536 PHASE 1 TRIAL OF TUMOR-INFILTRATING LYMPHOCYTE (TIL) THERAPY IN RECURRENT GLIOBLASTOMA: A SINGLE-CENTER EXPERIENCE USING CELLS DERIVED FROM PRIMARY SURGICAL SPECIMENS

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Background Glioblastoma (GB) is the most aggressive primary brain cancer subtype, characterized by rapid recurrence. Despite existing multiple therapies, recurrent GB has a median overall survival of only 6 to 10 months, underscoring the critical need for novel therapeutic strategies. Tumor-infiltrating lymphocytes (TIL), a novel immunotherapy, have shown promise in solid tumors and is now under investigation for its effectiveness in GB.

Methods We conducted a phase 1, open-label, nonrandomized clinical trial (NCT04943913) at the Second Affiliated Hospital of Soochow University to evaluate the safety and efficacy of TIL therapy in recurrent GB patients. Tumor tissues were resected and transported to a GMP facility. The cryopreserved infusion product was then shipped back to clinical center. The treatment protocol comprised a preconditioning regimen consisting of cyclophosphamide (20 mg/kg/day, intravenous infusion, administered from day -5 to day -3) and hydroxychloroquine (600 mg/day, oral administration, day -5). On day 0, following the administration of anti PD-1 antibody (100mg, sintilimab, Innovent) patients received a single intravenous infusion of TIL. The endpoints included safety and antitumor efficacy (RANO 2.0).

Results A 56-year-old male with left frontal lobe glioblastoma (IDH wild-type, WHO 4, EGFR amplification), whose tumor was resected on January 5, 2023, initially received stupp regimen treatment, resulting in transient stability before disease recurrence. Following recurrence, despite sequential administration of 17 cumulative CAR-T treatments targeting two distinct antigens (IL-13Rα2 and B7-H3), the patient ultimately experienced disease progression. The patient subsequently enrolled in our trial. TILs were generated from the initial resection specimen obtained in January 2023, yielding a total of 2.95×10^{10}cells, with 99.92% T cells and a predominant CD8+ T cell population (97.85%). Following preconditioning, TIL infusion occurred on December 12, 2023. Baseline MRI scans revealed a recurrent lesion with a maximum diameter of 2.8 cm. At 4 weeks post-infusion (January 8, 2024), the tumor was completely resected, and the patient demonstrated a sustained complete response lasting beyond 1.4 years (up to June 2025).

Conclusions Our findings indicate that despite GB being classified as a 'cold tumor', TILs can be effectively expanded ex vivo. The complete remission of intracranial lesions suggests that TILs possess the capability to cross the blood-brain barrier. Importantly, TILs derived from early surgical resection tissue (January 2023) facilitated remission in a recurrent tumor (enrollment in November 2023), underscoring the potential benefits of early tissue sampling for TIL therapy in recurrent GB.

Trial Registration https://clinicaltrials.gov/study/NCT04943913

Ethics Approval The trial obtained ethical approval from the Ethics Committee of The Second Affiliated Hospital of Soochow University (approval number: JD-LK-2021-051-01).

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal

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