Clinical Outcomes of Commercial CD19-Targeted CAR T-Cell Therapy in Patients With Secondary Central Nervous System Lymphoma

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Background

-The commercially available CD19-targeted CAR T-cell therapies have demonstrated remarkable response rates in patients with refractory or relapsed non-Hodgkin lymphoma.

-However, the data about the efficacy and safety of CAR T-cell therapies in patients who were diagnosed with secondary central nervous system lymphoma is limited. Therefore, we report our experience using tisagenlecleucel in patients with relapsed/refractory HGBCL with secondary CNS lymphoma involvement at our institution.

Objective

-The purpose of our study is to evaluate the safety and efficacy of CD19-targeted CAR T-cell therapy in patients with relapsed/refractory HGBCL with secondary CNS lymphoma involvement.

Materials & Methods

- Patients who had active CNS involvement at the time of CAR T-cell therapy were identified retrospectively in a single-institution database of 101 consecutive HGBCL patients who received either tisagenlecleucel (tisa-cel) or axicabtagene ciloleucel (axi-cel) between 2017 and 2021.

- The best overall post–CAR T-cell therapy response was defined as the lowest disease burden measured at any time between post-CAR T-cell therapy and additional salvage therapies.

- Survival analysis was conducted using the Kaplan–Meier method.

Results

-Overall, 19 HGBCL patients with active secondary CNS lymphoma (5 parenchymal, 9 leptomeningeal/CSF, 5 parenchymal and leptomeningeal) were identified.

- The median age was 59 years (16–79 years) at the time of apheresis.

- All patients in the cohort received tisa-cel with a pre-conditioning regimen of fludarabine and cyclophosphamide.

- The median follow-up was 5.2 months (range, 0.8–36.8 months) from the date of CAR T-cell infusion.

- Ten patients had concurrent systemic involvement at the time of infusion.

- Seventeen patients received bridging therapy, of whom four received radiation therapy (patients/radiation field: 2/craniospinal, 1/whole brain, 1/skull base).

- Cytokine release syndrome occurred in 16 patients, among whom no grade 3 or higher event was reported.

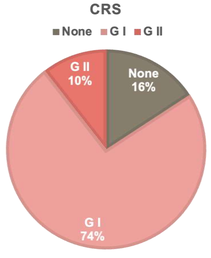
- Neurotoxicity syndrome occurred in 9 patients, one of whom reported a grade 4 event.

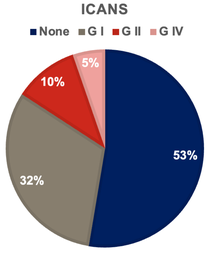
-The best objective CNS response (complete response and partial response) rate post-CAR T infusion as per MRI was 58% (n=11): parenchymal (n=3, 60%), leptomeningeal/CSF (n=5, 56%), parenchymal and leptomeningeal (n=3, 60%).

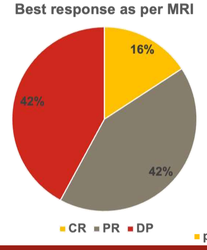
-The median overall survival and progression-free survival from the start of CAR T-cell therapy were 12.7 months (95% CI: 5.4 months–not reached) and 3.9 months (95% CI: 0.93 months–not reached), respectively.

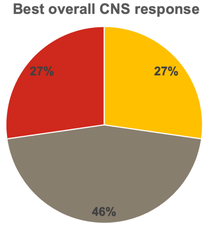
Table 1- Demographics and patient-related characteristics

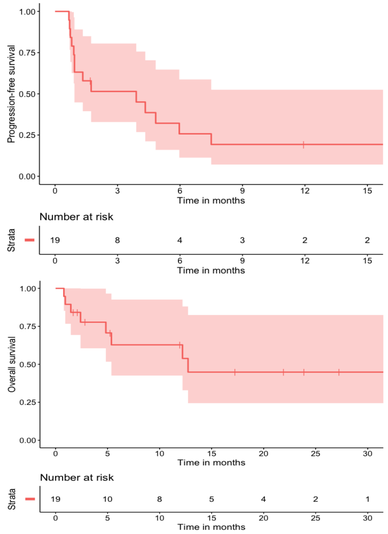
Variable	Value	Number (%)
Gender	Female Male	9 (47%) 10 (53%)
Histopathology	DLBCL TFL PMBCL Burkitt's lymphoma HGBCL with features intermediate between DLBCL and Burkitt's lymphoma	11 (58%) 4 (21%) 1 (5%) 2 (11%) 1 (5%)
Age at time of apheresis (years)	≥60 <60	9 (47%) 10 (53%)
ECOG PS pre-CAR T infusion	0-1 2-4	13 (68%) 6 (32%)
Elevated LDH at time of apheresis	Yes No	13 (68%) 6 (32%)
IPI score at time of apheresis	low risk low-intermediate risk High-intermediate risk High risk	3 (16%) 3 (16%) 7 (37%) 6 (31%)
Consolidative or Adjuvant RT pre-CAR T	Yes No	2 (11%) 17 (89%)
Salvage RT pre-CAR T	Yes No	5 (26%) 14 (74%)
Pre-CART transplant	Yes No	3 (16%) 16 (84%)
Bridging Therapy	Yes No	17 (89%) 2 (11%)
Concurrent systemic involvement pre-CAR T	Yes No	10 (53%) 9 (47%)
CNS involvement pre-CAR T	Parenchymal Leptomeningeal/CSF Parenchymal and leptomeningeal	5 (26%) 9 (47%) 5 (26%)
Salvage therapy Post-CAR T	Yes No	10 (53%) 9 (47%)
Alive Status	Dead Alive	8 (42%) 11 (58%)











Summary

Our data demonstrate that CD19-targeted CAR T-cell therapy is safe and feasible among HGBCL patients with secondary CNS lymphoma. Prospective cohort studies are required for validation.

References

Frigault MJ, Maus M v., Dietrich J, et al. Tisagenlecleucel CAR T-cell therapy in secondary CNS lymphoma. *Blood*. 2019;134(11):860-866. doi:10.1182/BLOOD.2019001694

Bennani NN, Maurer MJ, Nastoupil LJ, et al. Experience with Axicabtagene Ciloleucel (Axi-cel) in Patients with Secondary CNS Involvement: Results from the US Lymphoma CAR T Consortium. *Blood*. 2019;134(Supplement_1):763. doi:10.1182/BLOOD-2019-129097

Ahmed G, Hamadani M, Shah NN. CAR T-cell therapy for secondary CNS DLBCL. *Blood Adv*. 2021;5(24):5626-5630. doi:10.1182/BLOODADVANCES.2021005292