

eosinophils in bone marrow, gut and peripheral blood were analysed by using SPSS.

Results: The incidence of acute GVHD was 51% (36% grade 1, 27% grade 2, 15% grade 3 and 22% grade 4 out of it). One organ aGVHD was diagnosed in 42 (skin $n = 36$, gut $n = 4$, liver $n = 2$), two-organ aGVHD in 10 and three-organ aGVHD in 7 patients. The density of bone marrow eosinophils was increased after RIC-SCT in comparison to before it (6% vs 3.4%, $p < 0.001$, respectively). Bone marrow eosinophilia after RIC-SCT was found in 66% of patients with aGVHD and was a significant predictive factor ($p < 0.03$) for developing aGVHD. However, eosinophil density did not correlate with aGVHD severity. Peripheral blood eosinophilia was not predictive for developing aGVHD. Intestinal eosinophils were found in 15 of 20 patients with clinical signs of gut GVHD, which has been consequently histologically proven in 13 patients (87%, $p < 0.02$). The degranulation of eosinophils, determined by using anti-MBP was present in all patients with gut aGVHD.

Conclusions: Both gastrointestinal tract and bone marrow tissue eosinophilia after RIC-SCT predict aGVHD. In addition, gut eosinophil density and degranulation were increased in patients with higher grades of aGVHD thus indicating their role as a biological marker of GVHD. To our knowledge this is the first study showing that tissue eosinophil density might be a predictive marker for aGVHD after RIC-SCT.

368

IMMUNOMODULATORY EFFECTS OF VITAMIN D: IMPLICATIONS FOR THE TREATMENT OF GRAFT VERSUS HOST DISEASE

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Allogeneic transplantation is uniquely curative for some patients with hematologic malignancies. However, morbidity and mortality due to graft versus host disease remain substantial. Persistence of host dendritic cells (DCs) in the early post transplant period plays a role in the activation of alloreactive lymphocytes and the risk of GVHD. A focus of research involves the manipulation of DC recovery post-transplant to minimize activation of alloreactive lymphocytes while preserving the graft versus disease effect. Vitamin D is a hormone involved in bone metabolism. More recently, vitamin D has been shown to have immunomodulatory effects. We evaluated the effect of vitamin D on the phenotypic and functional characteristics of DC and T cell populations. Peripheral blood mononuclear cells were isolated from leukopaks obtained from normal donors. DCs were generated by culturing the monocyte enriched adherent fraction with GM-CSF and IL-4 for 5 days, followed by TNF α for 48 hours. DCs were generated in the presence and absence of 10nM of 1,25 hydroxyvitamin D. Mean expression of the costimulatory molecule CD80 and the maturation marker CD83 decreased from 60% to 37% and 53% to 27% respectively in the presence of vitamin D ($N = 3$). To assess the effect of vitamin D on the functional potency of DCs as antigen presenting cells, the capacity of DCs to stimulate allogeneic T cell proliferation in the presence of vitamin D was determined. Mature DCs were cultured with allogeneic T cells at a ratio of 1:10. After 5 days, cocultures were pulsed with tritiated thymidine overnight. The addition of vitamin D resulted in a blunted T cell proliferative response, with mean SI that decreased from 13 to 5 ($n = 10$). Similarly, the addition of vitamin D to a coculture of DCs and autologous T cells resulted in a 50% reduction in the T cell proliferative response to tetanus toxoid, a recall antigen. In addition, T cells stimulated by allogeneic DCs in the presence of vitamin D were polarized to secrete Th2 cytokines. The presence of vitamin D did not induce FOXP3 expressing regulatory T cell populations. These data suggest that exposure to vitamin D exerts a tolerizing influence on T cells mediated by its impact on antigen presenting cells. Vitamin D may therefore have a role in the prevention and treatment of graft versus host disease. A clinical trial evaluating the use of vitamin D in the early post-transplant period for the prevention of GVHD is planned.

369

ALLOGENEIC VERSUS AUTOLOGOUS STEM CELL TRANSPLANTATION (SCT) FOR FOLLICULAR LYMPHOMA (FL). THE JAMES COMPREHENSIVE CANCER CENTER EXPERIENCE

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Majority of the reported studies comparing allogeneic versus autologous SCT in patients with FL have short follow-up (median = or < 5-yrs). Patients with histologically confirmed FL ($n = 117$) undergoing SCT between 1985 and 2007 were eligible for this study. Patient characteristics including age, stage, LDH, number of prior therapies, remission status at SCT [CR, PR, untreated relapse (REL), refractory (REF)], and transplant characteristics were recorded. The median age was 49 years (range 23–71). 36 patients underwent allogeneic SCT (including 10 patients receiving reduced intensity conditioning), while 81 patients underwent autologous SCT. The median number of prior treatments for autologous and allogeneic SCT groups were 2 (range 1–5) and 3 (range 1–7) respectively. Median follow-up is 7-years. 5-year OS following autologous SCT for patients in CR1/PR1, CR>1/PR>1 and relapsed or refractory disease was 79%, 71% and 53% respectively. The respective OS for allogeneic SCT was 51%, 75%, and 49%. Relapse rates were lower following allogeneic SCT versus autologous SCT at 27% versus 55% respectively. 5 year progression free survival (PFS) was higher following allogeneic SCT at 46% versus 38%. Higher non-relapse mortality (NRM) with allogeneic SCT (25% versus 11%) resulted in a 5 year OS favoring autologous SCT (67% versus 57%). With prolonged follow-up a plateau was seen in allogeneic SCT curve at around 3-yrs, while autologous SCT patients continued to experience events. Hence the estimates of 10-yr OS for allogeneic SCT patients was 57% (unchanged from 5-yr OS), compared to 48% for autologous SCT. Our study shows that although the early results of allogeneic SCT (mostly with myeloablative conditioning) are negatively impacted with associated high NRM, it produces durable remissions, with eventual appearance of trends of improved survival with prolonged follow-up.

370

PHARMACOKINETICS (PK) OF IV AND PO MYCOPHENOLATE MOFETIL (MMF) IN AGE ADJUSTED PEDIATRIC AND ADOLESCENT ALLOGENEIC STEM CELL TRANSPLANT (ALLO-SCT) RECIPIENTS: SIGNIFICANTLY HIGHER CL_{SS} AND V_{SS} IN PATIENTS <6 YEARS OF AGE

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Children undergoing AlloSCT exhibit higher MMF dose requirements and significant interpatient variability in mycophenolic acid (MPA) PK (Jacobson P et al, *Ped* 2008). The objective of this study is to evaluate effects of age and conditioning intensity on the PK of MMF in pediatric AlloSCT recipients. From 1/04–5/08 we enrolled 38 pts: med age 8 yrs (0.33–16); M:F = 20:18; 22/16 malignant/non; 17/21 myeloablative (MA)/non-ablative (NMA); 16/22 related/unrelated. Cohort 1 (<6 yrs) $n = 14$; 2 (6–12 yrs) $n = 10$; 3 (12–16 yrs) $n = 12$. GVHD prophylaxis: tacrolimus Day –1 (5–20 ng/mL) and MMF 900 mg/m² IV Q6H starting on Day +1, then converted to PO (same dose) after Day +14. MPA serum samples were drawn on Days +1, +7, +14 (IV phase) and twice between Day +45–+100 (PO phase) at hour 0, 0.5, 1, 2, 3, 4, 6 post-dose. MPA plasma concentrations were determined by reverse-phase HPLC and LC/MS/MS. Non-compartmental PK analysis of total MPA was performed. Median time to myeloid and platelet engraftment was 18 and 31 d, respectively. KM probability of Grade II–IV acute GVHD (aGVHD) and extensive chronic GVHD