mcg/L (range: 32-263) 20 minutes post-CIS inhalation. Lung deposition studies showed the total deposited dose averaged 13% (range: 4-20%) of the inhaled dose. Of note, 5 subjects who showed a clinical benefit on study were subsequently enrolled onto a CIS extension protocol.

Conclusion: These data are the first to establish that CIS is safe and can stabilize or improve lung function in HSCT recipients with severe BOS, allowing systemic immunosuppression to be reduced. Importantly, lung deposition studies revealed substantial delivery of CIS could be achieved in the airways with only minimal systemic absorption.

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Early Post-Transplant Notch Signaling Activity Is Critical for the Differentiation of Pathogenic Alloantigen-Specific T Cells Mediating Acute Graft-Versus-Host Disease

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Blocking Notch signaling after allogeneic bone marrow transplantation prevents acute graft-versus-host disease (GVHD) in mice, with key roles for Notch1/2 receptors and Delta-like-1/4 ligands (DII1/4) (Zhang, Blood 2011; Tran, JCI 2013). To investigate the consequences of Notch inhibition in alloantigen-specific T cells, we identified a short 2-day window of Notch activity early after transplantation during which Notch blockade is critical for maximal prevention of acute GVHD. We describe new mechanistic models to study alloantigen-specific T-cells within this window, and provide insights into early events associated with Notch blockade. In a MHC-mismatched model, transgenic C57Bl/6 CD4+ 4C T-cells directly recognizing host I-Aa alloantigens induced lethal GVHD in BALB/c recipients. 4C CD4+ T-cells were sensitive to Notch blockade, which resulted in the downregulation of Notch target genes in and impaired production of inflammatory cytokines, concordant with findings in polyclonal responses (Zhang, Blood 2011; Tran, JCI 2013). Nonetheless, serial analysis revealed preserved 4C CD4+ T-cell activation, proliferation and expansion upon DII1/4 blockade. In the B10.D2->BALB/c MHC-matched model of sclerodermatous GVHD, donor-derived CD4+Vb3+ T-cells, responding to a Mtv6-encoded BALB/c superantigen, demonstrated massive expansion and dominant Th1 polarization of Vb3+ T-cells in lymphoid tissues and the liver. Despite this, Notch blockade in Vb3+ T-cells inhibited cytokine production, but preserved activation and proliferation. These findings document dissociated effects of Notch inhibition on proliferation and cytokine production in alloantigen-specific T-cells, allowing further focused evaluation of Notch signaling functions in alloimmunity.

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Is There a Stronger Graft-Versus-Leukemia Effect Using HLA-Haplo-Identical Donors Compared to HLA-Identical Sibling Donors?

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Purpose: Haplo-identical transplants are increasingly used in hematopoietic stem cell transplantation (HSCT). Do haplo-identical transplants have a stronger graft-versus-leukemia (GVL) effect?

Patients and Methods: We analyzed 10,679 patients with acute leukemia undergoing HSCT from an HLA-matched sibling donor (MSD, n=9,815), or a haplo-identical donor (≥2 HLA-antigen disparity, n=864) between 2007–2012, reported to the European Group for Blood and Marrow Transplantation. In a Cox regression model, acute and chronic GVHD were added as time-dependent variables.

Results: In the multivariate analysis, there was no difference in relapse probability between recipients of haplo-identical or MSD grafts. This was seen in T-cell replete and T-cell depleted grafts analyzed separately. Factors of importance for relapse among T-cell replete grafts included remission status at HSCT, Karnofsky score ≤80, acute GVHD >grade II, and chronic GVHD (p<10^-5). Among patients receiving T-cell depleted grafts, advanced disease (p<10^-5) and second remission (p=0.01) compared to first remission were the strongest factors for leukemic relapse. Non-relapse mortality was significantly higher in the haplo group versus MSD transplants among patients receiving T-cell replete or T-cell depleted grafts (p<10^-5). Subsequently, leukemia-free survival was superior in the MSD group of T-cell replete grafts (p<10^-5) and T-cell depleted grafts (p=0.0006).

Conclusion: Risk of relapse was the same in patients with acute leukemia in haplo-identical transplant recipients compared with MSD transplants, suggesting a similar GVL effect.

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Case Report: 52-Year-Old Male 11 Months after MUD for Angioimmunoblastic T Cell Lymphoma Developed Acute Fibrinous Organizing Pneumonitis Successfully Treated with Etanercept Suggesting TNF Alpha in the Pathogenesis in This Sub-Type of Pulmonary GVHD

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Introduction: We describe a case of a 52-year-old man with history of refractory angioimmunoblastic T-cell lymphoma 11 months after matched unrelated allogeneic hematopoietic cell transplant with acute fibrinous organizing pneumonitis successfully treated with high dose steroids, tacrolimus, and 8 doses of etanercept.

Case presentation: A 52-year-old Caucasian male with a history of refractory stage IV angioimmunoblastic T-cell lymphoma treated with CHOP, ICE and Romidepsin followed by ATG/TBI matched unrelated allogeneic hematopoietic cell transplant (HCT) in March 2013. He had an uncomplicated course with the exception of mild classic chronic GVHD of skin treated with topical steroids. Eleven months after HCT, he was off