

A REAL-WORLD CASE OF SECOND CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY

Jacinth Joseph, Dennis Marjoncu, Kori Holman, Sara Leidy*. *Methodist University Hospital, Memphis, TN, USA*

Background CD19-directed Chimeric Antigen Receptor T-Cell (CAR-T) therapy has emerged as a promising and novel treatment for relapsed and refractory (r/r) B-cell malignancies. Efforts are directed towards increasing persistence of CAR-T cells, which is known to lead to durable responses. Repeat CAR-T infusions have been explored in clinical trials.¹⁻¹⁴ Here, we report a second CD19-directed CAR-T treatment in a patient with diffuse large B-cell lymphoma (DLBCL).

Methods A 60-year old man diagnosed with r/r DLBCL received a CAR-T infusion with tisagenlecleucel having a cell viability of 75%, not meeting FDA specifications of $\geq 80\%$. After relapse, the same patient received a second CAR-T with axicabtagene ciloleucel (axi-cel). For both infusions, the patient received appropriate lymphodepletion. Throughout and following both infusions, the patient was monitored for cytokine release syndrome (CRS) or immune effector associated neurotoxicity syndrome (ICANS). mEASIX scores (figure 1) were calculated to evaluate association with developing CRS/ICANS and disease response. Appropriate imaging and additional follow-up of response was completed.

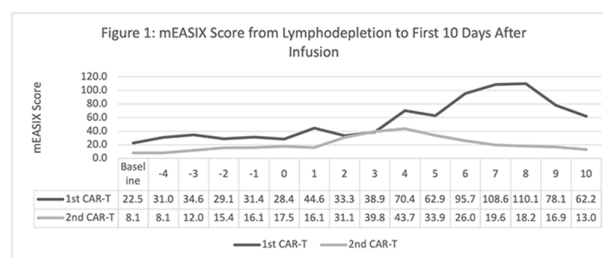
Results Following the patient's first CAR-T, he had no CRS or ICANS. He was discharged on day +9, then presented on day +84 with cough and dyspnea. Imaging showed an increase in lung lesion and pleural effusion. Biopsy of the lesion confirmed active lymphoma. Due to progression following CAR-T, he received two cycles of polatuzumab vedotin and rituximab for salvage. He then received his second CAR-T cell with axi-cel. On day +4, he developed grade 1 CRS, consisting of fever. CRS symptoms resolved on day +5 and he was discharged on day +12 without complications. Positron Emission Tomography (PET) scans on day +30, 3 and 6-months showed complete metabolic response (CMR), with persistently avid lesion at the L1 spine. This was biopsied showing no active lymphoma. Nine-month PET and 12-month CT showed no new findings to suggest active lymphoma and the patient remains in remission.

Conclusions Here, we present a case of a patient with r/r DLBCL who received two infusions of CAR-T cells. A second CAR-T treatment with a different product was used to treat relapse after first CAR-T in order to harness potential benefit from inherent differences between the 2 available commercial products, achieve adequate CAR-T cell dose, and avoid the higher-risk associated with the alternative treatment of allogeneic hematopoietic stem cell transplantation. As of 1-year post-second CAR-T the patient remains in a remission. This report reflects the benefit of a second infusion of CAR-T therapy in certain cases.

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