Clin Cancer Res. 2023 Jun 16;CCR-23-0203. doi: 10.1158/1078-0432.CCR-23-0203.
Online ahead of print.

Bavituximab decreases immunosuppressive myeloid-derived suppressor cells in newly diagnosed glioblastoma patients

K Ina Ly [1], Leland G Richardson [2], Mofei Liu [3], Alona Muzikansky [4], Jonathan Cardona [1], Kevin Lou [1], Andrew L Beers [5], Ken Chang [6], James M Brown [7], Xiaoyue Ma [8], David A Reardon [3], Isabel C Arrillaga-Romany [9], Deborah A Forst [1], Justin T Jordan [10], Eudocia Q Lee [3], Jorg Dietrich [11], Lakshmi Nayak [12], Patrick Y Wen [3], Ugonma Chukwueke [13], Anita Giobbie-Hurder [3], Bryan D Choi [1], Tracy T Batchelor [14], Jayashree Kalpathy-Cramer [15], William T Curry [2], Elizabeth R Gerstner [16]

Affiliations
PMID: 37327319 DOI: 10.1158/1078-0432.CCR-23-0203

Abstract

Purpose: We evaluated the efficacy of bavituximab - a monoclonal antibody with anti-angiogenic and immunomodulatory properties - in newly diagnosed glioblastoma (GBM) patients who also received radiation and temozolomide. Perfusion MRI and myeloid-related gene transcription and inflammatory infiltrates in pre-and post-treatment tumor specimens were studied to evaluate on-target effects (NCT03139916).

Patients and methods: Thirty-three adults with isocitrate-dehydrogenase-wild-type GBM received 6 weeks of concurrent chemoradiation, followed by 6 cycles of temozolomide (C1-C6). Bavituximab was given weekly, starting week 1 of chemoradiation, for at least 18 weeks. The primary endpoint was proportion of patients alive at 12 months (OS-12). The null hypothesis would be rejected if OS-12 was ≥72%. Relative cerebral blood flow (rCBF) and vascular permeability (Ktrans) were calculated from perfusion MRIs. Peripheral blood mononuclear cells (PBMCs) and tumor tissue were analyzed pre-treatment and at disease progression using RNA transcriptomics and multispectral immunofluorescence for myeloid-derived suppressor cells (MDSCs) and macrophages.

Results: The study met its primary endpoint with an OS-12 of 73% (95% CI 59-90%). Decreased pre-C1 rCBF (HR 4.63, p=0.029) and increased pre-C1 Ktrans were associated with improved OS (HR 0.09, p=0.005). Pre-treatment, overexpression of myeloid-related genes in tumor tissue was associated with longer survival. Post-treatment, tumor specimens contained fewer immunosuppressive MDSCs (p=0.01).

Discussion: Bavituximab has activity in newly diagnosed GBM and resulted in on-target depletion of intratumoral immunosuppressive MDSCs. Elevated pre-treatment expression of myeloid-related transcripts in GBM may predict response to bavituximab.