preliminary results from an IRB-approved prospective, open label, phase II trial to test the efficacy of montelukast, a leukotriene inhibitor, for the treatment of BOS after HSCT. BOS diagnostic criteria included: FEV1 < 75%, FEV1/VC < 0.7 or air trapping on CT and RV > 120% or RV/TLC > 120% in the absence of infection and presence of another cGVHD manifestation. Eleven patients have enrolled to date. One withdrew prior to medication initiation and 9/10 are currently on study medication (10 mg montelukast po nightly). Patient characteristics include age range 15-60 years, 7/11 female, baseline FEV1 range from 33 to 71% predicted, and 3/11 patients requiring oxygen supplementation. Sixty-four % (7/11) have reached the primary endpoint (6 months of study drug). FEV1 increased by 6-10% predicted in 3 patients, remained stable in 3, and declined by less than 15% in 1. Slope of the FEV1 value generated as linear regression of FEV1 volume vs. days post-transplant revealed: 5/7 increase in slope, 2/7 decrease in slope from pre-study FEV1 values. Three patients had immunosuppression reduced during this time period with complete cessation of tacrolimus in 1, cessation of steroids in 1, and decreased tacrolimus in 1(including 2 with stable FEV1 and 1 with increase in FEV1); 1 patient had an increase in steroid dose less than 1 mg/kg/day. Two patients had worsening of other cGVHD manifestations on study, including a skin flare that resolved without increasing systemic therapy (1) and gastrointestinal cGVHD flare that improved with increased steroids including local therapy (1). Montelukast was well-tolerated with one grade II attributable adverse event (insomnia) during the six-month collection period. Improvements were also noted in oral mucosa cGVHD manifestations in 3/7 and liver in 2/7. These preliminary findings suggest that montelukast may have a role in the therapy of BOS after allogeneic HSCT.

418 A PROSPECTIVE STUDY OF DONOR IMMUKNOW® AS A BIOMARKER FOR ACUTE GVHD IN HEMATOPOIETIC CELL TRANSPLANTATION RECIPIENTS

Kang, Y.1, DeOliveira, A.1, Peel, L.E.2, Chen, D.-F.2, Chao, N.1 1 Duke University Medical Center, Durham, NC; 2 Duke University Medical Center, Durham, NC

Introduction: Graft versus host disease (GVHD) occurs in ~40% of allogeneic hematopoietic cell transplantation (HCT) recipients and is associated with substantial morbidity and mortality. Immuno-logical parameters of donor cells that predispose a recipient to GVHD will be of great value. The Cylex® ImmunoKnow® assay determines the strength of immune function by quantifying the amount of ATP released from phytohemagglutinin-stimulated peripheral blood CD4+ cells. In our current study, we utilized the ImmunoKnow® to assess whether a donor’s immune response correlates with early outcomes in recipients post-HCT.

Patients and Methods: Twenty-six (26) donor-recipient pairs were included in our study (15 HLA identical sibling HCT and 11 haplo-identical HCT). Recipients received an average cell-dose of 10.7 ± 4.9 x 10^9 CD34+ cells/kg. Blood samples obtained prior to G-CSF mobilization and post-stem cell collection (approximately 2 weeks apart) were assayed for ImmunoKnow values and cell counts (WBC, ANC, ALC & CD34+ count).

Results: G-CSF mobilization led to a significant increase in ImmunoKnow® ATP values from 342 to 728 ng/mL (p < 0.001) along with an increase in all measured cell counts. Grade II acute GVHD occurred in 27% of haploidential HCT recipients (3/11 patients) and 20% of HLA identical HCT recipients (3/15 patients). In haploidential HCT, mobilized donor blood ImmunoKnow® ATP values did not correlate with GVHD. However, donor ImmunoKnow® values correlated with increased risk of acute GVHD in HLA identical sibling HCT. In HLA identical sibling HCT, ATP values in excess of 747 ng/mL predicted grade II or higher GVHD with a likelihood ratio of 4.00 (2.9-5.9, 95% confidence), sensitivity of 100%, and specificity of 75% (AUC = 0.889, p = 0.003).

Conclusions: If confirmed in larger studies, these data suggest that ImmunoKnow can serve as an independent predictor/biomarker for the development of GVHD in HLA identical HCT.

419 MYCOPHENOLATE MOFETIL AS THERAPY FOR STEROID DEPENDENT OR REFRACTORY GRAFT VERSUS HOST DISEASE: TEN YEARS EXPERIENCE FROM A SINGLE CENTER IN BRAZIL


Chronic graft-versus-Host-Disease (GVHD) is observed in up to 50% of long term survivors of hematopoietic stem cell transplants (HSCT) and is associated to important morbidity and mortality. Mycophenolate Mofetil (MMF) has been used as therapy for refractory chronic GVHD with good efficacy and tolerability. We describe our experience at Hospital de Clinicas of Federal University of Parana-Brazil during the last ten years on the use of this drug as rescue for refractory chronic GVHD.