**BACKGROUND**

Anti-HIV chimeric antigen receptor (CAR) T cell therapies are candidates to functionally cure HIV infection in people with HIV (PWH). Translating such therapeutic candidates successfully into PWH will require anti-HIV CAR-T cells to persist long term and eliminate reactivated HIV-infected cells. Interestingly, recent clinical studies have shown a positive correlation between the early-memory phenotype of cell therapy in humanized mouse models with productive HIV-1 infection. To test this hypothesis, we developed an 8-day CAR-T cell manufacturing process and profiled the T cell differentiation state of pre-infusion anti-HIV DuoCAR-T cell products using multiparametric flow cytometry and CyTOF analyses. The therapeutic efficacy of early-memory enriched anti-HIV DuoCAR-T cells was evaluated in a humanized NSG mouse model of intrasplenic HIV-1 infection.

**METHODS**

The ability of anti-HIV DuoCAR-T cells to functionally cure HIV infection in PWH was assessed in our ongoing phase I/IIa clinical trial of anti-HIV DuoCAR-T cell therapy in our open phase I/IIa clinical trial (NCT04648046, Steven Deeks, MD, PI).

**RESULTS**

The anti-HIV DuoCAR-T cells recognize and potentially kill HIV-infected monocytes. (A) DU144 cells from PBMC were cultured for 3 days in complete media and GM-CSF, then infected with HIVvar-Luc HIV for 3 days. (B) DU144 infected cells were cultured with anti-HIV DuoCAR-T cells at various E:T ratios for 48 hours. Percent suppression was shown above the DuoCAR bars.

**CONCLUSIONS**

1. Anti-HIV DuoCAR-T cells express an early-memory phenotype along with markers of T cell activation and effector function.
2. HIV DuoCAR-T are active in humanized mouse models i.v., can function in monocytes/macrophages, and are readily generated from PWH on suppressive ART.
3. Effector T cells population of this phenotype may be associated with a durable therapeutic response in PWH.
4. These studies support translation of anti-HIV DuoCAR-T cell therapy in our open phase I/IIa clinical trial (NCT04648046, Steven Deeks, MD, PI).

**ACKNOWLEDGEMENTS**

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