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Bevacizumab exerts dose-dependent risk for intracranial hemorrhage in patients with malignant gliomas

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Abstract

Purpose: Bevacizumab, an anti-VEGF monoclonal antibody, has become a mainstay therapeutic in the management of malignant glioma. It is unknown if the risk of intracranial hemorrhage (ICH), a major complication associated with bevacizumab use, is dose-dependent.

Methods: This was a single institution retrospective analysis of patients treated with bevacizumab for the management of gliomas between 2009 and 2022. Incidence rates of ICH between patients receiving low-dose (< 5 mg/kg/week) and conventional-dose (5 mg/kg/week) bevacizumab regimens were compared via competing risk analysis over time. We evaluated post-progression survival (PPS) as a secondary outcome using multivariate Cox regression.

Results: One hundred and seventy-three patients were identified (low-dose group, n = 51, conventional-dose group, n = 122) for inclusion in our analysis. Cumulative incidence rates of all cases of ICH and clinically symptomatic cases of ICH were higher in the conventional-dose (17.2% for all cases, 13.7% for symptomatic) relative to the low-dose group (3.9% for all cases, 2.0% for symptomatic); p-value 0.0296 for all cases, p-value 0.0274 for symptomatic cases. On multivariate Fine-Gray regression, conventional-dose bevacizumab therapy remained significantly associated with increased risk for symptomatic ICH (SHR 8.0560; p-value 0.0442). No difference in PPS was observed between the low-dose versus conventional-dose groups.

Conclusions: Conventional-dose bevacizumab therapy (5 mg/kg/week) is associated with increased incidence of ICH in patients with malignant glioma compared to lower dose bevacizumab (< 5 mg/kg/week) in this single center retrospective cohort. No difference in PPS was observed between the low-dose versus conventional-dose groups.

Keywords: Anti-VEGF therapy; Antiangiogenic therapy; Bevacizumab; Glioblastoma; Glioma; Intracranial hemorrhage.