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Phase I trial of IL13Rα2-targeted CAR-T cell therapy for recurrent malignant glioma: clinical results and pharmacokinetics

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Abstract

Purpose: This single-center, open-label, Phase 1 trial evaluated the safety and tolerability of chimeric antigen receptor (CAR)-T cells targeting interleukin-13 receptor α2 (IL13Rα2) in patients with malignant gliomas.

Patients and methods: Adults with World Health Organization Grade 3-4 gliomas, recurrent after standard treatment and expressing IL13Rα2 (confirmed by immunohistochemistry), received a single intravenous infusion of autologous CAR-T cells. Primary objectives were to measure the maximum-tolerated dose (MTD) and recommended Phase 2 dose. Secondary objectives included assessment of pharmacokinetics, objective response rate, progression-free survival (PFS), and overall survival (OS).

Results: Ten patients were sequentially assigned to three dosing cohorts (1.0×107, 3.0×107, 1.0×108 cells/kg). The MTD was not reached, as no dose-limiting toxicities were observed, and all adverse events (AEs) were Grade ≤3 without irreversible sequelae. The most common treatment-related AEs were pyrexia (70%) and elevated transaminase (70%). CAR-T cell levels in blood reached peak concentrations at a median of 7 days (range 3-14), and the transgene was detected in cerebrospinal fluid from five of six patients treated at the higher two doses. Nine patients were evaluable for survival analysis, among whom six were available for response assessment at 3 months; best response was stable disease in three cases. Median PFS was 2.6 months (95% confidence interval [CI]: 0.95-5.75), and median OS was 10.9 months (95% CI: 8.2-26.6).

Conclusions: Intravenous IL13Rα2-targeted CAR-T therapy was well tolerated and demonstrated preliminary safety. Further studies are warranted to optimize dosing and preconditioning regimens and identify exploratory biomarkers for efficacy evaluation.