

## **CAR T-cell Therapy for Primary and Secondary CNS Lymphomas**

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Chimeric antigen receptor (CAR) T-cell therapy has emerged as a promising approach for relapsed or refractory central nervous system lymphomas (CNSL), including both primary (PCNSL) and secondary (SCNSL) disease, addressing a historically poor prognosis with conventional treatment. Anti-CD19 CAR T-cells, already transformative in systemic B-cell lymphomas, have demonstrated encouraging efficacy in CNSL, with complete remission rates reported around 47–56% and meaningful proportions of patients maintaining remission at six months.

Toxicity profiles in CNSL largely mirror those seen in systemic lymphoma. The most frequent adverse events include cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). In aggregated data, around 70–72% of patients experienced CRS of any grade, and approximately half experienced ICANS, with severe (grade 3–4) events in a minority of cases. Importantly, no significantly elevated neurotoxicity signal has emerged specifically in CNSL cohorts compared with systemic disease.

Future directions in the field aim to optimize CAR constructs and delivery strategies to enhance durability and reduce relapse risk. Combining CAR T-cells with other modalities (e.g., autologous stem cell transplant or maintenance therapy) and refining understanding of neurotoxicity mechanisms are active areas of investigation. Continued prospective clinical studies will be critical to expand indications and improve outcomes for patients with CNS lymphomas.