE OF DIFFERENCE BETWEEN BONE MARROW OR PERIPHERAL STEM CELLS AS SOURCE OF HEMOPOIETIC SUPPORT FOR HIGH DOSE THERAPY IN BREAST CANCER

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From March 1992 to August 1994 62 patients received high dose therapy either as intensification for high risk breast cancer (31) or metastatic disease (31). Combination chemotherapy employed was: Cyclophosphamide (1.5 g/m^2 × 4 days), carboplatin (200 mg/m^2 × 4 days continuous infusion) and thiotepa (125 mg/m^2/4 days, continuous infusion). Conventional bone marrow harvested was used as a source of hemopoietic support in 37 patients. In all cases subcutaneous G-CSF was administered from day +1 until neutrophil engraftment at a dose of 5 microg/k/day. In the rest 25 patients G-CSF mobilized peripheral blood stem cells were infused after high-dose therapy. Eleven out of 25 received G-CSF after the transplant in the same schedule than bone marrow transplant patients. The aim of this study was to analyze if there were difference in terms of engraftment, days of hospitalization, and requirements of transfusion between this groups.