823

ALLOGENEIC BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOGENOUS LEUKEMIA.

van Aelst F., Löwenberg B., Sizoo W., van den Anker P.J., van 't Veer M., Hagenbeek A.
Dr Daniel Den Hoed Cancer Center, Dept of Hematology, Rotterdam, The Netherlands.

Twenty eight patients with a Philadelphia chromosome (Phi) positive chronic myelogenous leukemia were transplanted between April 1983 and April 1992. The donors were HLA-identical siblings (26), or HLA-matched unrelated (2). Median age at transplantation was 37 years (range 15-55). Median time between diagnosis and BMT was 13 months (range 5-76). In the earlier years an induction treatment was given with daunorubicin and cytosine arabinoside followed by the conditioning with Total Body Irradiation (TBI; 2x5 Gy). Later on, no induction treatment was given, and the dose of the TBI was changed (2x6 Gy, lungs 8.5 Gy, kidneys 10 Gy). In most patients the conditioning consisted of etoposide 20 mg/kg or cytosine arabinoside 1 g/m² q 12 hours, followed by endoxan 60 mg/kg, each for two days. The graft was T-cell depleted in 26 patients. Cyclosporin-A (CyA) was prescribed in 21 patients.

	all patients	latter period
Number of patients	28	15
Disease status		
first chronic phase	20	13
accceleration	6	2
blastic phase	2	0
Treatment outcome		
complete remission	21	12
subsequent relapse	7	3
No take, Phi negative, alive	1	0
early death	6	3
First chronic phase		
number of patients	19	13
median follow-up (days)	171	171
disease free survival (%)	42	62
(median duration, days)	540+	522+

The main causes of death were recurrent disease (5), interstitial pneumonitis (8), pneumococcal meningitis (1) and acute cardiac arrest (1). The disease free survival of 62% at 522+ days (median) with the recent conditioning regimen compares favourably with the literature. To even improve these results, partial T-cell depletion is envisaged to maintain the graft-versus-leukemia effect and/or the use of short-course CyA only.

824

SPLENIC IRRADIATION PRIOR TO BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOGENOUS LEUKEMIA

J Ravalese, M Ling, D Schenkein, J Erban, K Miller & H Madoc-Jones
Departments of Radiation Oncology and Medicine, New England Medical Center Hospitals and Tufts University School of Medicine, Boston, Massachusetts, USA.

PURPOSE: Splenomegaly is a common finding in CML and may represent a site of high tumor burden in patients being considered for allogeneic bone marrow transplantation, which is the only potentially curative therapy for patients with CML. We decided to irradiate the spleens of CML patients prior to their allogeneic BMT.

MATERIALS AND METHODS: We report on 14 patients who received pre-transplant splenic irradiation before allogeneic BMT for CML. The mean age was 41, range 32-56. Of the 14 patients, 11 had clinical splenomegaly. All patients received splenic irradiation mainly consisting of 500 cGy prior to BMT. The preparative regimen for all patients consisted of fractionated total body irradiation (1200 cGy) following cytoxan 60 mg/kg x 2 days. Median follow up is 23 months.

RESULTS: Twelve of 14 patients are in clinical and cytogenetic remission. Overall survival is 100% with a projected 80% disease free survival at 24 months.

CONCLUSION: These results suggest a benefit from splenic irradiation for patients with CML before allogeneic BMT.

825

RECOMBINANT HUMAN INTERFERON-ALPHA AND INTERFERON BETA/ INTERLEUKIN-6 BUT NOT INTERFERON-GAMMA INDUCE MEGAKARYOCYTIC DIFFERENTIATION OF THE ACUTE MEGAKARYOBLASTIC LEUKAEMIA BLAST CELLS.

H.T. HASSAN, S. GRELL, U. BORMANN-DANSO and M. FREUND.
Department of Hematology/Oncology, University of Hannover Medical School, Konstanty-Gutschow-Str.8, W-3000 Hannover 61, Germany.

The effects of interferon-alpha (IFN-alpha), interferon-beta2 interleukin-6 (IL-6) and interferon-gamma (IFN-gamma) in inducing megakaryocytic differentiation of blast cells from acute megakaryoblastic leukaemia (AMegL) patient determined by the increase in CD41 and CD42b expressions using monoclonal antibodies in APAAP technique were investigated in liquid suspension culture. After six days of culture, the percentage of CD41 and CD42b positive cells increased in control cultures from 15.2% and 10.6% on day 0 to 32.0 ±4.3% and 22.1 ±2.6%, respectively. The addition of IFN-alpha significantly increased the number of CD41 and CD42b positive cells by two to three fold compared to control cultures, $p < 0.01$ and by four to six fold compared to day 0, $p < 0.001$. Similarly, IFN-beta2/IL-6 induced a significant increase in CD41 and CD42b positive cells. On the other hand, IFN-gamma failed to increase the number of CD41 and CD42b positive cells in comparison to control cultures on day 6 and instead induced a significant increase in the number of monocytes/macrophages, $p < 0.001$. The present results suggest that megakaryocytic differentiation of blast cells in AMegL could be induced by IFN-alpha and IL-6 and support a clinical role for IL-6 in the treatment of AMegL patients. Also, the present results showed that monocytic differentiation of blast cells in AMegL could be induced by IFN-gamma, supporting the multipotent stem or progenitor cell origin of the AMegL subtype of acute myeloid leukaemia.

Dr. H.T. Hassan is supported by a research fellowship from the Alexander von Humboldt-Stiftung, Bonn, Germany.

826

EORTC-GIMEMA AML8 PROTOCOL: PARALLEL PHASE III TRIALS IN ACUTE MYELOGENOUS LEUKEMIA (AML).

R. Zittoun, F. Mandelli.

On behalf of the EORTC and GIMEMA Leukemia Cooperative Groups.
Service d'Hématologie - Hôtel-Dieu - 75181 Paris 04 - France.

The AML8 protocol, intended to prospectively assess the value of allogeneic BMT (ALLO), autologous BMT (ABMT) and intensive chemotherapy (IC) during 1st complete remission (CR) of AML, was activated in November 1986. It is based on 2 parallel trials for patients aged 12-45 (AML 8A) and 46-60 (AML 8B) yrs old : Following one or two courses of induction with daunorubicin (DNR) 45 mg/sq m d 1-3 and Ara-C 200 mg/sq m cont. IV inf. d 1-7, patients in AML 8 A received one intensive consolidation with Ara-C 500 mg/sq m q 12 hrs d 1-6 and AMSA 120 mg/sq m d 5-7. Then they were eligible for ALLO if a HLA identical sibling was available : if not they were randomized for ABMT using an unpurged bone marrow or for a second IC course combining Ara-C 2 g/sq m q 12 hrs d 1-4 and DNR 45 mg/sq m d 5-7. In AML 8B, patients achieving a CR were randomized for the same 2 courses IC or standard post-CR chemotherapy with 6 courses DNR-Ara-C in EORTC, 4 courses DNR-Ara-C-TG in the GIMEMA. During the 2 last years the value of GM-CSF during induction was also assessed.
As of March 1993, 1720 patients were registered, 1063 in AML 8A and 657 in AML 8B. The CR rate for patients not treated with GM-CSF is 66.4 % in AML 8A and 60.9 % in AML8B, most CR being achieved after a single course. In AML 8A, 142 pts were eligible for ALLO (121 performed), 126 were randomized for ABMT (89 performed) and 124 for IC (100 performed). The main reasons for non-completion of treatment protocol were excess toxicity, refusal, or early relapse. The disease-free survival (DFS) was significantly higher for ALLO and ABMT (50 % at 3-4 yrs) than for IC (29 %) ($p : 0.04$). However the overall survival following CR is identical in the 3 arms, more patients in the IC arm achieving a 2nd CR and being transplanted secondarily. In AML 8B, the DFS was not significantly different between the 2 randomized arms, but the causes of failure were different, with more relapses and less death in CR in the standard post-CR arm (66.9 % and 2.7 % respectively), than in the intensive arm (45.8 % and 20.5 % respectively).

827

REEVALUATION OF THE GASTROINTESTINAL SELECTIVE DECONTAMINATION EFFECTIVENESS ON THE COURSE OF NEUTROPENIA IN HEMATOLOGICAL MALIGNANCIES

Kubešová H., Vorlíček J., Zemanová J.,
Masaryk University Hospital, Dept. of Medicine, Jihlavská 20, 639 00 Brno, Czech Republik

The importance of the selective decontamination (SDD) is one of the most discussed topics in supportive care in oncology. Two regimens were administered (colistin+nystatin or gentamicin+ nystatin) during 100 courses of chemotherapy in 48 patients. The effect of SDD on the microbial flora in the digestive tract, further on microbiological findings in the urogenital tract, in oropharynx and on skin was evaluated. The occurence of infective complications, their infection agents and susceptibility to antibiotics were compared with historical control group. SDD reduces significantly (34.1%) the number of infective complications, the number of days with fever and the consumption of antibiotics (47%). These effects were followed by an increase of fungal infections and fever of unknown origin. The results suggest, that SDD remains to be a method improving the course of neutropenia following cytostatic therapy.

828

INTENSIVE CHEMOTHERAPY(CT) AFTER REMISSION INDUCTION WITH ALL-TRANS-RETINOIC ACID (ATRA) IN ACUTE PROMYELOCYTIC LEUKEMIA (APL)

AB Sousa,JP Fernandes,V Mesquita,G Ferreira,P Ribeiro,M Bernardo,O Nunes,F Aveiro,E Cruz,J Veiga,A Neves,A Conduto,AS Rodrigues,A Monteiro,VH Soares,AM Pereira,M Sousa,AJ Gonçalves,I Costa,M Machado,J Gouveia.
Unidade de Hematologia, Hospital dos Capuchos, Lisboa, Portugal

Although ATRA induces a high CR rate in APL, most patients (pts) relapse despite maintenance with ATRA or mild CT, and the best postremission therapy is unsettled. To assess the value of short-term intensive consolidation CT, we gave pts in whom CR was induced with ATRA (45 mg/m2/d), one course of Ara-C 3g/m2 q12h d 1-4 and mitoxantrone 10 mg/m2 d 2-5, with no further treatment. Since November 91 we prospectively treated 10 pts with APL (8 newly diagnosed, 2 in first relapse), median age 40(31-75). 7 of 9 evaluable pts (one too early) entered CR, after a median of 51 days; there were 2 early deaths from CNS bleeding. Hyperleukocytosis during therapy occured in 5 pts and was uncomplicated in 4 ; in one pt (the only non-leukopenic pt at entry) it was associated with a "retinoic acid syndrome" and probably contributed to death. The drug was otherwise well tolerated. Of 7 CR pts, one 75 year-old pt was maintained on ATRA, and 6 were given CT (without ATRA) as soon as they entered CR; non-hematologic toxicity was modest (namely no CNS side effects) and main toxicity was myelosuppression (with WBC<1000 for a median of 16 days). As of January 93, one pt [treated in first relapse, and whose karyotype showed -2, -5, in addition to t(15;17)] relapsed after 10 weeks. All other pts remain in CR after 15+ to 45+ weeks (median 25). These preliminary data are encouraging; further accrual of pts and longer follow-up will show if this approach improves outcome in APL.