SCID model, comparing transplantation of 1×10^6 CD34+ cells, cotransplantation of 5×10^5 untransduced mesenchymal cells and 1×10^6 CD34+ cells and cotransplantation of 5×10^5 IL-7 engineered stromal cells with 1×10^6 CD34+ cells, the last improved engraftment in terms of CD45+ cells and significantly increased the CD3+ cell count in peripheral blood (1.4 ± 1.6 vs 7.4 ± 3; $P < .05$), bone marrow (0.8 ± 1 vs 5.5 ± 2; $P < .05$) and spleen (0.08 ± 0.1 vs 6.2 ± 2; $P < .05$). No significant differences emerged in CD19+ cell recovery. IL-7 serum concentrations did not vary at any time point posttransplantation. These data demonstrate that IL-7-transduced stromal cells maintain the naive T-cell phenotype (CD45RA+/CD45RO−) in vitro and serve to improve immunologic reconstitution after HSCT in NOD/SCID mice, thus emerging as an ideal scaffold for hastening immunological recovery in T-cell-deficient hosts.

LATE EFFECTS/QUALITY OF LIFE

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LIMITING ALLOGENEIC BONE MARROW TRANSPLANTATION BASED ON PSYCHOSOCIAL CRITERIA: A COMPARISON OF PROFESSIONAL ATTITUDES

McLellan, L.[1]; Foster, L.[2]; Kuczkowski, E.[1]; Dabney, J.[1]; Welsh, E.[1]; Bell, K.[1]; Rini, B.[1]; Bates, J.[1]; Curtis, J.[1]; Bolwell, B.J.[1] 1. The Cleveland Clinic Foundation, Cleveland, OH; 2. Cleveland State University, Cleveland, OH.

Oncologists specializing in bone marrow transplantation (BMT) make decisions about who is an appropriate medical candidate for an allogeneic BMT based on clinical criteria. It is not clear how and if decisions are made as to whether a patient is an appropriate candidate based on psychosocial criteria. Although setting limits based on such criteria has been researched in solid organ transplantation, this is not the case in BMT. Presented will be results from survey research comparing responses of BMT physicians, social workers, and nurses regarding acceptability of select psychosocial screening criteria in allogeneic BMT. An IRB-approved survey was mailed to members of ASBMT (North America), AOSW, BMT Special Interest Group, and ONS BMT Special Interest Group. Respondents were asked whether they would recommend proceeding or not proceeding with allogeneic BMT in 17 case vignettes, all of in which the patient has leukemia and had a matched donor. Based on 262 physician surveys returned (40% response rate), the following are 7 case vignettes in which the majority stated that they would recommend not proceeding: active suicidal ideation (84%), current use of addictive illicit drugs (76%), noncompliance (76%), no caregiver available posttransplantation (69%), active alcoholism (61%), early onset of Alzheimer's disease (55%), and no means to pay for BMT (51%). In 10 of 17 case vignettes, most physician respondents would recommend proceeding: history of prior suicide attempts but not currently suicidal (86%), mild mental retardation (84%), major depression (84%), controlled schizophrenia (82%), daily marijuana use (82%), history of a violent felony crime (81%), borderline personality disorder (79%), tobacco smoking (79%), morbid obesity (71%), and caregiver with mental health problem (65%). These initial findings infer that whether or not physicians decide to proceed with allogeneic BMT may be contingent on the currency and acuity of psychosocial risk factors predictive of impaired patient ability for informed, competent decision-making. Responses of physicians, nurses, and social workers are compared and implications for clinical practice in BMT discussed.

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HSCT FAMILY CAREGIVER QUALITY OF LIFE INFLUENCED BY HIGH CAREGIVING STRAIN AND LOW PREDICTABILITY OF CAREGIVING

Eldredge, D.H.[1], Nail, L.M.[1], Grant, M.[2], Maziarz, R.T.[1] 1. Oregon Health Science University, Portland, OR; 2. City of Hope Comprehensive Cancer Center, Duarte, CA.

Background/Purpose: Family caregivers (FCGs) provide much of the outpatient care for allogeneic HSCT recipients during the first year after transplantation. Despite the importance of family caregiving, there is little information about the types of care activities required during this period and the effect of caregiving role strain (CRS) on FCGs' quality of life (QOL). The purpose of this study is to describe relationships among preparedness for caregiving, predictability of caregiving, recipient function and CRS on FCG QOL. **Methods:** FCGs (N = 56) were recruited from 2 academic medical centers on the West Coast and completed a single questionnaire between 3 and 15 months (mean, 7.7 months) after family members' allogeneic HSCT. Descriptive statistics, correlation, and simultaneous regression techniques were used in this cross-sectional study. **Results:** Three types of caregiving were inductively derived from 100 activities: (1) performing usual care (eg, supervising scheduled medications, keeping house clean), (2) providing emotional support (eg, talking with HSCT recipients when sad, discussing how people respond to recipients' illness), and (3) making care-based decisions (eg, giving prn medications, noticing subtle changes). Providing emotional support was the most difficult type of caregiving activity (mean, 1.81; range, 0 = not done, 1 = easy, to 5 = very hard). FCGs had little difficulty performing usual care (mean, 0.90) and making care-based decisions (mean, 1.28). FCGs felt moderately well prepared for caregiving (mean, 2.9; range, 1–4). Together, preparedness, recipient function, predictability, and the 3 types of caregiving accounted for 37% of the variance in FCG QOL ($F6,48= 7.3$; $P < .001$). FCG QOL was uniquely predicted by predictability of caregiving ($t48 = 2.5$; $P = .02$) and strain from providing emotional support ($t48 = -1.9$; $P = .05$). **Conclusions:** During the first year after allogeneic HSCT, FCGs need ongoing assistance providing emotional support to HSCT recipients and recognizing predictability of recipients' caregiving needs.

LEUKEMIA

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EARLY ALLOGENEIC STEM CELL TRANSPLANTATION FOR YOUNG ADULTS WITH ACUTE MYELOBLASTIC LEUKEMIA IN FIRST COMPLETE REMISSION: AN INTENT-TO-TREAT ANALYSIS OF THE LONG-TERM EXPERIENCE OF THE BGMT GROUP

Jourdan, E.[1]; Boiron, J.M.[2]; Dastugue, N.[3]; Vey, N.[4]; Marit, G.[2]; Rigal Huguet, F.[3]; Molina, L.[5]; Fegueux, N.[6]; Pigneux, A.[2]; Recher, C.[3]; Rossi, J.F.6; Attal, M.[3]; Sotto, J.J.[5]; Maraninchi, D.[4]; Reiffers, J.[2]; Bardou, V.J.[4]; Blaise, D.[4] 1. Centre Hospitalier de Caremeau, Nimes, France; 2. Groupe Hospitlier du Haut Leveque, Bordeaux, France; 3. Hopital Purpan, Toulouse, France; 4. Institut Paoli-Calmettes, Marseille, France; 5. Hopital Michalon, Grenoble, France; 6. Hopital Lapeyronie, Montpellier, France.

We evaluated the outcome of early allo-SCT through 4 successive protocols over 17 years by an intent-to-treat analysis based on donor availability in patients younger than 45 years with CR1 AML. Of the 472 patients achieving CR, 182 had an HLA-identical sibling identified, and allo-SCT was carried out in 171 (94%) after Cy-TBI. Of the 290 patients without donor, 88% were intended (and 63% received) to receive autologous auto-SCT. With a median follow-up of 114 months, the 10-year probabilities of relapse, nonrelapse death, overall survival (OS), and leukemia-free survival (LFS) were 27% versus 55% ($P < .001$), 24% versus 6% ($P < .001$), 51% versus 43% ($P = .11$), and 48% versus 40% ($P < .03$), respectively, for alloSCT and non-alloSCT treatment. Cox analysis identified initial WBC, FAB subtypes, cytogenetic risk group, and number of induction courses to achieve CR as significant prognostic predictors. We calculated the statistical risk of each combination of these 4 factors for patients not having a suitable donor and identified 3 groups of patients with different outcome (poor, intermediate, and standard risk group). This analysis allowed us to reclassify 21% of the patients as compared with

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 trough a simple classification based on common parameters.

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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)

Mori, T.; Yokoyama, A.; Aisa, Y.; Yamane, A.; Yamazaki, R.; Nakazato, T.; Ikeda, Y.; Okamoto, S. Division of Hematology, Keio University School of Medicine, Tokyo, Japan.

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 (3g/m^2 every 12 hours for 4 consecutive days). Recombinant G-CSF (lenograstim; 5 μg/kg/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

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

Bollard, C.M.[1,3]; Straathof, K.C.[1]; Huls, H.[1]; Gresik, V.[3]; Carrum, G.[1,2]; Gottschalk, S.[1,3]; Gee, A.[1]; Brenner, M.K.[1,2,3]; Rooney, C.M.[1,3]; Heslop, H.E.[1,2,3] 1. Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX; 2. Methodist Hospital, Houston, TX; 3. Texas Children's Hospital, Houston, TX.

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 IFNγ 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

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REPAIR OF CROHN'S DISEASE WITH EMBRYONIC STEM CELLS

Feng, Z.; Arrunategui-Correa, V.; Kim, H.S.; Carrier, E. University of California, San Diego, La Jolla, CA.

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 piroxicam. The colitis in this model is patchy and progressive and leads to death unless rescue therapy is provided. Enhanced yellow fluorescent protein (EYFP)