seasonal influenza (SFlu) in HM patients versus HSCT recipients are lacking.

Methods: We evaluated characteristics, diagnostic results, management and outcomes of all influenza A infections (pandemic H1N1 versus SFlu) and determined the risk factors associated with pneumonia and all-cause mortality in HM patient and HSCT recipients at MD Anderson Cancer Center (MDACC) from April 2009 to July 2013.

Results: A total of 259 patients were identified, including 134 (52%) HM patients and 125 (48%) HSCT recipients. Majority of patients (242, 93%) were adults, males (147, 57%) with underlying diseases in remission (160, 64%). About half of patients required hospitalization for outcomes including pneumonia 28% (72 pts) and death 6% (16 pts). Majority of patients (214, 83%) received antiviral therapy within a median of 3 days (range, 0d − 28d) after onset of first symptom. Compared to HCT recipients, a significantly higher percentage of HM pts were in active stages of cancer with severe neutropenia (26, 20%) and severe lymphopenia (25, 19%) and required hospitalization (76, 57%). Multivariable logistic regression analysis identified hematologic malignancy (AOR: 2.5 (95% CI: 1.2, 5.28), decreased albumin (AOR: 2.2 (95% CI: 1.0, 4.64), and delay in initiation of antiviral therapy (AOR: 1.3 (95% CI: 1.12, 1.47) as significant risk factors for development of pneumonia ($P = 0.05$), after adjusting for the virus strain. Interestingly, H1N1 infections were more prevalent in Hispanic population (26, 31%) and required more mechanical ventilation (9, 11%) compared to SFlu, but no significant differences were observed with respect to pneumonia or mortality between these two viruses.

Conclusions: Influenza remains a significant cause of morbidity and mortality in HM patients and HSCT recipients. Compared to HCT recipients, HM patients were more likely to progress to pneumonia, probably owing to active cancer stage and pancytopenia. H1N1 patients did not have higher mortality rate compared to SFlu in either of the groups. Early antiviral therapy remains crucial in preventing morbidity in this population.

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Favorable Outcomes from Allogeneic Hematopoietic Cell Transplantation in Thailand for Thalassemias and Hemoglobinopathies

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Background: Thalassemia syndromes are very prevalent in many parts of the world including Asia. Allogeneic hematopoietic cell transplantation (HCT) is the only curative therapy accepted worldwide.

Objectives: To assess outcomes of HCT for thalassemias and hemoglobinopathies in single medical center in Thailand.

Methods: Case series study for thalassemia and hemoglobinopathy patients undergoing HCT at Bangkok Hospital Medical Center from February 2009 thru October 2013.

Results: There were totally 14 patients. 10 cases were Thais, 1 was French-Thai, 1 was Bangladeshi, 1 was Lao, and 1 was Omani who had sickle cell disease (SCD). 12 cases were diagnosed as beta-thalassemia/hemoglobin E diseases, 1 as transfusion-dependent alpha-thalassemia, and 1 as SCD. Among 14 HCTs, 9 patients underwent bone marrow transplant (BMT), 4 patients underwent umbilical cord blood transplant (CBT), and 1 patient underwent combined cord blood and marrow transplantation. All 14 related donors were fully-HLA-matched, 4 had normal typing, 9 had thalassemia trait, and 1 had sickle cell trait. Male to female patients ratio were 11:3. Patients' ages at transplant varied from 2 years to 15 years 11 months with median of 4 years 10 months. Patient's body weight varied from 11.1 to 50 kilogram (median 17.2 kilogram). According to Pesaro classification, among 13 thalassemia patients there were 8 class I, and 5 class II patients. Busulfan, fludarabine, and rabbit ATG were mainly used as myeloablative conditioning regimen. Cyclosporine and short-course methotrexate were mainly used as graft-versus-host disease (GvHD) prophylaxis in BMT group, while cyclosporine alone was used in CBT group. CD34+ cell doses per kilogram body weight recipients were ranged from 5.6 to 34.7×10^6 (median 11.3×10^6) in BMT group (n=9), and from 1.6 to 3×10^5 (median 2.3×10^5) in CBT group (n=4). Complete donor engraftments were achieved in 11 patients. Mixed-chimerism states with donor predominance were present in 2 patients from BMT and 1 patient from CBT group. No patients experienced graft failure. Neutrophil recoveries were evident on days +10 to +23 (median day +14), and platelet recoveries were observed on days +19 to +64 (median day +40). 2 patients had mild veno-occlusive diseases and were later completely reversible. No patients developed acute or chronic GvHD. There were no mortalities. 1 patient had treatable pneumocystis pneumonia at 4 months post CBT. Median follow-up time for all patients was 2 years (1 month to 4 years 8 months). Overall (OS) and disease-free survival (DFS) were 100% and 100% for all patients (n=14). Based on risk class, the OS and DFS for class I thalassemia patients (n=9) were 100% and 100%, and class II patients (n=4) were 100% and 100%, respectively.

Conclusions: Our experiences in HCT for thalassemias and hemoglobinopathies were very favorable. Regular follow-up visits are encouraged to determine long term outcomes.

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Engraftment and Immune Recovery (IR) in Good Risk Patients Undergoing Hematopoietic Stem Cell Transplantation (HSCT): Comparison of Two Different Approaches Using Cyclophosphamide (CY) for T-Cell Tolerization

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We developed a 2 step haploidentical HSCT where 76 patients received myeloablative or reduced intensity regimens followed by a DLI containing a fixed dose of 2.0×10^8/kg T cells (HSCT step 1). After 2 days, 60mg/kg/d x 2 of CY was infused, followed a day later by a CD34 selected PBSC product [HSCT step 2 median dose 5×10^6/kg (range 1.64-10)]. We concurrently used a 1 step HSCT approach in a group of 16 patients, 8 with unrelated donors (URD) and 8 patients (6 with haploidentical, 2 with matched related donors) with comorbidities precluding eligibility for the 2 step protocol. The 1 step patients were given the same conditioning, but afterwards received unmanipulated PBSC's [median CD 34 dose 7.18×10^6/kg, (range 4.41-10); median T cell dose 2.9×10^8/kg, (range 1.4-3.90)]. CY 60mg/kg/d x 2 was infused 48

hours later. Because avoidance of stem cell exposure to CY occurs only in the 2 step approach, we compared engraftment rates and IR between the 2 groups. All 92 patients had good risk disease. In the 1 step vs the 2 step study, median time to ANC > 500/ul was 19(range 15-28 days) vs 11[range 9-16 days (p=0.000-Mann-Whitney)], and for platelets > 20,000/ul, 29(range 18-52 days) vs 17(range 12-173 days) respectively (ns). The significant difference in time to ANC recovery in the 1 step group was possibly from the exposure of the donor PBSC's to CY. When we accounted for the later occurrence of day 0 in the 2 step group, the median time to ANC recovery was still 3 days longer in the 1 step group even though this group received a higher median CD 34 dose. Possibly due to the earlier count recovery in the 2-step group, the median CD3/4 count at day 28 was 20(range 5-50/ul) in the 1 step group vs 54(range 11-299/ul) in the 2 step group. By day 90, differences between the groups resolved, with a median CD3/4 count of 157(range 29-397/ul) vs 147(range 10-814/ul) in the 1 and 2 step groups respectively. Median CD3/8 count at day 28 was 40 (range 3-157/ul) vs 57 (range 4-2682/ul) and at day 90 was 239(range 12-1439/ul) vs 204(range 2-2379/ul) in the 1 and 2 step groups respectively. The percentages of patients on steroids for GVHD at day 28 (13% in the 1 step group vs 31%) and 90 (18% vs 33%) was not significantly different between the two groups (p=0.215 and 0.413 respectively, Pearson Chi Square). The median length of stay (LOS) was 41(range 15-99 days) vs 32(range 15-156 days) in the 1 and 2 step groups respectively. The 2 step approach to HSCT allows for the administration of a fixed dose of T cells from which to optimize outcomes and circumvents exposure of donor cells to the effects of CY. Our experience with a 1 step approach suggests later ANC recovery and possibly initial T cell recovery versus the 2 step approach. There may be a slightly longer LOS in the 1 step group possibly from longer time to count recovery. Formal analyses of the differences between the two approaches will be performed when more patients are treated at our institution with the 1 step approach.

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END Organ Disease in the Context of Human Herpes VIRUS 6 Viremia in Pediatric Allogeneic Hematopoietic STEM CELL Transplant Patients: A Case Series

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Introduction: HHV6 (Human Herpes Virus 6) reactivation occurs in approximately one-half of patients following allogeneic hematopoietic stem cell transplant (HSCT). The target tissues of HHV6 and the extent to which HHV6 causes disease in those with viremia is not resolved.

Methods: Biopsies or body fluid sampling are routinely performed at our center to determine the cause of otherwise unexplained end-organ disease. We describe 14 pediatric HSCT patients who were found with HHV6 PCR end-organ tissue positivity on these studies. Of these 14 patients, 13 had received myeloablative conditioning, 12 had received an unrelated donor graft, 10 had underlying malignant disease, 9 patients had acute GVHD, and 3 were diagnosed with chronic GVHD.

Results: Robust statistical partitioning identified two distinct subgroups within this population based on the highest HHV6 viral load in blood. In 10 of the 14 patients, a peak blood viral load (>28,000 copies/mL) occurred developed while the other 4 patients had peak blood viral loads <2000 copies/ml. All patients received antiviral treatment to treat their viremia. At the time of biopsy and/or fluid sampling, only 1 patient out of 14 had a blood viral load >28,000 copies/mL and the remainder had very low (<1500 copies/ml) or undetectable HHV6 virus in the blood despite having detectable virus in their tissues. In total, 8/14 patients biopsied patients who had tissue/body fluid viral positivity did not have concurrent detectable virus in blood, in 5/14, the blood viral load was <1500 copies/ml, while only in one patient who had encephalitis there was a high copy number of 344,488 copies/ml detected in blood at the time of detection of the virus in the cerebrospinal fluid (CSF).

HHV6 was found in CSF (3 patients), BAL fluid (3 patients), GI tract (5 patients), bone marrow (5 patients), pericardial fluid (3 patients), liver (1 patient), and gallbladder (2 patients). Statistical analysis showed no difference between the two subgroups with respect to age, gender, stem cell graft, stem cell donor, HLA compatibility between the donor and the recipient, acute/chronic graft-versus-host disease, or survival. Of note, 4 out of 14 patients had co-existent CMV viremia. There was a decreasing linear trend (Cochran-Armitage P=0.015) in the association (Fisher's exact P=0.041) between CMV viremia and HHV6 viral load group: 3 patients with CMV viremia were in the low HHV 6 viral load group versus 1 patient in the high group. Five of the fourteen patients died (one of whom relapsed), suggesting a high non-relapse mortality rate (28%) in this population.

Conclusion: End-organ disease/dysfunction with HHV6 positivity can persist despite a decrease in peripheral viral load after antiviral treatment. Further studies will elucidate whether prolonged or intensive antiviral treatment is warranted in such cases.

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Impact of Adenovirus Viremia in Bone Marrow Transplant Patients, 2010-2013

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Table 1
Patient characteristics comparing cases and controls

	Cases (n=5)	Controls (n=15)	*P* value
Age (Median with range)	43 (21-68)	47 (27-71)	0.646
Male gender	5 (100%)	13 (86.7%)	1.000
Type of transplant			
Allogeneic – Related, Unmatched	0 (0%)	3 (20%)	0.539
Allogeneic – Unrelated, Matched	3 (60%)	2 (13.3%)	0.073
Allogeneic – Unrelated, Unmatched	1 (20%)	7 (46.7%)	0.603
Autologous	1 (20%)	3 (20%)	1.000
Immunosuppressive therapy on day + 14			
Tacrolimus	4 (80%)	11 (73.3%)	1.000
Corticosteroids	0 (0%)	1 (6.7%)	1.000
Mycophenolate	1 (20%)	2 (13.3%)	1.000
GvHD	3 (60%)	2 (13.3%)	0.073
WBC	4.1 (0.2-9)	4.7 (0.8-9.2)	0.668
ANC	3.0 (0.7-5.3)	3.2 (0.1-9.3)	0.882
Hemoglobin	8.7 (6.8-10)	10.7(7.2-14)	0.066
Platelets	70 (7-165)	120 (35-236)	0.147
Cr	1.25 (0.83-1.97)	0.84 (0.38-1.29)	0.081
Alk Phos	85 (36-138)	69 (50-95)	0.243
Total bilirubin	1.2 (0.6-2)	0.6 (0.3-0.9	0.003
ALT	71(10-151)	29 (8-71)	0.026
Albumin	2.6(2.2-3.1)	3.7 (2.7-4.2)	< 0.001