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J Neurooncol. 2023 Feb 7. doi: 10.1007/s11060-023-04248-z. Online ahead of print.

Dose-dependent efficacy of bevacizumab in recurrent glioblastoma

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PMID: 36749445 DOI: 10.1007/s11060-023-04248-z

Abstract

Background: Bevacizumab (BEV), at a standard dose of 10 mg/kg every 2 weeks is associated with prolonged progression-free survival (PFS) but no improvement in overall survival (OS) in recurrent glioblastoma (rGBM). Few studies have examined the potential dose-dependent efficacy of BEV. In Ontario, reimbursement for the costs of BEV varies, and as a result, our practice began to routinely use lower dose regimens. The main aim of this study was to ensure that there was no harm to patients who received the low dose protocol.

Methods: A single-center retrospective study of patients given BEV for rGBM between 2015 and 2020 was performed. Clinical and treatment data including BEV dose regimen [SD (10 mg/kg every 2 weeks) vs. LD (5 mg/kg every 2-3 weeks or 10 mg/kg every 3 weeks)] received at the time of rGBM diagnosis were captured. Overall survival (OS) and progression-free survival (PFS) on BEV were compared using the Kaplan-Meier product-limit method. Log-rank test was used to compare potential predictive factors. Cox regression model was performed for multivariable analysis of OS and PFS.

Results: A total of 96 patients were included with a median follow-up duration of 6.84 months (range 1.12-50.63 months) from the date of the first infusion. The LD group consisted of 55 of the 96 patients. By virtue of funding mechanisms for BEV, the median age in the LD group was significantly higher (62 vs. 54 years p = 0.009). There was no difference in MGMT status between the two groups (p = 0.60). The LD group had prolonged median PFS (5.89 months versus 3.22 months; p = 0.0112) and OS (10.23 months versus 6.28 months; p = 0.0010). Multivariable analysis including the dose of BEV, the extent of resection, gender, and age revealed that standard dose of BEV, subtotal resection, and female sex were associated with worse overall survival. Nine patients in the SD group vs. 18 patients in the LD group reported an adverse event related to BEV.

Conclusion: For patients with recurrent GBM, we found that a low dose regimen of BEV was associated with prolonged OS and PFS compared to the standard dose regimen. Lower dose schedules may be a better and more cost-effective option for patients with rGBM. Lower costs might

provide more equitable access to this very important palliative drug.

Keywords: Antiangiogenic therapy; Cost-effectiveness; Dose dependence; Glioblastoma.

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