patients dosed by adjusted body weight were more likely to under-shoot the goal AUC (-12.8 % vs. +19.5 %, $P = .018$), and require busulfan dose increases (+20% vs. -19.9%, $P = .012$) compared to those dosed on actual body weight. A subgroup analysis confirmed this result for patients receiving Bu/Cy (-23.6 % vs. +2.2%, $P =<.001$ for goal AUC and +36.2% vs. -4.5 %, $P = .008$ for busulfan dose changes in adjusted vs. actual body weight groups, respectively), but not Flu/Bu conditioning regimens (-0.8 % vs. +25.3%, $P = .123$ for goal AUC and +3.4% vs. -25.1 %, $P = .174$ for busulfan dose changes in adjusted vs. actual body weight groups, respectively). Notably, two patients dosed by actual body weight in the Flu/Bu group experienced an AUC of > 9000 μmol*min. Time to neutrophil or platelet engraftment, progression-free survival and overall survival were not significantly different between those dosed on actual versus adjusted body weight ($P > .05$). No neurologic adverse events or VOD incidents were observed in any group.

Conclusions: Our prospective analysis of IV busulfan PK data in various myeloablative and non-myeloablative busulfan based conditioning regimens for HSCT provides important insight into the choice of appropriate busulfan dosing weight. Further studies are warranted to elucidate which weight is most likely to achieve goal area-under-the curve and subsequent optimal patient outcomes.

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Description of Adverse Drug Events Associated with High-Dose Undiluted Etoposide (VP-16) Among Hematopoietic Stem Cell Transplant Recipients

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Background: Etoposide is an important drug in the conditioning regimen for hematopoietic stem cell transplant (HSCT). The administration of etoposide in this patient care setting presents a challenge due to limited aqueous solubility. As a result of the high doses utilized in myeloablative regimens, administration is accompanied by large volumes of intravenous fluids which increase the risk for volume overload, cardiac dysfunction, and electrolyte abnormalities. There are published reports that describe unchanged pharmacokinetic parameters between diluted and undiluted drug, as well as data describing the safe use of undiluted drug in the transplant population.

Methods: We report our experience with eleven patients who received undiluted etoposide (20 mg/mL) over 4 hours through a central line in preparation for HSCT. All patients received an antihistamine and corticosteroid as premedication, as well as another dose of each and acetaminophen when half of the volume had infused. The etoposide was infused through DEHP-free tubing into a dedicated lumen. Vital signs were monitored at baseline, regularly throughout the infusion, and after the infusion was complete.

Results: Between April 2 and June 15, 2012, eleven patients received undiluted etoposide at a dose of 60 mg/kg. The most common adverse events documented were gastrointestinal toxicities. All patients reported nausea and most cases were accompanied by emesis, requiring an average of 4.4 antiemetic doses for treatment of breakthrough nausea/vomiting. Hypotension was documented in nine patients, with an average drop in systolic blood pressure of 35 mm Hg (range: 15-46 mm Hg) occurring 6.6 hours (range: 1.7-18.8 hours) after the start of etoposide infusion. Nine patients required fluid resuscitation with an average of 1400 mL (range: 500 mL-3500 mL) of normal saline.

Conclusion: Despite published reports of successful administration of undiluted etoposide in myeloablative conditioning regimens, we report numerous adverse events in our patient population. All patients treated at our institution with undiluted etoposide as part of the conditioning regimen experienced side effects related to the drug. The benefits of administering undiluted etoposide should be carefully weighed against the possibility of related toxicities.

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Delaying the Start of Triazole Prophylaxis 7 Days After Allogeneic HCT Does Not Affect Outcomes, Including Risk of Invasive Fungal Infection

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Introduction: Antifungal prophylaxis with azoles is considered standard in patients undergoing allo-HCT. However, azoles have significant interactions with immunosuppressive drugs used for graft-versus-host disease (GVHD) prophylaxis. Since the risk of GVHD is increased in the setting of sub-therapeutic immunosuppressant levels, we changed our standard practice from initiating the triazole on day +3 to day +7 after allo-HCT in order to make the change at steady state and limit the occurrence of non-therapeutic levels.

Methods: We retrospectively evaluated 196 patients treated from Jan 2009 to Nov 2011 to assess the impact of delaying the start of azole antifungals on immunosuppressive levels, acute GVHD, and rate of invasive fungal infections (IFI). Micafungin was given from admission until azole initiation. Patients received voriconazole (n=162), posaconazole (n=17), fluconazole (n=9) or were maintained on micafungin (n=8). Stem cell sources included PBSCT from related/unrelated donors (n=139) and cord blood grafts (n=57). GVHD prophylaxis was with tacrolimus (tacro) + sirolimus (siro) + methotrexate (MTX) (n=76), tacro + MTX (n=42), cyclosporine (CSA) + mycophenolate mofetil (MMF) (n=57), tacro + MMF (n=9), tacro + siro (n=7), CSA + MTX (n=3), CSA (n=1), siro + MMF (n=1). Results were analyzed by intent-to-treat (ITT) for patients treated before (day+3 switch, n=69) or after February 2010 (day+7 switch, n=127) as well as by actual day of switch + 1 (day+2,3,4: n=49 vs. day+6,7,8: n=70). Cumulative incidence (CI) functions estimated day 200 grade II-IV aGVHD. Gray's test was used to compare aGVHD incidence for individuals in the day +3 and day+7 treatment categories for both the ITT and as-treated analyses.

Results: Median levels two weeks after HCT were therapeutic in 19/19 (100%), 50/52 (96%), 31/32 (97%) patients on CSA, Tacro, and Siro, respectively, prior to Feb 2010 and in 43/44 (98%), 82/83 (99%), 47/52 (90%), for CSA, Tacro, and