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High Donor and Recipient Age Are Not Risk Factors for Chronic Graft-Versus-Host Disease in the Setting of Anti-Thymocyte Globulin-Conditioned Hematopoietic Stem Cell Transplantation

Andrew Boon Ming Lim [1], Jan Storek [2], Ashanka Beligaswatte [3], Marnie Collins [4], Kate Mason [5], Emily Peizhen Li [6], Ahsan Chaudhry [7], James A. Russell [2], Andrew Daly [2], Jeffrey Szer [8], Ian Lewis [9], David Stuart Ritchie [1,10]. [1] Clinical Haematology & Bone Marrow Transplant Service, Royal Melbourne Hospital, Parkville, Australia; [2] Blood and Bone Marrow Transplant Program, Tom Baker Cancer Centre/ Foothills Hospital, Calgary, AB, Canada; [3] Department of Haematology, Royal Adelaide Hospital, Adelaide, Australia; [4] Centre for Biostatistics and Clinical Trials, East Melbourne, Australia; [5] Royal Melbourne Hospital, Parkville, Victoria, Australia; [6] Royal Melbourne Hospital, Parkville, Australia; [7] Alberta Blood and Marrow Transplant Program, Calgary, AB, Canada; [8] Clinical Haematology & BMT Service, Royal Melbourne Hospital, Parkville, Australia; [9] Haematology, Royal Adelaide Hospital, Adelaide, SA, Australia; [10] Peter MacCallum Cancer Centre, East Melbourne, Australia

Rabbit anti-thymocyte globulin (ATG) given with conditioning for allogeneic haematopoietic stem cell transplantation (alloHSCT) is effective in reducing the risk of chronic graft-versus-host disease (cGVHD). Whether conventional risk factors for cGVHD apply to ATG-conditioned alloHSCT is not known. Between the years 2004 and 2011, 356 adults (median age 48) from 3 centres received 4.5 mg/kg of Thymoglobulin prior to alloHSCT for haematologic malignancy (acute leukaemia 58%, chronic myeloid leukaemia 6%, other myeloid malignancy 15%, other lymphoid malignancy 21%). Donors were unrelated in 64%. Conditioning was myeloablative in 94%. Peripheral blood grafts were used in 97%. At 3 years, overall survival was 61.0% (95% CI 55.3-67.3%), cumulative incidence of relapse was 32.6% (95% CI 26.2-38.5%) and transplant-related mortality was 18.8% (13.2-24.1%). 342 patients were evaluable for the primary endpoint of cGVHD requiring systemic immunosuppression (cGVHD-IS). The cumulative incidence of cGVHD-IS at 3 years was 37.2% (95% CI 31.1-42.7%). On multivariate analysis, only prior grade 2-4 aGVHD (HR 3.08, 95% CI 2.10-4.52, $P < .001$) was associated with a significant increase in risk of cumulative incidence of cGVHD-IS. Recipient age of greater than 40 years was associated with significantly less cGVHD-IS (HR 0.66, 95% CI 0.45-0.97, $P = .03$) in univariate but not multivariate analysis. The use of unrelated donors, donor age over 40, female donor/male recipient gender combination and recipient CMV seropositivity were not associated with increased cGVHD-IS. There was insufficient power to determine the effect of graft type (peripheral blood vs bone marrow) on cGVHD-IS, but the incidence did not appear higher in peripheral blood graft recipients. In summary, in this cohort, traditional pre-transplant risk factors for cGVHD were not predictive. In patients undergoing *in vivo* T-cell depleted alloHSCT, novel predictors of cGVHD may be needed.

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Sub-Therapeutic Levels of Oral Tacrolimus Prophylaxis Prior to Allogeneic Stem Cell Transplant Do Not Predict the Incidence of Chronic Graft Versus Host Disease

Jill MacPherson, Carlos Bachier, Ashley Simpson, Paul J. Shaughnessy. Adult Blood and Marrow Transplant, Texas Transplant Institute, San Antonio, TX

Chronic graft versus host disease (cGVHD) is a common complication of allogeneic stem cell transplantation (ASCT). Tacrolimus prophylaxis has been proven to be instrumental in the prevention of acute graft versus host disease (aGVHD) a common precursor to developing cGVHD. Our institution uses oral tacrolimus prior to ASCT because we perform ASCT in the outpatient setting and increases ease of administration. We retrospectively reviewed our experience in 94 consecutive patients (pts) who received ASCT from 10 /10 HLA matched donors, 47 were matched sibling donors (MSD) and 47matched unrelated donors (MUD) with a median age of 50 and 52 respectively. All patients received GVHD prophylaxis with tacrolimus started orally between day -3 and day -1 at a dose of 0.06mg/kg per day divided twice daily. Standard short course methotrexate (MTX) was prescribed for all pts (D1 dose 15mg/m2, D3, 6, and 11 doses at 10mg/m2). Pts who had sub-therapeutic tacrolimus levels (less than 5ug/L) on the day of transplant (D0) were compared to pts who had therapeutic tacrolimus levels (greater than 5ug/L) for incidence of cGVHD and overall survival. Sixty-eight pts had tacrolimus levels less than 5ug/L on D0 and 26 pts had tacrolimus of 5ug/L or greater. Fifty eight of the 94 patients developed cGVHD and 36 did not develop cGVHD indicating that there was no significant difference in the incidence of cGVHD in these patients despite the level of tacrolimus on D0. The 58 pts that developed cGVHD, 42/68 (62%) had a tacrolimus level less than 5ug/L.The 36 pts that did not develop cGVHD, 26/68 (38%) had a tacrolimus level less than 5ug/L. With a median follow up of 463 days 54/94 pts (57%) survive; 40/68 pts (59%) with D0 tacrolimus levels that were less than 5ug/L, and 14/26 pts (54%) with D0 tacrolimus levels were greater than or equal to 5ug/L. In conclusion, oral tacrolimus prophylaxis prior to ASCT at our institution results in sub-therapeutic levels on the day of transplant in the majority of patients, however, this does not appear to impact the overall incidence of cGVHD or survival. As an incidental finding, those who developed cGVHD had longer overall survival versus those who did not develop cGVHD. This study was limited by its retrospective nature, small size and single center experience.

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The Expansion of Gastrointestinal-Associated αβ T Cell Clones in Peripheral Blood Associates with Severe Steroid Refractory GVHD

Everett H. Meyer [1,2], Joanna A. Lilienta [3], Mareike Florek [1], Andrea Lohr [2], Ando Hsu [2], David Johnson [2], Philip Lavori [4], James L. Zehnder [5], David B. Miklos [1], Samuel Strober [6], Robert Negrin [1]. [1] Department of Medicine, Division of Blood and Marrow Transplantation, Stanford University School of Medicine, Stanford, CA; [2] GigaGen, Inc, San Francisco, CA; [3] Department of Medicine, Translational Research and Applied Medicine Program, Stanford University School of Medicine, Stanford, CA; [4] Health Research and Policy, Biostatistics, Stanford University School of Medicine, Stanford, CA; [5] Dept. of Pathology, Stanford University School of Medicine, Stanford, CA; [6] Department of Medicine, Rheumatology Division, Stanford University School of Medicine, Stanford, CA

Donor T cell alloreactivity in hematopoietic stem cell transplantation (HCT) can result in acute graft-versus-host disease (GVHD) which is a major cause of morbidity and mortality in HCT. We hypothesized that using T cell receptor repertoire sequencing, we could identify the most frequent T cell clones in the gastrointestinal (GI) tract of human patients with GVHD and subsequent tracking of these disease-associated