Abstract 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. Eligible participants are adults aged 18 to 75 years with histologically confirmed primary glioblastoma; Karnofsky Performance Status ≥60% or ECOG score of 0–2; patients must have be suitable candidates for biopsy or resection to obtain TILs, and possess at least one evaluable tumor lesion before TIL infusion; adequate organ function; and must discontinue any prior antitumor therapy at least 28 days before TIL infusion. The procedure of the trial was showed in Figure 1. The endpoints included safety and antitumor efficacy (RANO 2.0).

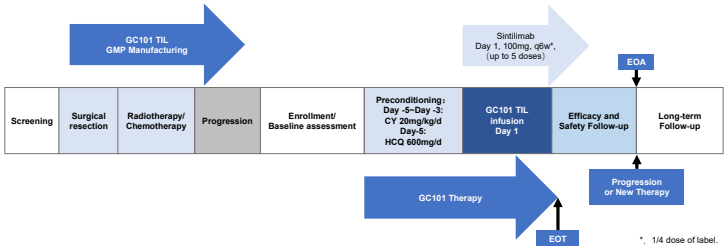

Figure 1. Treatment Schema
Tumor tissues were resected and transported to a GMP facility. The cryopreserved infusion product was then shipped back to clinical center. The treatment protocol comprised a preconditioning regimen consisting of cyclophosphamide (20 mg/kg/day, intravenous infusion, administered from day -5 to day -3) and hydroxychloroquine (600mg/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.

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 eliminated, and the patient demonstrated a sustained complete response lasting beyond 1.8 years (up to October 2025).

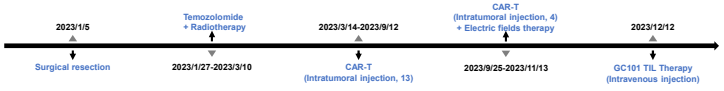

Figure 2. The treatment history.

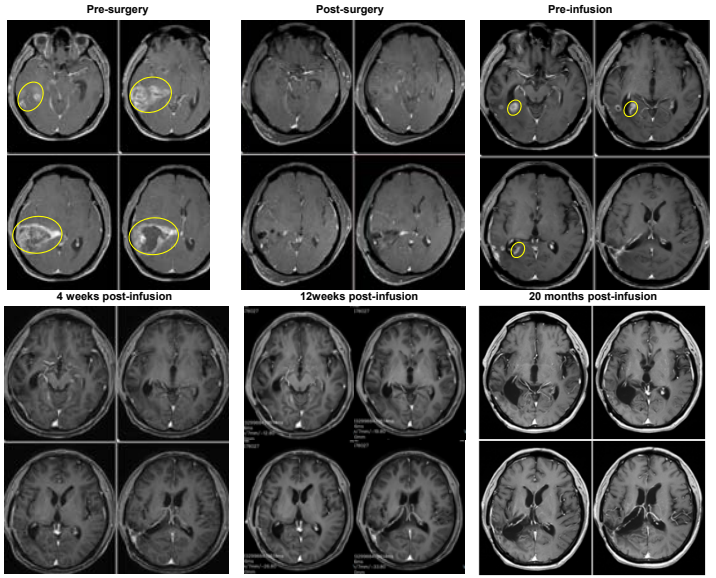

Figure 3. The MRI images during treatment process. At 4 weeks post-infusion (2024/1/8), the patient achieved complete remission, and the patient demonstrated a sustained complete response lasting beyond 1.8 years (2025/9/9).

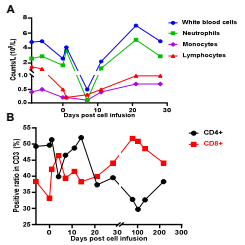

Figure 4. Peripheral blood profile.
A), Complete blood count (CBC) analysis, including neutrophils, white blood cells, monocytes, lymphocytes, showed transient decreased, and with normalization observed within two weeks after cell infusion.
B), Longitudinal monitoring of peripheral blood CD4+/CD8+ T-cell ratios demonstrated a reversal post-TIL infusion, suggested the antitumor activity.

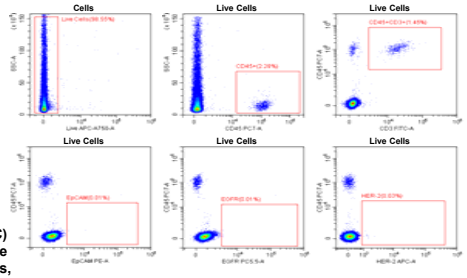

Figure 5. Cerebrospinal fluid (CSF) analysis performed at the 12-week follow-up post-TIL infusion demonstrated no detectable malignant cells, aligning with negative imaging results.

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.

Abbreviations
GB, glioblastoma; TIL, tumor-infiltrating lymphocytes.

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