Bevacizumab, temozolomide, and radiotherapy for newly diagnosed glioblastoma: comprehensive safety results during and after first-line therapy.

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Abstract

BACKGROUND: The proposed use of bevacizumab with radiotherapy/temozolomide for newly diagnosed glioblastoma raised potential safety concerns. Bevacizumab has been linked with stroke, bleeding events, and wound-healing complications in other tumor types; these events are of particular concern for glioblastoma (highly vascular tumors that are usually resected). Published data on the interaction of bevacizumab with radiotherapy/temozolomide are also limited. We report safety data from a phase III randomized trial (Avastin in Glioblastoma), focusing on these considerations.

METHODS: Eligible patients received: radiotherapy and temozolomide plus bevacizumab/placebo, 6 cycles; a 4-week treatment break; temozolomide plus bevacizumab/placebo, 6 cycles; and bevacizumab/placebo until progression. Data on adverse events (AEs) were collected throughout.

RESULTS: Bevacizumab-treated patients (n = 461) had a longer median safety follow-up time (12.3 vs 8.5 mo), and a higher proportion completed 6 cycles of maintenance temozolomide (64.6% vs 36.9%) versus placebo (n = 450). The incidences of relevant AEs (bevacizumab vs placebo, respectively) were: arterial thromboembolic events (5.9% vs 1.6%); cerebral hemorrhage (3.3% vs 2.0%); wound-healing complications (6.9% vs 4.7%); thrombocytopenia (34.1% vs 27.3%); radiotherapy-associated skin injury (8.2% vs 9.3%); alopecia (39.0% vs 36.0%); gastrointestinal perforation (including gastrointestinal abscesses and fistulae, 1.7% vs 0.4%); and radiotherapy-associated injury (0.4% vs 0.0%). Overall, 15.8% and 23.8% of bevacizumab- and placebo-treated patients had surgery (including biopsy) after progression. Within 30 days of postprogression surgery, AE incidence was 10.9% (bevacizumab) and 23.4% (placebo).

CONCLUSION: The safety profile was consistent with that expected from radiotherapy/temozolomide plus bevacizumab. The increased AE incidence with bevacizumab did not impact patients’ ability to receive standard-of-care treatment or to undergo further surgery.

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