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)

Y. Morishima

Nagoya Bone Marrow Transplantation Group, Nagoya, Japan

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

M. Ohira[1], J. Takayama[1], Y. Kuroda[2], Y. Takaue[2], K. Kawano[2], T. Matsumura[3], T. Sawada[3]

[1]Department of Pediatrics, National Cancer Center, Tokyo, Japan

[2]Department of Pediatrics, Tokushima University, Tokushima, Japan

[3]Department of Pediatrics, Kyoto Prefectural University, Kyoto, Japan

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

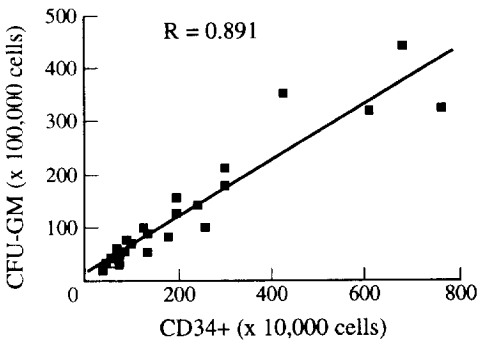
COMPARISON BETWEEN CD34+ CELLS AND CFU-GM GROWTH IN LEUKAPHERETIC PRODUCTS OF PATIENTS UNDERGOING CPC TRANSPLANT

P. Pedrazzoli, C. Perotti[1], C. Zibera, G. Poggi, P. Preti, G. Robustelli della Cuna

IRCCS Fondazoine Clinica del Lavoro

[1]IRCCS Policlinico S. Matteo, Pavia, Italy

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

S. Singhal, R. Powles, J. Treleaven, J. Prendiville, P. Glynne, J. Mehta

Royal Marsden Hospital, Surrey, U.K.

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

J.F. Tomás, R. Pérez-Carrión, G. Pérez-Manga, J. Jalón, R. Arranz, A. Alegre, C. Mendiola, J.L. López-Lorenzo, A. Escudero, J. López-Pascual, J.M. Fernández-Rañada

Clínica Ruber and Hospital La Princesa, Madrid, Spain

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.

	BONE MARROW G-CSF (n = 37)	PBSC G-CSF (n = 11)	PBSC No G-CSF (n = 14)
Neutrophils >500/mm^3	12 (10–33)	11 (9–14)	12 (7–16)
Platelets >20000/mm^3	21 (18–36)	17 (10–25)	18 (9–33)
Days Antibiotics	12.5 (6–29)	11 (5–19)	10.5 (5–26)
Days Hospitalization	25 (20–43)	22 (19–30)	25 (20–49)
Packed red blood cells	5 (0–32)	3 (2–4)	4 (2–9)
Random Platelets units	38 (7–247)	32 (8–98)	30 (5–200)

Although this is not a randomized survey, no difference with statistical significance could be proven for any of the other variables analyzed.

1136 PUBLICATION

LIMITED MOBILIZATION EFFECT OF G-CSF (LENOGRASTIM) FOR BLOOD STEM CELLS IN CHILDREN WITH SOLID TUMORS

Y. Kawano, Y. Takaue, Y. Kuroda, M. Ohira
Department of Pediatrics, University of Tokushima and National Cancer Center Hospital, Japan

Autografts with G-CSF mobilized blood stem cell (PBSC) has been widely applied for cancer therapy. However, its dose response effect has not been fully tested. To address this, we gave various doses of G-CSF to 31 children with solid tumors (age, 1 to 15 y) including 17 neuroblastoma, with concomitant measurement of circulating CD34+ cells. Eleven of 31 patients has >6 mo history of chemotherapy. They received a regimen incorporating CDDP and G-CSF was started from the nadir of WBC. Blood was drawn 3 times a week for CD34+ cell assay and CBC. There was no dose response effect for shortening the duration of neutropenia with 2 to 12.5 μg/kg of G-CSF. Increase of circulating CD34+ cells (>100/μl) was observed in patients whose platelet recovery was fast, reaching to a level of 10×10^9/l within 2 weeks (n = 14), but no apparent dose response effect was observed. While in the rest of slowly recovering patients, its effect was marginal. Comparing our historical data for children with ALL/NHL, these may suggest that G-CSF has only a limited effect for mobilizing PBSC in children with a solid tumor and/or those who were treated with a regimen specific for solid tumors.

Bladder cancer

1137 ORAL

A PROSPECTIVE, RANDOMIZED, MULTICENTER, PHASE III CLINICAL TRIAL OF THE EFFECT OF DIFFERENT INITIAL THERAPY REGIMES AND MAINTENANCE PROPHYLAXIS IN SUPERFICIAL BLADDER CANCER USING MITOMYCIN C

D.W.W. Newling, D. Mulder
The Flemish Mitomycin C Study G-roup, Amsterdam, The Netherlands

Doubts still exist over the appropriate initial regime and the length of maintenance necessary with intravesical chemotherapy for the best prophylaxis against recurrence in superficial bladder tumor. All patients with superficial bladder cancer were eligible apart from those with a solitary Ta lesion, in whom the protocol regimes would be generally unacceptable. After resection of tumors in the bladder, 1287 patients were randomized into 4 different groups. Group A received 8 weekly instillations with 40 mgs Mitomycin C in 50 cc's 0.9% saline, followed by 4 months, monthly prophylaxis with the same dose. Group B received 4 weeks initial therapy, followed by 5 months, monthly prophylaxis. Group C received the same therapy as group A but the prophylaxis was continued to 12 months and group D the same initial regime as group B but again with maintenance continued to 12 months. Groups were evenly matched with regard to stage and grade of their tumors and there was no significant sex difference between the 4 groups. The side-effects were similar in groups A and B, and groups C and D, but almost twice as many patients in groups C and D missed one or more instillations due to side-effects, compared with the two groups with the shorter maintenance regime. All patients have been treated for a minimum of 12 months and there are no significant differences in the recurrence rate of rate of progression between patients in group A and B compared with those in C and D.

1138 ORAL

CLINICAL SIGNIFICANCE OF PROLIFERATING CELL NUCLEAR ANTIGEN EXPRESSION IN TRANSITIONAL CELL CARCINOMA OF THE BLADDER

H. Shiina, S. Urakami, H. Shirakawa, M. Igawa, T. Ishibe
Department of Urology, Shimane Medical University, 89-1 Enya-cho, Izumo 693, Japan

To elucidate the clinical significance of cellular proliferation in transitional cell carcinoma (TCC) of the bladder, the proliferating cell nuclear antigen (PCNA) expression, p53 and nm23 immunoreactivities, 2c deviation index (2cDI) and 5c exceeding rate (5cER) were evaluated using an image analyzer. The paraffin embedded materials obtained from 77 patients with non-metastatic untreated TCC of the bladder who received total cystectomy were used in this study. The PCNA expression significantly correlated with the p53 and nm23 immunoreactivities, 2cDI value and 5cER, respectively. The grade significantly correlated with all of the 5 parameters. Similarly, the stage as well as disease progression significantly correlated with all of the parameters except for the nm23 immunoreactivity. In univariate analysis, the prognostic relevance was noted in grade, stage, PCNA expression, p53 immunoreactivity, 2cDI value and 5cER, whereas not in nm23 immunoreactivity. In multivariate analysis, the PCNA expression, followed by 2cDI value, was the most important variable, however, the p53 immunoreactivity and 5cER were not of independent significance. The results suggest that the tumor growth fraction as assessed by the PCNA expression is an important and independent predictor for survival in patients with TCC of the bladder.

1139 ORAL

EFFECT OF PREOPERATIVE RADIOTHERAPY ON CLINICAL-TO-PATHOLOGIC DOWNSTAGING IN MUSCLE-INVASIVE BLADDER CANCER

A. Pollack, G.K. Zagars, C.J. Cole, C.P. Dinney, D.A. Swanson, H.B. Grossman
Departments of Radiotherapy and Urology, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas 77030, U.S.A.

Downstaging (DS) after preoperative radiotherapy is well-established; however, the prognosis of such patients relative to those who exhibit DS in the absence of any radiotherapy has not been described. The relationship between DS and local control for 301 patients treated with preoperative radiotherapy and cystectomy (PREOP) from 1960–1983, was compared to that for 225 patients treated with radical cystectomy alone (CYST) from 1984–1990. PREOP patients received 50 Gy in 25 fractions 4–6 weeks prior to cystectomy. DS was found in 73% treated with PREOP and 29% treated with CYST ($p < 0.0001$, chi-square). The only potential prognostic factors that correlated with DS were clinical stage and creatinine level ($p < 0.05$, chi-square). Multivariate analysis revealed that treatment (PREOP vs CYST) correlated with DS independently of these covariates. In terms of 5 yr actuarial local control, those who were downstaged fared better than those who were not; 93% vs 85% for PREOP ($p = 0.01$) and 91% vs 83% for CYST ($p = 0.13$). Local control for clinical Stage T2 and T3a patients was not related to the treatment, regardless of whether DS was documented. In contrast, downstaged T3b patients treated with PREOP had significantly greater local control rates than those receiving CYST. These data indicate that preoperative radiotherapy for clinical Stage T3b patients had a significant impact on local control beyond selection based on downstaging.