Stem Cell Gene Therapy for HIV Related Lymphoma

AMC-097: A Phase I Study of Stem Cell Gene Therapy for HIV Mediated by Lentivector Transduced, Pre-Selected CD34+ Cells

ClinicalTrials.gov Identifier: NCT02797470

Key Eligibility Criteria:

- ≥ than 18 years
- HIV-1 related lymphomas refractory/resistant to first line of therapy or relapse after achieving a remission
- Eligible for an autologous HSCT as a part of their routine therapy
- Must be on a multi-drug anti-HIV regimen
- HIV-1 viral load < 50 copies/mL

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Dear Fellow AMC Investigators,

We would like to update you on the progress of AMC-097. This study is enrolling subjects at Memorial Sloan Kettering Cancer Center, University of California San Diego, University of California San Francisco, and University of California Davis. Eleven subjects have been enrolled and dosed on this study with ***one slot remaining in the third cohort*** **and three slots in the upcoming expanded third cohort**. We envision this as a trial to create the underpinnings for future cure intent studies for HIV patients without cancer.

Hypothesis:
Anti-HIV gene expressing stem cells can safely reconstitute the hematopoietic system of the recipient and can produce a pool of mature myeloid and lymphoid cells that harbor anti-HIV genes capable of resisting HIV-1. Transduced HIV-resistant immune cells will have a selective survival advantage as compared to non-transduced cells in the face of a viral load.

Objective
The primary endpoint of the study is safety, defined as timely engraftment of absolute neutrophil count and platelet count.

Study Agent
The anti-HIV study agent combines three anti-HIV genes into a single lentiviral vector that is designed to block HIV-1 infection at different stages of the HIV-1 life cycle (entry, uncoating, and viral transcription).

- CCR5 shRNA
- chimeric TRIM5α
- TAR decoy

This vector also contains a pre-selective molecule, a truncated and mutated form of human CD25, which marks transduced cells so they can be separated from untransduced cells.

The number of cells in the transduced products is based on CD34 counts after transduction of the stem cells and before freezing.

Study Cohorts	Ratio of Transduced vs Un-transduced Stem Cells	Minimum Number of Transduced/Un-transduced cells CD34 cells/kg	Range for Number of Transduced Cells/Unmanipulated. CD34 cells/kg
3	1:0	2 X 10^6: 0	2 to 10 X 10^6: 0
3+	1:0	3.0 X 10^6: 0	3.0 to 10 X 10^6: 0

The initial follow-up period for this clinical trial will be two years; however, all participants will be followed for 15 years for safety, as mandated by FDA for all gene therapy study participants.

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AMC AIDS Malignancy Consortium