Chimeric Antigen Receptor T-cell Therapy for HIV-associated Diffuse Large B-cell Lymphoma: Case Report and Management Recommendations

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Introduction

Chimeric antigen receptor-expressing autologous T cells (CAR-Ts) have shown remarkable efficacy in patients with relapsed/refractory diffuse large B cell lymphoma (DLBCL). HIV-positive patients, who have significantly increased risk of DLBCL despite adequate viral control[1], have been excluded from all CAR-T clinical trials, leaving uncertainty regarding safety and efficacy of using autologous CAR-Ts in this high risk population. To date, only three HIV+ patients with DLBCL treated with CAR-T have been reported in the literature.[2,3]

Case Description

- A 50-year-old, well-controlled HIV-positive male on antiretrovirals presented with aggressive DLBCL relapsed at D+100 post-autologous transplant.
- His disease was classified as a relapsed/refractory stage-IV high-grade DLBCL, non-germinal center subtype, expressing CD19, CD20 and MYC in >40% of cells. Ki67 was 90%. FISH showed no evidence of rearrangements. IPI = 1
- Quantitative serum HIV was undetectable and CD4 count was 378 cells/uL at relapse.
- He remained on continuous triple agent anti-retroviral therapy for HIV throughout his CAR-T clinical course.
- He underwent apheresis for T cell collection with absolute lymphocyte count of 0.9x10^9/L with successful manufacture of axicabtagene, a CD19-targeting CAR-T.
- He received lymphodepleting chemotherapy followed by axicabtagene infusion

Clinical Response

- Patient tolerated CAR-T infusion well except for grade-I cytokine release syndrome (CRS) and grade-II Immune-associated Neurotoxicity syndrome (ICANS) that both resolved with steroids.

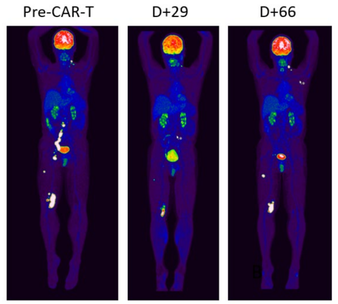

Figure 1 - PET images demonstrating tumor metabolic activity as well metabolic tumor volume (MTV) quantitation based on PET/CT measurements prior to CAR-T, at D+29 and D+66

- Day+28 restaging scans demonstrated a partial response with a **78% reduction** in metabolic tumor volume (130cm3 to 26cm3).
- Day+66 PET imaging demonstrating increasing tumor volume indicative of progressive disease. Repeat biopsy confirmed relapse with preserved expression of CD19.

Immune Reconstitution

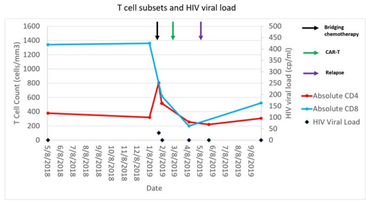

Figure 2 - A) Absolute CD4 / CD8 T cell counts and HIV viral load through CAR-T therapy

- Pt experienced no therapy related infections or apparent organ toxicity from lymphodepleting chemotherapy or CAR-T cellular product
- CD4 count remained stable and CD8 count recovered post-lymphodepletion
- HIV remained undetectable except one minimally positive (32 copies/ml) prior to CAR-T.

Conclusion

- Commercially available CAR-T therapy demonstrated adequate safety and evidence of clinical efficacy in a patient with HIV-associated R/R DLBCL.
- Available data supports the use of CAR-T for patients with controlled HIV who have thus far been excluded from clinical trials.
- Further research is needed, including focused clinical trials, to fully assess efficacy and safety of CAR-T in HIV-associated DLBCL

Management Recommendations

Pre-CAR-T

1) Assess HIV control and T cell repertoire
- Establish a management team including oncologist, infectious disease physician, pharmacist and cell therapy physician.
- Review ART and check HIV viral load; establish effective viral control.
- Assess peripheral T cell subsets including absolute CD4 count to assess repertoire. ALC >100 is recommended (but not required) for Axicabtagene manufacturing.

2) Infection control
- Screen for and treat any active immunodeficiency-associated infections.
- Initiate appropriate antimicrobial prophylaxis based on CD4 count and current infectious disease guidelines.

3) Assess drug-drug interactions
- In collaboration with team, review and adjust cART regimen for interactions with therapy plan.

Post-CAR-T

1) Monitor HIV control
- Recommend assessing HIV viral load at least q3 months for 1 year, more frequently with changes in cART regimen

2) Assess immune reconstitution
- Administer G-CSF for ANC <1000 cells/uL after 14 days post-CAR-T
- Monitor total T and B cell counts as well as CD4 count post-CAR-T

3) Infection prophylaxis
- Inhaled Pentamidine (or equivalent) 1 month prior and monthly for 6 months post-CAR-T
- Anti-fungal with mold activity if high dose steroids to be used for more than 7 days, if heavily pre-treated or prior autologous transplant within 1 year
- Acyclovir for HSV and VZV prophylaxis for minimum 6 months

Citations: 1) Gibson et al. AIDS 2014 2) Abramson et al. Cancer 2019. 3) Abbasi et al. Journal of Hematology & Oncology, 2020.

Acknowledgments: This work supported in part by T32 HL007062