Fisher's exact test. Disease free (DFS) and overall survival (OS) were estimated using Kaplan-Meier methods, and time-to-relapse and non-relapse mortality (NRM) were estimated using cumulative incidence functions. Cox regression was used to further investigate the association between chimerism and the risk of NRM adjusted for key covariates.

Results: Of 161 patients identified, 96 were disease free and had PB TC chimerism at 3 month Table 1 lists transplant characteristics and outcomes. PB TC MC was observed in 64 (66%) at 3 month There was no difference in chimerism based on disease, stem cell source, HLA-match, donor-recipient gender pairing, or conditioning regimen. Relapse and DFS were not different between the MC and full donor chimerism groups. However, NRM was significantly higher (*P*-value 0.001) and OS was significantly lower (*P*-value 0.01) in the full donor chimerism group at 2 years. Using Cox regression, the association between chimerism and NRM remained after adjusting for DLI, disease, conditioning regimen and donor-recipient sex (*P* value 0.03). Analysis of 6 month PB TC chimerism also showed patients with MC in the PB at 6 months had less NRM and improved OS than patients with full donor chimerism.

Conclusions: In this analysis of PB TC chimerism following TCD transplant, both NRM and OS were significantly better in patients with MC. These data suggest that DLI for the conversion of MC to full chimerism may be unnecessary.

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Intramural Duodenal Haematoma After Upper Gastrointestinal Endoscopic Biopsy in a Bone Marrow Transplant Recipient

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Intraduodenal haematoma (IDH) has been noted usually after blunt abdominal trauma. It has been recognized as a complication of endoscopic biopsy and the risk is high in patients with bleeding disorders. History of bone marrow transplantation seems to be relevant risk factor. The incidence is estimated to be 1/1250 upper gastrointestinal endoscopies. The diagnosis is likely if symptoms of acute abdominal pain and vomiting occur within 48 hours after duodenal biopsy. The symptoms are usually caused by duodenal obstruction. Pancreatitis may develop. Conservative management is the preferred approach if perforation is excluded. Complete resolution generally occurs within 2-3 weeks.

A-18-year old girl with acute lymphoblastic leukemia underwent allogeneic peripheral blood stem cell transplantation. Diarrhea developed on the third month and gastrointestinal endoscopic biopsies were performed for GVHD evaluation. The mucosa of stomach was reddish and edematous but other parts looked normal. Three hours later the patient had severe vomiting, intense abdominal tenderness and massive haematemesis which required red cell transfusions. A second look revealed active hemorrhage from biopsy side at the cardioesophageal junction. Epinephrine injection was performed and the clinical status was related to Mallory-Weiss tear due to severe vomiting. However her complaints persisted despite full supportive treatment. Abdominal CT scan revealed a 9 cm mass with diameter of 5 cm within the second and third duodenal portions consistent with an intramural haematoma. There was also hemoperitoneum. Since perforation was excluded conservative management was initiated including bowel rest, parenteral nutrition and nasogastric decompression. On day 14 serum bilirubin levels reached 7.5 mg/dl with GGT:393 U/L, ALP:329 U/L values. MRI revealed 8x4 cm haematoma compressing the ampulla of Vater. She improved in the following days. Haematoma regressed to 3 cm on the 4th week and the patient was discharged.

In our patient blood counts and coagulation tests were within normal limits at the time of endoscopic intervention. Biopsies were consistent with GVHD and the mucosal damage caused by this condition may have been contributed to duodenal vulnerability. Depending on other reported cases with bone marrow transplantation we can conclude that endoscopic interventions should be carefully employed in this subgroup of patients.

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BK Virus-Associated Nephropathy (BKVN), an Under-Recognized Cause of Renal Dysfunction in Severely Immunosuppressed Hematopoietic Stem Cell Transplant (HSCT) Patients: Report of 5 Cases of Bkvn and the Potential Role of CMX001 for Treatment

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BKVN is reported in 8% of renal transplant (RT) patients (pts) and leads to renal failure/graft loss if untreated. In HSCT BKV is mainly associated with hemorrhagic cystitis (HC), with few BKVN cases reported to-date. In RT, treatment (tx) is primarily immunosuppression reduction, not feasible in HSCT due to the risk of graft versus host disease (GvHD). IV cidofovir (CDV) is used as adjunctive tx, but is associated with significant nephrotoxicity. At MSKCC, we have had 5 HSCT pts with tissue-proven BKVN in past 6 yrs. Diagnosis (dx) was by biopsy in 2, autopsy in 2 and nephrectomy in 1. Three pts received T-cell depleted (TCD) grafts, 3 had GvHD and 3 CMV disease. Three had severe HC with clot obstruction. Two pts developed end-stage renal disease (ESRD) requiring hemodialysis (HD) despite tx with CDV. ESRD preceded the BKVN dx. We present 1 HSCT pt treated for BKVN with CMX001 in an open-label, expanded access study (CMX001-350; ClinicalTrials.gov ID: NCT01143181). CMX001 is an orally bioavailable, broad spectrum, lipid acyclic nucleoside phosphonate converted intracellularly into the active antiviral CDV. The pt (58 YO white male) with history of chronic lymphocytic leukemia/small lymphocytic lymphoma (SLL) transformed to a diffuse, large B-cell lymphoma received a TCD graft from a matched, unrelated donor. He had SLL relapse +6 mos post-HSCT (tx with chemotherapy, donor lymphocyte infusion and lenalidomide), complicated by grade IV steroid-refractory acute

Table

Parameter	BL	Change from BL at:										
		Wk2	Wk3	Wk4	Wk5	Wk7	Wk9	Wk11	Wk13	Mo4	Mo5	Mo6
BK viremia* (log_{10} c/mL)	6.2	-0.6	-1.4	-1.8	-2.1	-2.4	-2.7	-3.0	-3.0	-3.9	-3.9	-3.3
BK viruria* (log_{10} c/mL)	8.7	ND	ND	-0.7	-1.0	-1.1	-1.5	ND	-1.9	-2.1	ND	ND
Cr (mg/dL)	2.6	+0.5	+0.3	+0.6	+0.5	+1.0	+0.8	+1.1	+1.2	+0.9	+1.0	+1.3
BUN (mg/dL)	39	-2	-3	0	-2	0	-4	-4	-2	+2	-7	-9
GFR (mL/min/1.73m^2)	27.1	-5.0	-3.2	-5.8	-5.0	-8.5	-7.2	-9.1	-9.6	-7.9	-8.5	-10.2

ND indicates not determined

* Viracor BKV qPCR assays in plasma (LLOD, 2 log_{10} c/mL) or urine (LLOD = 2.7 log_{10} c/mL)

GvHD (treated with alemtuzumab/mycophenolate mofetil [MMF]). He has remained on sirolimus and MMF. At +16 mos serum creatinine (Cr) was increasing, BKVN was diagnosed by biopsy and he was enrolled in CMX001-350.

Methods: CMX001 was given orally at 100 mg twice-weekly for 6 mos (max tx duration under CMX001-350). Pt was assessed weekly (Wks 2-5), biweekly (Wks 7-13), and monthly (Mos 4-6).

Results: Baseline (BL) and changes from BL in BK viremia/viruria, Cr, BUN and estimated glomerular filtration rate (GFR, MDRD4) are shown below. No drug-related adverse events (AEs) or serious AEs were reported. The pt continues on CMX001 under separate EIND provisions and has stable renal function and no HD.

Conclusions: BKVN may be underdiagnosed in HSCT. In 1 pt treated with CMX001, the drug was well tolerated and controlled the BK viremia. After 6 mos therapy, he has stable renal function without HD. Our data supports a potential role for CMX001 in the tx of BKVN.

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Dose Intensification of Busulfan in the Preparative Regimen Is Associated with Improved Outcomes: A Phase I/II Controlled, Randomized Study

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Dose intensity is important for disease control in allogeneic stem cell transplant (AlloSCT). There is no prospective data to determine the ideal dose for intravenous busulfan to be used in reduced intensity AlloSCT. We conducted a phase I/II controlled randomized study to determine the optimal dosing schedule of intravenous busulfan. Patients with advanced hematologic malignancies, ≤75 years with HLA-compatible donor were eligible. In the phase 1 portion, seven dose levels were explored. All patients received fludarabine at 30mg/m^2/d for 4 days. Dose level 5 (11.2mg/kg) was chosen to be tested for phase II cohort. Eighty patients with a median age of 56 years were enrolled with 40% having relapsed/refractory disease. Engraftment occurred in 91% and complete response was documented in 79% patients after undergoing transplant. At a median follow up of 91 months, no significant difference was seen in terms of non-relapse mortality of 34% for dose level 5 (11.2mg/kg) vs. 23% for all other dose levels ($P = .4$). Significant improvement in cumulative incidence of relapse of 43% vs. 68% ($P = .02$); relapse-free-survival of 25% vs. 9% ($P = .017$) and overall-survival of 27% vs. 9% ($P = .037$) (Figure 1) was demonstrated with the dose intensification of busulfan. We conclude that optimizing intravenous busulfan dose intensity in the preparative regimen leads to improvement in PFS and OS of patients with advanced hematologic malignancies and may overcome disease associated poor prognostic factors.

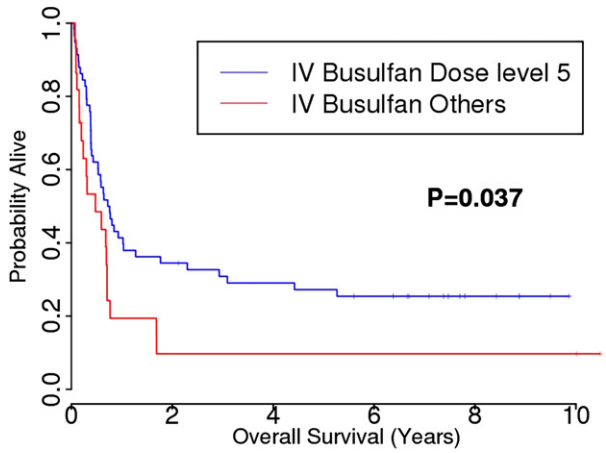

Figure 1.

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Assessment of a Disease Risk Index in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation After Fludarabine and Pharmacokinetically Dose-Targeted Intravenous Busulfan: Effect On Overall and Progression-Free Survival

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Background: Several methods are employed to predict the outcome of patients undergoing allogeneic hematopoietic cell transplantation (HCT), including patient characteristics (e.g., age, performance status, concurrent comorbidities), diagnosis, and disease status. Armand, et al. (Blood 2012;120:905-913) validated a disease risk index using diagnosis, cytogenetics, and disease status, which predicted for overall and progression-free survival. To test this disease risk index in our patient population, we applied it to patients receiving fludarabine and pharmacokinetically dose-targeted intravenous busulfan myeloablative conditioning followed by allogeneic peripheral blood HCT.

Methods: We analyzed a cohort of 322 patients transplanted between 2004 and 2009 and assigned them to disease (low, intermediate, and high) and stage (low and high) risk groups