Review Trends Cancer. 2025 Nov 13:S2405-8033(25)00254-7. doi: 10.1016/j.trecan.2025.10.003.

Online ahead of print.

The promise of TIL therapy for glioblastoma

Emma L Pristo [1], Kelly M Hotchkiss [1], Anna M Corcoran [1], Pamela Noldner [2], Hideho Okada [3], John W Hickey [4], Jose Conejo-Garcia [5], Beth Shaz [6], Mustafa Khasraw [7]

PMID: 41238472 DOI: 10.1016/j.trecan.2025.10.003

Abstract

Tumor-infiltrating lymphocyte (TIL) therapy has demonstrated efficacy in refractory melanoma and durable responses in lung cancer. Glioblastoma presents distinct challenges for immunotherapy, including profound tumor heterogeneity, low T cell infiltration, and an immunosuppressive microenvironment, but these same features highlight the unique rationale for TILs. Unlike monoclonal engineered approaches, TILs retain natural polyclonality, enabling recognition of a diverse set of tumor-associated antigens and potential adaptation to the evolving antigenic landscape. Preliminary studies have already shown that tumor-reactive TILs can be successfully isolated and expanded from glioblastoma specimens, providing feasibility for clinical translation. This review discusses the current landscape of TIL therapy in glioblastoma, highlights recent advancements, and discusses future directions and clinical translation to position TIL therapy as a promising and adaptable cellular immunotherapy for one of the most treatment-resistant human cancers.

Keywords: T cell therapy; glioblastoma; immunotherapy; tumor-infiltrating lymphocytes.