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# Change in Pattern of Relapse After Antiangiogenic Therapy in High-Grade Glioma.

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### Abstract

**PURPOSE:** Local recurrence is the dominant pattern of relapse in high-grade glioma (HGG) after conventional therapy. The recent use of antiangiogenic therapy has shown impressive radiologic and clinical responses in adult HGG. The preclinical data suggesting increased invasiveness after angiogenic blockade have necessitated a detailed analysis of the pattern of recurrence after therapy.

**METHODS AND MATERIALS:** A total of 162 consecutive patients with HGG, either newly diagnosed ( $n = 58$ ) or with recurrent disease ( $n = 104$ ) underwent therapy with bevacizumab at 10 mg/kg every 2 weeks and conventional chemotherapy with or without involved field radiotherapy until disease progression. The pattern of recurrence and interval to progression were the primary aims of the present study. Diffuse invasive recurrence (DIR) was defined as the involvement of multiple lobes with or without crossing the midline.

**RESULTS:** At a median follow-up of 7 months (range, 1-37), 105 patients had recurrence, and 79 patients ultimately developed DIR. The interval to progression was similar in the DIR and local recurrence groups (6.5 and 6.3 months,  $p = .296$ ). The hazard risk of DIR increased exponentially with time and was similar in those with newly diagnosed and recurrent HGG ( $R(2) = 0.957$ ). The duration of bevacizumab therapy increased the interval to recurrence ( $p < .0001$ ) and improved overall survival ( $p < .0001$ ). However, the pattern of relapse did not affect overall survival ( $p = .253$ ).

**CONCLUSION:** Along with an increase in median progression-free survival, bevacizumab therapy increased the risk of DIR in HGG patients. The risk of increased invasion with prolonged angiogenic blockade should be addressed in future clinical trials.

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