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Antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma: Analysis of single-agent and combined modality approaches.

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Abstract

ABSTRACT: Surgical resection followed by radiotherapy and temozolomide in newly diagnosed glioblastoma can prolong survival, but it is not curative. For patients with disease progression after frontline therapy, there is no standard of care, although further surgery, chemotherapy, and radiotherapy may be used. Antiangiogenic therapies may be appropriate for treating glioblastomas because angiogenesis is critical to tumor growth. In a large, noncomparative phase II trial, bevacizumab was evaluated alone and with irinotecan in patients with recurrent glioblastoma; combination treatment was associated with an estimated 6-month progression-free survival (PFS) rate of 50.3%, a median overall survival of 8.9 months, and a response rate of 37.8%. Single-agent bevacizumab also exceeded the predetermined threshold of activity for salvage chemotherapy (6-month PFS rate, 15%), achieving a 6-month PFS rate of 42.6% ($p < 0.0001$). On the basis of these results and those from another phase II trial, the US Food and Drug Administration granted accelerated approval of single-agent bevacizumab for the treatment of glioblastoma that has progressed following prior therapy. Potential antiangiogenic agents-such as cilengitide and XL184-also show evidence of single-agent activity in recurrent glioblastoma. Moreover, the use of antiangiogenic agents with radiation at disease progression may improve the therapeutic ratio of single-modality approaches. Overall, these agents appear to be well tolerated, with adverse event profiles similar to those reported in studies of other solid tumors. Further research is needed to determine the role of antiangiogenic therapy in frontline treatment and to identify the optimal schedule and partnering agents for use in combination therapy.

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