The Use of BPX-501 Donor T-Cell Infusion (with Inducible Caspase 9 Suicide Gene) Together with HLA-Haploidentical Stem Cell Transplant to Treat Children with Hemoglobinopathies and Erythroid Disorders

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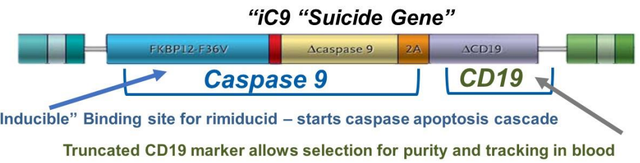
Background

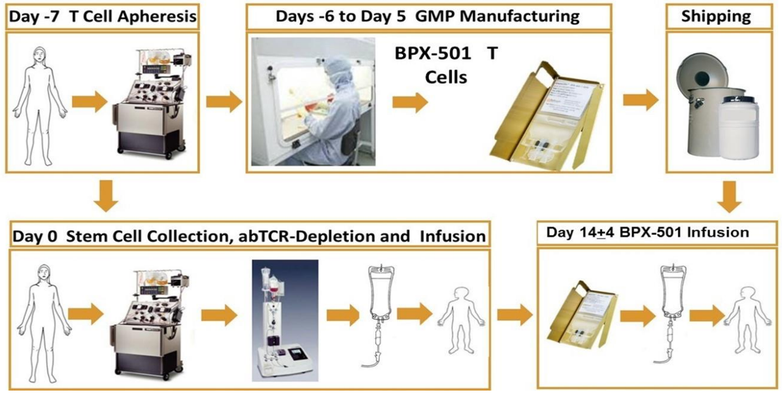
Allogeneic HSCT from either an HLA-identical sibling or an unrelated donor is a potentially curative treatment for patients with hemoglobinopathies and erythroid disorders. An ongoing Phase I/II trial, BP-004, evaluates the safety and efficacy of post-transplant infusion of donor T-cells transduced with the iC9 suicide gene (BPX-501 cells) after αβTCR depleted haplo-HSCT in order to optimize the recovery of adaptive immunity (ClinicalTrials.gov identifier: NCT02065869).

We report, as of April 24, 2017, on 15 patients with hemoglobinopathies, and Diamond Blackfan Anemia and who had received an αβTCR depleted HSCT, did not receive any post-transplantation pharmacological GVHD prophylaxis, received BPX-501 after HSCT and were ≥180 days post-transplant follow-up.

BPX-501 Technology



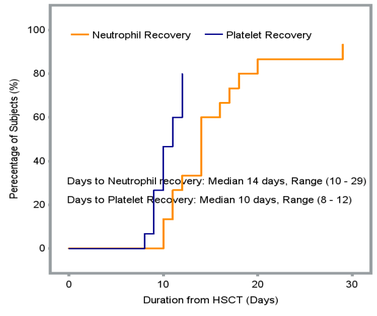
- **From normal donor leukapheresis -- GMP facilities US / Europe**
- **Activated and expanded in culture, transduced with the iC9 suicide gene and selected for CD19+ cells**
- **Cryopreserved and stored in liquid nitrogen**
- **Maintain characteristics of normal T cells**
  - Broad T cell repertoire
  - Antiviral and antigen specific activity



Demographics

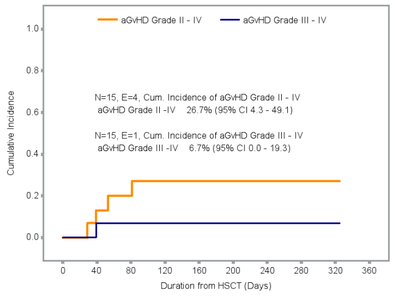
Disease	N= 15
Thalassemia Major	8 (53.3%)
Sickle Cell Disease	5 (33.3%)
Diamond Blackfan Anemia	2 (13.3%)
Male/Female	6/9 (40%/60%)
Median Age at HSCT (yrs)	8.9 (2.5-19)
Conditioning	
Busulfan-based	13 (86.7%)
other	2 (13.3%)
Donor Median Age	36 (18-44)
Donor Relationship	
Parent	13 (86.7%)
Sibling	2 (13.3%)
Median CD34 (X10^6/kg)	21 (4-36)
Median αβTCR (X10^5/kg)	0.3 (0.04 - 0.8)

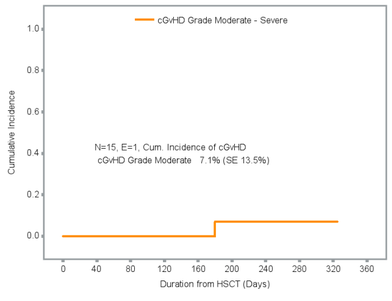
Hematopoietic Recovery



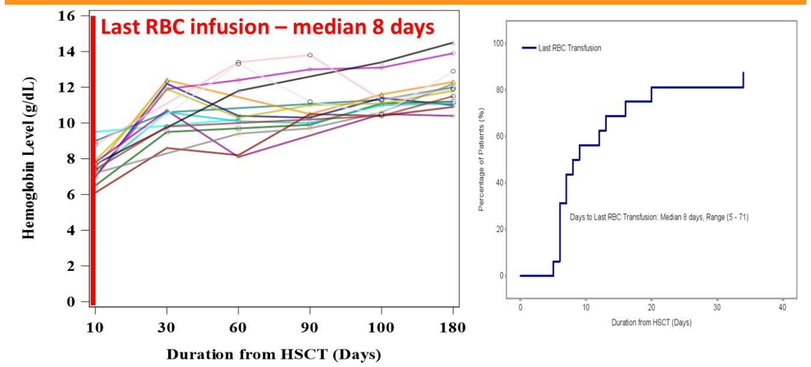
- **Median neutrophil recovery - day 14 (10-29).**
- **Median PLT recovery – day 10 (8-12).**
- **Median day of hospital discharge - 23 days (14-55).**
- **No TRM in this patient group with hemoglobinopathies and erythroid disorders.**

GVHD





Hemoglobin Levels



-Normal hemoglobin in all 15 patients, and transfusion free at 180 days.

-Last red cell transfusion median 8 days (range 5-71).

- 15/15 patients had full donor chimerism at 180 days.

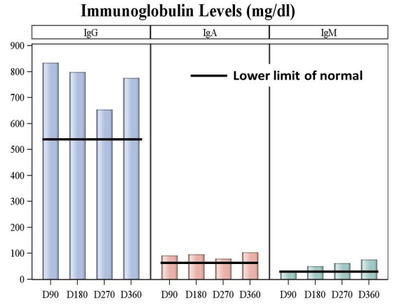
Immune Reconstitution

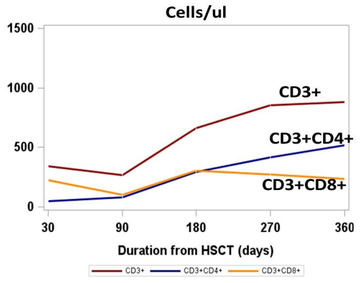
-Normal T cell recovery and normal humoral immunity.

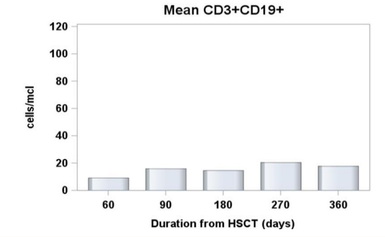
BPX-501 CD3+CD19+ donor T cells expand and persist over time.

-Detectable by flow cytometry.

-Both CD4+CD19+ and CD8+CD19+ populations expand.







Conclusions

Children with hemoglobinopathies, and erythroid disorders can benefit from curative haplo-HSCT after depletion of α/β T-cells followed by infusion of BPX-501 cells, which, expanding and persisting over time, contribute to the overall immune reconstitution and favorable transplantoutcomes.