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 control1, 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/μL at relapse.
• He remained on continuous triple agent anti-retroviral therapy for HIV throughout his CAR-T clinical course.
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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.
• Day+28 restaging scans demonstrated a partial response with a 78% reduction in metabolic tumor volume (130cm³ to 26cm³).
• Day+66 PET imaging 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

Immune Reconstitution

• Phenytoinacd 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

• Commerically 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
2) Assess immune reconstitution
3) Infection prophylaxis

Post-CAR-T
1) Monitor HIV control
2) Assess immune reconstitution
3) Infection prophylaxis

Figure 1 - PET images demonstrating tumor metabolic activity as well as metabolic tumor volume (MTV) quantitation based on PET/CT measurements before and after CAR-T therapy.

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

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