Background

- Despite effective antiretroviral therapy, the cellular HIV reservoir persists.
- CD4ζ is a chimeric antigen receptor (CAR) T cell composed of the extracellular and transmembrane domains of CD4 linked to the cytoplasmic zeta signaling domain of the CD3 T cell receptor.

Method

- Randomized controlled trial, laboratory-blinded.
- Conducted at Walter Reed Army Medical Center, Washington D.C.

Results

- I:CD4ζ transgene was detected in PBMCs and RT at LTF in recipients of NA transgene transduction followed using a MMV.
- Previously we have reported:
  - CD4ζ transgene persists in PBMCs for 7 years (Scholler 2012).
  - Synergy of low dose IL-2 with cells caused large but transient increases in CD4ζ T cells (Aronson 2008).
- Other CAR-T cell studies have reported:
  - CD4ζ transgene is present in gut lymphocytes at 1 year (Mitsuyasu 2000).
  - Slight decrease in HIV reservoir (Deeks 2002).

We report on the FDA-mandated 15 year follow up.

Conclusions

- Persistence of the CD4ζ transgene was measured in all 13 subjects’ PBMC and RT at 15 years.
- Low levels of HIV RNA and DNA were detected in PBMC and/or RT at the long term follow up in all arms.
- In recipients of CAR-T cells, there is a trend towards transitional memory cells harboring more integrated HIV DNA compared to the IL-2 arm.
- Findings are limited by the small heterogeneous study population with intra subject variability, low transduction efficiency, low cell dose, methodologic limits of detection of the HIV reservoir, and the absence of a HAART-only comparison arm.

References


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