Real-world outcomes of axicabtagene ciloleucel (axi-cel) for the treatment of relapsed/refractory (R/R) secondary central nervous system lymphoma (SCNSL).

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Abstract

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Background:

Axi-cel is an autologous anti-CD19 CAR T-cell therapy that demonstrated durable, long-term efficacy and manageable safety in R/R LBCL. However, there is paucity of data using axi-cel in SCNSL, a subset associated with poor clinical outcomes. Here, we describe effectiveness and safety outcomes of axi-cel in R/R SCNSL.

Methods:

Patients (pts) receiving commercial axi-cel for R/R active SCNSL from 2018-2023 were selected from the CIBMTR database. Pts with primary CNS lymphoma and diseases other than LBCL were excluded. Outcomes included overall response rate (ORR), complete response (CR) rate, cumulative incidence of relapse (CIR), duration of response (DOR), progression-free and overall survival (PFS and OS), cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) per ASTCT consensus grading, other adverse events, and non-relapse mortality (NRM). Outcomes were analyzed descriptively.

Results:

At May 2024 data cutoff, 65 pts from 28 centers were identified. Median age at infusion was 63 y (range, 21-79) with 66% male and 81% white. Few pts (9/58, 16%) had ECOG PS ≥2; 52/65 (80%) had clinically significant comorbidities. Double-/triple-hit lymphoma was seen in 12/50 pts (24%), and 51/58 (88%) had Stage III/IV disease. CNS sites involved preinfusion were brain (51%), cerebrospinal fluid (12%), epidural space (15%), leptomeninges (11%), eyes (9%), and spinal cord (5%). Median number of prior lines of therapy was 4 (IQR, 3-5); 12/65 pts (18%) had prior autologous stem cell transplantation. Median time from leukapheresis to infusion was 28 days (IQR, 26-34). Bridging therapy was given to 47/65 pts (75%; systemic, 40 [63%]; intrathecal, 12 [19%]; radiation, 17 [27%]).

At 48.2-mo median follow-up, ORR was 72% (95% CI, 60-83); CR rate was 51% (95% CI, 38-63). Median (95% CI) DOR, PFS, and OS were 4.0 (2.3-NE), 3.6 (2.2-4.9), and 8.4 mo (6.6-18.2), respectively. CIR was 66% (95% CI, 51-77) at 1 and 2 y. At 2 y and 3 y, PFS (95% CI) was 26% (16-38) and 23% (13-35), respectively, and OS (95% CI) was 36% (24-49) and 32% (20-44). Among pts without progression at 1 y, PFS was 100% and 90% (47-99) at 2 y and 3 y, respectively; OS was 82% (59-93) and 72% (48-86). Grade ≥3 CRS and ICANS occurred in 14% and 37% of pts, respectively (any grade, 81% and 62%). Of 56 pts with CRS and/or ICANS, tocilizumab, corticosteroids, and anakinra were used in 68%, 73%, and 7% of pts, respectively. Prolonged cytopenia (by Day 30) was reported in 25/63 pts (40%; thrombocytopenia, 37%; neutropenia, 11%), and 39/65 (60%) had clinically significant infections. Subsequent cancers were found in 3/39 pts (8%); 2 were myeloid. NRM at 3 y was 12%.

Conclusion:

With 4-y median follow-up, this real-world study highlights the potential use of axi-cel as an option to treat this challenging group of pts. Further studies are needed to improve response durability.