**IMMUNOTHERAPY AND TRANSPLANTATION FOR MULTIPLE MYELOMA: EARLY RECOVERY OF AGGRESSIVE CYTOTOXIC CELLS AND IMPROVED IMMUNE RECOVERY**

Bengtson, E.M.1, Wu, J.-Y.2, Fitzmaurice, T.F.1, Cornell, C.J.1, Elly, P.1, Gautier, M.1, Lazery, C.H.1, Mekan, K.R.1 1Dartmouth–Hitchcock Medical Center, Lebanon, NH; 2Dartmouth Medical School, Hanover, NH.

Autologous peripheral blood stem cell transplantation (APBSCT) is effective for the treatment of multiple myeloma (MM); however, the majority of patients relapse. Recent evidence shows that immediate following APBSCT in patients with a hematologic malignancy. We designed a Phase II trial evaluating a dose escalation of SQ IL-2 and standard-dose GM-CSF posttransplantation for myeloma patients. Patients (n = 18) received melphalan 200 mg/m² with GM-CSF 250 mg/m²/day beginning on day 5. IL-2 began on day 0 and continued for 5 days per week for 4 weeks. Peripheral blood samples were obtained at baseline (pretreatment) and every week for 4 weeks posttransplantation and evaluated using flow cytometry for cell subsets with antibodies directed against CD3, CD4, CD8, CD25, and CD56. Control patients (n = 11) consisted of MM patients who received melphalan 200 mg/m² with either GM or GM-CSF without IL-2. IL-2 at a dose of 1 × 10⁶ U/m²/day was not tolerated in 2 of 6 patients due to grade 4 fatigue and diarrhea (n = 1) and grade 4 SVT (n = 1). A dose of 6 × 10⁴ U/m²/day was well tolerated by 12 patients. At this dose, level 3 or greater toxicities included nausea (n = 5), diarrhea (n = 3), anorexia (n = 11), and mucositis (n = 9). Engraftment of neutrophils occurred on day 12 (median; range, 11–17 days) and platelets on day 14 (median; range, 9–74 days). Only 3 of 18 patients have relapsed/progressed, with a median follow-up of 16.4 months. Absolute lymphocyte counts on days 10–15 were increased by 152% in the IL-2 cohort (mean; range, 25%-390%) compared with the control group. At day 21, there was a marked increase in the number of CD8+ T cells (43% ± 7.5%), CD56 NK cells (78.3% ± 9.1%), and CD6+CD56+ NKT cells (36.8% ± 9.8%) compared with baseline levels. Cytotoxicity of day 21 PBMCs in the IL-2 cohort was strikingly increased at 28.1%, compared with baseline levels. Cytotoxicity of day 21 PBMCs in the IL-2 cohort was strikingly increased at 28.1%, compared with baseline levels. These results demonstrate a very-well-tolerated regimen of immediate posttransplantation immunotherapy with marked increase in the number and function of early cytotoxic effector cells. The enhanced immune recovery may translate into an improved outcome.

**HEMATOPOIETIC STEM CELL TRANSPLANTATION IS EFFECTIVE CURATIVE TREATMENT IN PEDIATRIC REFRactory/AGGRESSive LANGERHANS CELL HISTIOCYTOSIS**

Camiglia, M.1, Pinto, R.M.1, Rana, L.1, Zimmo, F.1, Peluso, G.1, Lombardi, A.1, Angioni, A.1, Iacchi, G.1, Arvace, W.2, De Rosa, G.1 1Hematology Unit, “Bambino Gesù” Children’s Hospital, Rome, Italy; 2Hematology Tor Vergata University, Roma, Italy.

Although the new strategies for the management of LCH have been made considerable advances in the outcomes of pediatric patients, the best therapeutic approach for aggressive/refractory multisystem LCH patients remains controversial. Antiproliferative and immunosuppressive therapy in combination with HSCT has been proposed as the appropriate treatment for these patients with poor prognosis. Because of the appreciable morbidity and mortality of allogeneic HSCT, this strategy has heretofore been reserved for the few LCH patients with a very poor prognosis. In this report we describe 4 children, age 14 months (patient 1), 27 months (patient 2), 96 months (patient 3), and 48 months (patient 4), with refractory aggressive MS-LCH who were treated with allogeneic HSCT in our institution between 2001 and 2003. Disease activity score, as well as Karnofsky status, were retrospectively calculated for all patients at diagnosis and before HSCT. All patients presented with MSD progression with single or multiple agents or immunosuppressive therapy. Allogeneic HSCT was performed 10, 22, 72, and 47 months, respectively, from onset. Patients 1 and 3 received umbilical cord blood transplantation (UCBT) from HLA 4/6 and 5/6 mismatched unrelated donors. Patients 2 and 4 received bone marrow transplantation (BMT) from related HLA-identical donors. A conditioning regimen including busulfan 4 mg/kg and fludarabine 30 mg/m² from day −7 to day −4 and thiopeta 10 mg/kg on day −3 was used as preparative regimen. All patients received horse ATG 15 mg/kg from day −6 to day −2, cyclosporine A 3 mg/kg from day −1 to day +180, and PDN 1 mg/kg until day +10. After HSCT, all patients are alive with a median follow-up of 30 months (51, 39, 19, and 11 months, respectively). The conditioning regimen was well tolerated without major complications. Donor engraftment was demonstrated in all 4 patients by PCR DNA analysis, and progressive improvement of disease symptoms were observed after 18, 6, 8, and 6 months, respectively. Patients 1 and 2 are disease-free, patient 3 presented with grade III AGVHD and reduction of esophagomuscular and skin lesions, bone lesions are stable as well as for patient 4. Disease progression was not evident in any of the patients during long-term follow-up. We conclude that HSCT is a good curative treatment for these patients with poor prognosis. Progressive clinical improvements were evident a long time after HSCT. Selection of patients based on early response to conventional chemotherapy and timing of HSCT remains controversial.