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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 Ifosfamide 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).

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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/m², Mitoxantrone 25 mg/m² and Thiotepa 600 mg/m² 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. Pentoxifylline 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; Diarrhea: 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: 0. **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.

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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 myeloid leukemia -AML, chronic

myeloid 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 bifractionated 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 thyroid 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.

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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.

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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/m² 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