Review J Neurooncol. 2024 Dec 5. doi: 10.1007/s11060-024-04865-2. Online ahead of print.

# Angiogenesis inhibitors effects on overall survival and progression-free survival in newly diagnosed primary glioblastoma multiforme: a meta-analysis of twelve randomized clinical trials

Ali Motamed-Sanaye [1], Ali Mortezaei [1], Amir R Afshari [2], Zahra Saadatian [3], Amir H Faraji [4], Jason P Sheehan [5], Ali Mohammad Mokhtari [6]

Affiliations

PMID: 39636552 DOI: 10.1007/s11060-024-04865-2

## Abstract

**Background:** Glioblastoma multiforme (GBM) is the most common malignant brain tumor in adults. Typically treated with initial surgical resection, and chemoradiotherapy, despite current treatments, patients typically survive only 12-14 months, necessitating new therapeutic approaches. Our meta-analysis evaluates combining antiangiogenic medications with chemoradiotherapy versus using chemoradiotherapy alone in treating newly diagnosed GBM.

**Methods:** A comprehensive literature search was conducted using PubMed/MEDLINE, Scopus, Cochrane and the Web of Science databases. The search aimed to identify studies reporting overall survival (OS), progression-free survival (PFS), and hazard ratio (HR) with corresponding confidence intervals (CIs) in patients with newly diagnosed GBM. We employed random-effect meta-analysis.

**Results:** Twelve randomized clinical trials (RCTs) involved 3,309 patients included in the study. The findings showed that angiogenesis inhibitors significantly prolonged PFS [HR 0.85, 95% CI (0.73, 0.99), p-value = 0.04], while there was no significant difference on OS [HR 1.014, 95%CI (0.89, 1.15), p-value = 0.84]. Bevacizumab (BEV) exhibited the highest [HR 0.67, 95% CI (0.56, 0.79), p-value < 0.0001] and thalidomide exhibited the lowest [HR 1.46, 95% CI (1.004, 2.1), p-value = 0.048] improvements of PFS. Meta-regression revealed that age, white race, study sample size, infection, vascular disease complications, KPS > 60, biopsy, gross and subtotal resection can significantly influenced the PFS, while only the year of publication affected OS.

**Conclusions:** The current study showed that improve the PFS with no significant effect on OS. Our findings may provide some evidence for decision-making regarding the utilization of angiogenesis inhibitors for the treatment of adult patients with newly diagnosed GBM.

**Keywords:** Angiogenesis inhibitors; Glioblastoma multiforme; Overall survival; Progression-free survival.