characterizing the effector (cytolytic capacity) profile of the expanded cells, and plan to map immunodominant T cell epitopes. Finally, to verify the importance of T cell immunity in providing in vivo protection against PIV-3 we isolated blood from 2 post-HSCT recipients who naturally controlled their infections and in both cases, detected an amplification of endogenous T cells directed to M, HN, N, F and PC coincident with viral clearance. Thus, we have demonstrated the feasibility of generating PIV-3-directed VSTs in vitro and have preliminary evidence demonstrating the protective capacity of reactive cells in vivo. Our ultimate goal is to develop an immune-based therapy for allogeneic HSCT recipients with active infections whose endogenous immunity is lacking.

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Clinical Outcome and Immune Recovery after Adoptive Infusion of BPX-501 Cells (donor iC9-transduced T cells) in Children with Wiskott-Aldrich Syndrome (WAS) Given Alfa/Beta T-Cell Depleted HLA-Haploidentical Hematopoietic Stem Cell Transplantation (HSCT)

Alice Bertaina [1], *Barbarella Lucarelli* [1], *Pietro Merli* [1], *Valentina Trevisan* [1], *Carmelo Gurnari* [1], *Valentina Bertaina* [2], *Matilde Sinibaldi* [2], *Giuseppina Li Pira* [3], *Concetta Quintarelli* [4], *Mauro Montanari* [5], *Letizia Pomponia Brescia* [1], *Annemarie Moseley* [6], *Franco Locatelli* [7]. [1] *Stem Cell Transplant Unit, Ospedale Bambino Gesu', Rome, Italy;* [2] *Laboratory of Immunology, Ospedale Bambino Gesu', Rome, Italy;* [3] *Stem Cell and graft manipulation Laboratory, Ospedale Bambino Gesu', Rome, Italy;* [4] *Laboratory of Immunotherapy, Ospedale Bambino Gesu', Rome, Italy;* [5] *Hematology and Oncology, Ospedale Bambino Gesu', Rome, Italy;* [6] *Bellicum Pharmaceuticals, Houston, TX;* [7] *Ospedale Pediatrico Bambino Gesu, University of Pavia, Rome, Italy*

Background: Both gene therapy and allogeneic HSCT are suitable options to treat children with WAS. We recently developed a novel method of selective T-cell depletion of the graft based on physical elimination of α/β T cells (Clinical Trial.gov identifier: NCT01810120), which was shown to be safe and effective for preventing life-threatening infections in children given an-HLA haploidentical HSCT. To further optimize the approach, we are exploring innovative approaches able to accelerate recovery of adaptive immunity. We designed an ongoing phase I/II trial aimed at testing the safety and efficacy of post-transplant infusion of BPX-501 cells in children with malignant or non-malignant disorders (ClinicalTrials.gov identifier: NCT02065869). BPX-501 cells can easily track in patient peripheral blood since they are CD3/CD19 positive. We report on 3 WAS children who were enrolled in the phase I of the study.

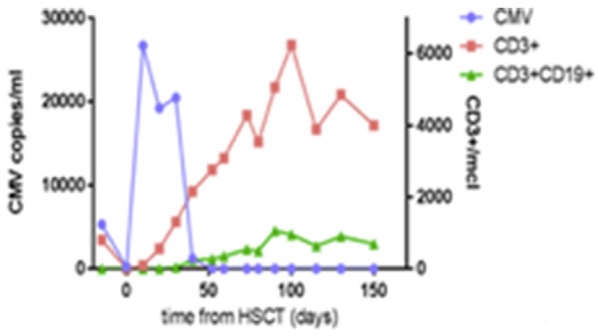

Figure 1.

Table 1

	PLT 10^{-9}/L	CD3+/ µL	CD4+/ µL	CD8+/ µL	CD3+ CD19+/ µL	IgA mg/ dL	IgA mg/ dL	IgM mg/dL
Patient #1	557	8791	3430	2316	1339	53	906	45
Patient #2	213	1488	380	424	14	21	627	49
Patient #3	346	1522	579	420	5	49	606	28

Patients and Methods: Patient #1, before HSCT, developed CMV retinitis and hepatitis with high levels of CMV-DNAemia. Patient #2 experienced intestinal vasculitis, which led to surgery due to ileo-ileal invagination and developed also CMV infection. Patient #3 had experienced recurrent infectious episodes before the allograft. In all patients, the conditioning regimen consisted of a combination of busulfan (16 mg/Kg), thiotepa (10 mg/Kg) and fludarabine (160 mg/sqm). No post-transplantation graft-versus-host disease (GvHD) prophylaxis was administered. All patients were transplanted from the father and received 1 x 10^6/kg BPX-501 cells in the first 3 weeks after HSCT (Pt#1 on day +15, Pt#2 on day +15 and Pt#3 on day +18). Phenotype of circulating lymphocytes was assessed on day +10, 20, 30, 60, 90, 120 150 and 180 post haplo-HSCT. In patient #1, CMV specific reconstitution was monitored through the INFγ ELISPOT assay.

Results: All patients engrafted, reaching full donor chimerism; none experienced acute or chronic GVHD, or organ inflammatory-related toxicity. The pre-existing CMV infection in Pt#1 and 2 was progressively cleared once BPX-501 cells were infused. These cells expanded *in vivo* and are still persisting, contributing to the recovery of adoptive immunity. The increasing number of both CD3+ T lymphocytes and BPX-501 cells over time in Pt #1, together with the modifications of CMV DNAemia, is reported in Figure 1. At day 30 after HSCT, the PLT count was 221, 48 and 127x10^9/L respectively. All children are alive and disease-free, without infections or autoimmune manifestations, at day +210, +200 and +190, respectively. The lymphocyte and PLT counts at last follow-up are shown in Table 1.

Conclusions: In children with WAS given haplo-HSCT after depletion of α/β T cells both PLT and lymphocyte recovery is fast. Infusion of BPX-501 cells contributes to accelerate recovery of adaptive T-cell immunity and clearance of viral infections, thus rendering the procedure safer.

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Preemptive T-Rapa Cell DLI after Low Intensity Allogeneic HCT May Allow for Improved Overall Survival in High Risk Lymphoid Malignancies

David Halverson [1], *Scott Rowley* [2], *Michael R. Bishop* [3], *Brenna Hansen* [4], *Stephanie Cotton* [5], *Bazetta Blacklock Schuver* [1], *Seth M. Steinberg* [6], *Fran T. Hakim* [7], *Juan Gea-Banacloche* [4], *Nancy Hardy* [8], *Claude Sportes* [9], *Steven Z. Pavletic* [7], *Hanh Khuu* [10], *David F. Stroncek* [10], *Bruce L. Levine* [11], *Carl H. June* [12], *Michele L. Donato* [2], *Andre Goy* [2], *Andrew Pecora* [2], *Ronald Gress* [13], *Daniel Fowler* [1]. [1] *Experimental Transplantation and Immunology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD;* [2] *John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ;* [3] *Section of Hematology/Oncology, University of Chicago, Chicago, IL;* [4] *Experimental Transplantation and Immunology Branch, NCI, Bethesda, MD;* [5] *ETIB, NCI, Bethesda, MD;* [6] *Biostatistics and Data Management Section, Center for Cancer Research, National Cancer Institute, National Institutes of*