**Table.**

| | No-VGC (n = 136) | VGC (n = 136) | p-value |
|---|---|---|---|
| Age, median | 53 | 54 | 0.8 |
| Active disease | 69 (51%) | 68 (50%) | NR |
| Recipient/Donor CMV serostatus | | | |
| R+/D+ | 66 (48%) | 68 (50%) | |
| R-/D+ or R+/D- | 66 (48%) | 63 (46%) | |
| R-/D- | 4 (3%) | 5 (4%) | 0.5 |
| Diagnosis | | | |
| Acute Leukemia | 96 (70%) | 96 (70%) | |
| Chronic Leukemia | 18 (13%) | 18 (13%) | |
| Other | 22 (17%) | 22 (17%) | NR |
| Regimn Intensity *† | | | |
| Myeloablative | 87 (64%) | 95 (70%) | |
| Reduced-Intensity | 26 (19%) | 21 (15%) | |
| Non-Myeloablative | 23 (17%) | 20 (15%) | 0.6 |
| Donor Type | | | |
| Matched related | 55 (40%) | 55 (40%) | |
| Matched unrelated | 72 (54%) | 72 (54%) | |
| 1 Antigen mismatched unrelated | 3 (2%) | 3 (2%) | |
| Haploidentical | 5 (4%) | 5 (4%) | NR |
| CMV reactivation | 56 (41%) | 63 (46%) | 0.4 |
| Median days to CMV reactivation | 26 (range 0-85) | 34 (range 2-97) | 0.008 |
| CMV disease | 1 (0.7%) | 5 (4%) | 0.1 |
| Day 100 Survival | 91% | 90% | 0.8 |

*Pasquini MC, Wang Z. Current use and outcome of hematopoietic stem cell transplantation: Part I CIBMTR summary slides, 2009. CIBMTR Newsletter (serial online), 2009; (15)1:7-11.
†Bacigalupo A, et al. Defining the Intensity of Conditioning Regimens: Working Definitions. Biol Blood Marrow Transplant 2009; 15: 1628-1633.

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### EXTENDED USE OF APREPITANT IN PEDIATRIC PATIENTS

*Williams, D.[1], Rohatgi, R.[1], Seaton, A.[2], Makonnen, T.[3] [1]Children's National Medical Center, Washington, DC; [2]University of Maryland; [3]Virginia Commonwealth University*

**Purpose:** This will report a single center experience of safety and efficacy of aprepitant used for treatment of nausea and vomiting in pediatric stem cell transplant patients, used for greater than 4 days.
**Background:** Aprepitant is a nuerokinin-1 receptor antagonist that is FDA approved to prevent nausea and vomiting with moderate to highly emetogentic chemotherapy. Aprepitant is utlized in combination with standard antiemtic therapy for a 3 day dosing schedule in adult patients. This is a case series in which pediatric stem cell transplant patients were prescribed aprepitant for the treatment of nausea and vomiting.
**Methods:** This is a retrospective review of patient charts and data. Patients prescribed aprepitant fore extended dosing at Children's National Medical Center between the dates of January 1, 2009 and December 31, 2010 were included.
**Inclusion Criteria:** Aprepitant prescription for greater than 4 days
Age between 1 year and 17.9 years at the initiation of aprepitant therapy
**Results:** Six patient therapy encounters were observed. Patient ages ranged from 2 years to 16 years of age at the time of therapy. The duration of aprepitant usage ranged from 5 to 12 days. The doses of aprepitant ranged from 45mg per body surface area daily to 70mg per body surface area daily. Five out of six (83%) patient encounters demonstrated an improvement of emesis with the addition of aprepitant, both during aprepitant therapy and for 72 hours following the discontinuation of aprepitant. (See Table). The number of rescue antiemetics required did not differ with the addition of aprepitant. There were no adverse events attributed to aprepitant usage.
**Conclusion:** In a single center experience, aprepitant therapy is effective at decreasing episodes of emesis during therapy and the time period up to 72 hours after aprepitant discontinuation, in pediatric stem cell transplant patients. Use of aprepitant therapy for greater than three days is not associated with any significant adverse events. Variations in patient age and standardized dosing based on body surface area need to be further investigated and developed. Additional larger studies are warranted to determine the most appropriate dosing scheme based on pediatric developmental pharmacokinetic principles.

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### DOSING OF BUSULFAN IN OVERWEIGHT AND OBESE PATIENTS COMPARED TO NORMAL WEIGHT PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (alloHSCT)

*Tkacz Brown, V.[1], Zahurak, M.[2], Hatfield Seung, A.[1], Rosner, G.[2], Jones, R.J.[2], Luznik, L.[2], Lombardi Thomas, L.[1] [1]The Johns Hopkins Hospital, Baltimore, MD; [2]The Sidney Kimmel Comprehensive Cancer Center at The Johns Hopkins Hospital and University, Baltimore, MD*

Busulfan has a narrow therapeutic index, making dosing in obesity a therapeutic dilemma. The busulfan pharmacokinetic (PK) profile is related to many variables including body size. By normalizing dosing to body size, variability in clearance is reduced. The difficulty is the selection of an appropriate measure of body size for normalization. The objectives of this study were to determine if busulfan dosed on ideal body weight (IBW) in overweight patients (BMI $\geq$ 25 kg/m$^2$) leads to differences in the PK parameter area under concentration-versus-time curve (AUC) for the first dose and dosing adjustments compared to normal weight patients (BMI < 25 kg/m$^2$). Secondary objectives include comparison of transplant outcomes including sinusoidal obstruction syndrome (SOS), non-relapse mortality (NRM), event-free survival (EFS), and overall survival (OS). A retrospective chart review included 131 patients with hematologic malignancies, 69 of whom were not in remission, who received an alloHSCT with our busulfan/cyclophosphamide preparative regimen and post-transplant cyclophosphamide alone as GVHD prophylaxis. Oral or intravenous busulfan was administered to 72 and 59 patients, respectively, with routine first dose PK assessment performed with a goal AUC/dose of 800 – 1400 μMol-min/L. The majority of the population was overweight (67%) and had similar characteristics, with the exception of a higher portion of males in the overweight group (37% vs. 58%; p = 0.026). The median first dose busulfan AUC was 1153 μMol-min/L (range: 659-1805 μMol-min/L) in the normal weight patients and 915 μMol-min/L (range: 482-1875 μMol-min/L) in the overweight patients (p = 0.0001); this did not translate into a difference in dose adjustments at first assessment (p = 0.522). Ten cases of SOS were observed with a trend to higher incidence in the normal weight patients (12% vs. 6%; p = 0.30). The two year EFS and OS were improved in overweight patients EFS: 35% (95% CI: 21, 49%) vs 40% (95% CI: 30, 51%) and OS: 42% (95% CI: 27, 57%) vs 56% (95% CI: 44, 66%), but these differences were not significant (EFS p = 0.37 and OS p = 0.26). Two year NRM was lower in overweight patients NRM: 23% (95% CI: 12, 37%) vs 12% (95% CI: 6, 19%) p = 0.18. These results demonstrate that when busulfan is dosed on IBW, overweight patients may have a lower initial busulfan AUC than normal weight patients, but these pharmacokinetic differences may not translate into differences in clinical outcomes.

**Table. Efficacy Results**

| Patient Encounter | Duration of Aprepitant Therapy | Average Number of Emesis Prior to Aprepitant Therapy* | Average Number of Emesis During Aprepitant Therapy | Average Number of Emesis after Aprepitant Therapy* | Aprepitant Daily Dosage (mg/BSA) | Patient Age (Years) |
|---|---|---|---|---|---|---|
| 1 | 5 | 1.67 | 0 | 1 | 70 | 13 |
| 2 | 6 | 2 | 0.16 | 0.66 | 45 | 16 |
| 3 | 6 | 2 | 1.6 | 0 | 50 | 3 |
| 4 | 6 | 0 | 0.16 | 2 | 63 | 3 |
| 5 | 9 | 5.33 | 0.22 | 0 | 63 | 3 |
| 6 | 12 | 0.66 | 0.25 | 0 | 63 | 4 |

*72 hour observation period before and after therapy.