served as controls. Using samples from over 20 patients in four groups, we first conducted a discovery study to identify peptide variables that were significant across disease development (control vs. IPS) and time (day 0 vs. day of Dx or day 14 for controls). This revealed a set of 81 IPS-associated proteins that were verified by a number of methods, analyzed by ingenuity pathway analysis (IPA) and mapped to relevant immune pathways. IPA underscored a significant contribution of the acute phase response (TNFα / IL-6) signaling pathway during disease progression and revealed striking similarities between inflammation engendered during IPS in humans and mice. In the second verification analysis, we used only samples collected on day 0 from a larger cohort of patients to identify proteins that were effective variables for patient stratification. Identified peptides were subjected to predictive model building using the Ishwaran & Rao approach, which identified a set of robust plasma proteomic markers that could 1) predict the development of IPS, and 2) identify individuals who would ultimately respond to etanercept therapy. Analysis also revealed a number of novel proteins including attractin, lumican and LBP (the expression of which was verified by ELISA) that were significant in the discovery analysis and classifiers for disease development and or response to therapy. In sum, data generated in this translational research endeavor confirm previous clinical and experimental observations, provide new insights into the pathophysiology of IPS and identify a set of robust markers predictive for disease progression and response to therapy. As anti-TNF therapies are being developed as treatment for GVHD and other immune-mediated disorders, these results uncover a set of robust markers for patient stratification as a basis for individualized therapy that is ripe for further development.

296

CMX001 AS THERAPY FOR SEVERE ADENOVIRUS INFECTIONS IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS: SINGLE EXPERIENCE IN 5 PATIENTS

Grimley, M.S.[1], Marsh, R.A.[1], Bleesing, J.J.[1], Mehta, P.A.[1], Jodele, S.A.[1], Myers, K.M.[1], Kumar, A.[1], Jordan, M.B.[1], Edwards, S.L.[1], Kennedy, R.[1], Wilhelm, J.[1], Painter, W.[2], Anderson, M.[2], Filipovich, A.H.[1], Davies, S.M.[1] [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH; [2]Chimerix, Inc., Durham, NC

Background: Adenovirus infection is a serious and often fatal complication in immunocompromised patients. There are currently no FDA-approved therapies for adenovirus infection. Cidofovir has been reported to have variable efficacy in treating Adenovirus but is associated with significant toxicity, especially renal and possible marrow toxicity. CMX001 is an oral Lipid -Antiviral-Conjugate that generates high intracellular levels of the active cidofovir-diphosphate without evidence of cidofovir-like nephrotoxicity. CMX001 is under investigation for the prevention of adenovirus disease.
Methods: We report on 5 patients with adenovirus disease treated with CMX001. Data were available for > 4 weeks of treatment. The median age was 1.9 years (Range 1.5 -11.8). The preparative regimen for the transplant patients consisted of Alemtuzumab, Fludarabine and Melaphalan. The graft source was bone marrow. GVHD prophylaxis was cyclosporine and methylprednisolone. Virologic response (VR) was defined as 99% drop from baseline or undetectable adenovirus DNA by PCR in plasma. Patient characteristics are shown in Table 1.
Results: Adenovirus disease was diagnosed at a median of 38 days (range -7 to 300) after transplantation. All patients received intravenous cidofovir for a median of 27 days (range 22-47) prior to starting CMX001. Four of five patients (80%) had a > 1 log drop in viral load at the end of 1 week of therapy. VR was seen in all patients with a median time to achieve VR was 2 weeks (range 1-3). Four patients received doses exceeding those currently being studied. No adverse events felt to secondary to CMX001 were seen with the 4 mg/kg/ doses. Two patients developed diarrhea that was likely related to CMX001 therapy while receiving the 2 mg/kg/dose twice weekly. Both patients had resolution of the symptoms when CMX001 was stopped and were able to resume therapy without recurrence of symptoms. No other significant side effects were observed.
Discussion: Our data demonstrates that CMX001 has efficacy against adenoviral infections with a favorable safety profile. In this critically ill group of patients, morbidity was high which may reflect that CMX001 is an investigational medicine and was not used as first line therapy for adenoviral infections in our institution for these patients. Clinicians caring for immunocompromised individuals with adenovirus infections should consider early use of CMX001 for severe adenovirus infections.

297

PREVALENCE OF VIRAL INFECTIONS IN CHILDREN UNDERGOING FIRST ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: TWO YEAR SINGLE CENTER EXPERIENCE

Ozdemir, N., Jodele, S., Myers, K.C., Mehta, P.A., Bleesing, J.J., Jordan, M.B., Marsch, R.A., Kumar, A.R., Bellman, D., Filipovich, A.H., Davies, S.M., Grimley, M.S. Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Viral infections are a major cause of morbidity and mortality in patients receiving allogenic hematopoietic stem cell transplantation (HSCT). With the introduction of newer conditioning regimens, increasing use of reduced intensity protocols and T cell depletion, the risk of post-transplant viral infections may be increasing and specific high risk groups may need to be identified as candidates for intensive viral monitoring and pre-emptive strategies. Here we report our experience of viral infections in children undergoing their first allogenic HSCT from January 2009-December 2010.
Methods: One hundred twenty four patients, median age 4.9 years (range: 0.2-25.4) were identified and charts retrospectively reviewed. Ninety-five patients underwent HSCT for non-malignant disease, 29 for malignant disease. Graft source was unrelated donor in 102 (82%) and matched related in 22 (18%). Stem cell source was bone marrow in 94 (76%), peripheral blood stem cells in 16 (13%) and cord blood in 14 (11%). Sixty-four patients (35 with non-malignant disease, 29 with malignant disease) received myeloablative conditioning regimens. Forty-six patients (all with non-malignant disease)

Table 1. Patient Characteristics

Patient	Diagnosis	Days post HSCT of ADV detection	Sites of ADV infection	Viral Load (copies/ml)	Dose of CMX001	Adverse Events	Current Status/Followup (months)
1	SCID	N/A	Blood and Stool	770 million	4 mg/kg/dose BIW	None	Died of Disseminated Aspergillosis infection
2	SCID due to RAG2 mutation	-7	Blood and Stool	1.2 million	4 mg/kg/dose BIW	None	Alive and Well/ 8 months
3	FHL	300	Blood, Stool and Nasal Secretions	32,000	1 dose of 4 mg/kg/dose BIW then 11 doses of 2 mg/kg/dose BIW	Diarrhea	Died of Progressive Bronchiolitis Obliterans
4	XLP/MDS	70	Blood and Stool	89,000	5 doses of 4 mg/kg/dose BIW then 32 doses of 2 mg/kg/dose BIW	Diarrhea	Alive and Well/7 months
5	XLP	5	Blood and Stool	102,000	2 mg/kg/dose BIW	None	Died of Pulmonary TMA

SCID: Severe Combined Immunodeficiency; FHL: Familial Hemophagocytic Lymphohistiocytosis; MDS: Myelodysplastic Syndrome; XLP: X-Linked Lymphoproliferative Disorder; BIW: twice a week; QW: weekly; TMA: Thrombotic Microangiopathy.