

Oral Presentations

the standard cytogenetics classification (unfavorable, intermediate, favorable). We then compared each of this subgroup with the corresponding population of patients presenting the same risk factors but owning a HLA identical sibling. In the standard risk group ($n = 66$), no-donor patients presented a favorable 10-year survival (74%) compared with patients with a donor (51%) ($P =$ not significant), and allo-SCT should not be recommended. In the poor risk group ($n = 131$), patients without a donor presented a poor outcome (10-year OS = 17%), which was not better if a donor existed (28%) ($P = .29$); in these patients with a poor outcome whatever the treatment, investigational studies should be recommended. In the intermediate risk group ($n = 275$), allo-SCT offered a better outcome; the 10-year probabilities of relapse, nonrelapse death, OS, and LFS (no donor vs donor) were 47% versus 18% ($P < .0001$), 7% versus 17% ($P = .02$), 47% versus 63% ($P = .02$), and 45% versus 64% ($P = .001$), and the 10-year OS was 56% versus 41% ($P = .01$). Allo-SCT represent a real chance of long-term outcome and might benefit from recent advances. We conclude that long-term outcome might be achieved in some subgroups of patients and that the indication for allo-ASCT could be assessed through a simple classification based on common parameters.

50

TOTAL BODY IRRADIATION (TBI) AND G-CSF-COMBINED HIGH-DOSE CYTARABINE AS A PREPARATIVE REGIMEN FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOGENOUS LEUKEMIA (AML) AND ADVANCED MYELODYSPLASTIC SYNDROME (MDS)

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The most common reason for failure in later-stage patients after allogeneic hematopoietic stem cell transplantation (allo-HSCT) for AML and advanced MDS is leukemic relapse, demonstrating the inability of preparative regimen to completely eradicate leukemic cells. We report the outcome of allo-HSCT for myeloid malignancies using myeloablative preparative regimen including TBI and high-dose cytarabine. In addition, granulocyte colony-stimulating factor (G-CSF) was simultaneously administered with cytarabine to increase the susceptibility of leukemic cells to cytarabine. **Patients and Methods:** Patients with myeloid malignancies, including AML, AML evolving from MDS, and advanced MDS (RAEB, RAEB-t, CMML) were eligible. For conditioning, patients received TBI (12 Gy) followed by intravenous high-dose cytarabine ($3\text{g}/\text{m}^2$ every 12 hours for 4 consecutive days). Recombinant G-CSF (lenograstim; $5\ \mu\text{g}/\text{kg}/\text{day}$) was administered intravenously by continuous infusion for 4 days, starting 12 hours before the first dose of Ara-C and continued until the last dose of Ara-C. For the prophylaxis of acute graft-versus-host disease, cyclosporine A or tacrolimus with or without short-term methotrexate was given. **Results:** Seventy-nine patients were evaluable, with a median age of 39 years (range, 15–58 years). Their diagnoses were AML in 57, AML from MDS in 11, and MDS in 11 (RAEB in 8, RAEB-t in 1, CMML in 1). Five-year overall survival (OS), disease-free survival (DFS), and relapse rate (RR) were 79.1%, 76.3%, and 15.2% in AML in remission, and 41.9%, 34.4%, and 46.4% in AML not in remission. These rates were 43.6%, 43.6%, and 0% in AML from MDS and 71.6%, 72.7%, and 10% in advanced MDS. For AML in remission, no risk factor affecting OS and RR was observed, whereas both high-risk karyotype abnormality and high numbers of blasts in the peripheral blood negatively affected OS, and these 2 factors and absence of chronic GVHD significantly increased RR in AML not in remission. **Conclusions:** These data suggest that TBI and G-CSF combined high-dose cytarabine is a highly effective regimen for allo-HSCT for AML in remission, AML evolving from MDS, and advanced MDS with a notably low incidence of relapse.

LYMPHOMA/MULTIPLE MYELOMA

51

THE USE OF AUTOLOGOUS LMP2-SPECIFIC CYTOTOXIC T LYMPHOCYTES FOR THE TREATMENT OF RELAPSED EBV+ HODGKIN'S DISEASE AND NON-HODGKIN'S LYMPHOMA

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EBV-associated Hodgkin's disease (HD) and some cases of non-Hodgkins lymphoma (NHL) show type II latency expressing the subdominant EBV antigens EBNA1, LMP1, and LMP2, which may serve as targets for immunotherapy approaches. In previous studies, we used polyclonal EBV-specific CTL in patients with relapsed EBV+ HD and saw 2 complete and 1 partial responses in 11 patients. Analyses of EBV-CTL lines showed that small populations of T cells reactive against the tumor-associated antigen LMP2 were present in most of the infused lines, with some expansion in the peripheral blood after infusion. We therefore hypothesized that CTL specifically targeting LMP2 might have greater efficacy in these patients. LMP2-CTLs were generated from 10 patients using dendritic cells and lymphoblastoid cell lines (LCLs) that had been genetically modified to overexpress LMP2 by transduction with an Ad5f35LMP2 vector. Polyclonal LMP2-CTL lines recognized 2–6 (median, 4) LMP2 epitopes, as determined using overlapping LMP2 peptide pools in ELISPOT assays. A mean of 22.8% (range, 5%–42.1%) of CD8+ T cells bound HLA-restricted LMP2 tetramers, compared with a mean of 0.11% (range, 0.01%–0.24%) of LMP2-tetramer positive CD8+ T cells found in CTLs generated with genetically unmodified LCLs from the same patients. So far, 6 patients have been treated with 2 doses of 2×10^7 CTL/ m^2 2 weeks apart. No immediate toxicity was observed. In patients with identified LMP2 epitopes, measurement of IFN γ secretion by CD8+ T cells after stimulation with appropriate LMP2 peptides in ELISPOT assays showed a 4- to 25-fold increase in spot-forming cells after infusions. In contrast, frequencies of CMV and superantigen-specific T cells did not increase. Four patients without radiologic evidence of disease who received CTL as adjuvant therapy post-SCT or chemotherapy remain well up to 12 months post-CTL. Two patients with measurable disease at the time of CTL infusion had stable disease 8 weeks post-CTL. They received 2 further doses of LMP2-CTL. One patient continues with stable disease, and the other patient had a complete radiologic response. This patient had a supraclavicular lymph node resection that showed selective accumulation of LMP2 tetramer-positive cells (0.3%, compared to 0.01% in the peripheral blood) with few residual tumor cells. Immunotherapy with autologous LMP2-CTL is therefore well tolerated in patients with relapsed EBV+ HD/NHL, and infused LMP2-CTL cells can localize to the tumor and induce a clinical response.

STEM CELL BIOLOGY

52

REPAIR OF CROHN'S DISEASE WITH EMBRYONIC STEM CELLS

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The primary objective of this work is to determine differentiation and repair potential of murine embryonic stem cells (ES) in murine Crohn's disease (CD) model. **Methods:** Colitis was induced in IL10 $^{-/-}$ knock-out mice using prolixicam. The colitis in this model is patchy and progressive and leads to death unless rescue therapy is provided. Enhanced yellow fluorescent protein (EYFP)