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Title: Bevacizumab Monotherapy in Recurrent Glioblastoma: Real-World Outcomes in Patients 60 Years and Older

Publication Type

Clinical Trial (Phase IV Real-World Evidence Study)

Year of Publication

2024

Patient Demographics

- **Age Group**: 60-81 years (median age: 69 years)
- **Sample Size**: 134 patients
- **Condition**: First recurrence glioblastoma following standard chemoradiotherapy
- **Gender Distribution**: 56% male, 44% female
- **Time to Recurrence**: Median 8.4 months from initial diagnosis (range: 3.2-24.7 months)
- **Karnofsky Performance Score**: 60-90 (median: 70)
- **Prior Treatment**: All patients received surgery/biopsy + radiotherapy + temozolomide

Disease Focus

Recurrent glioblastoma multiforme with focus on anti-angiogenic therapy outcomes in elderly patients in routine clinical practice setting

Treatment Discussed

Bevacizumab (Avastin), a humanized monoclonal antibody targeting vascular endothelial growth factor (VEGF), administered at 10 mg/kg intravenously every 2 weeks as monotherapy until disease progression, unacceptable toxicity, or clinical deterioration.

Treatment Duration: - Median number of cycles: 8 (range: 1-34) - Median treatment duration: 4.1 months (range: 0.5-17.2 months)

Study Outcome Summary

Primary Endpoints: - Median overall survival from bevacizumab initiation: 8.6 months (95% CI: 7.3-10.1) - Median progression-free survival (PFS): 4.2 months (95% CI: 3.6-5.1) - 6-month PFS rate: 38.8% - 6-month OS rate: 71.6% - 12-month OS rate: 33.6%

Radiographic Response (RANO Criteria): - Complete response: 0% - Partial response: 26.1% (n=35) - Stable disease: 41.0% (n=55) - Progressive disease: 32.8% (n=44) - Overall response rate: 26.1% - Disease control rate (CR+PR+SD): 67.2%

Pseudo-Response Phenomenon: Radiographic response observed in 26.1% of patients; however, clinical benefit did not always correlate with imaging improvement. Median time to radiographic response: 6.3 weeks.

Clinical Benefit: - Reduction in corticosteroid dose achieved in 58.2% of patients - Improvement in performance status (≥10 point KPS increase): 32.1% - Neurological symptom stabilization or improvement: 52.2%

Safety Profile: Treatment-related adverse events occurred in 68.7% of patients: - Hypertension (Grade 3: 14.9%, Grade 1/2: 41.8%) - Fatigue (Grade 3: 10.4%, Grade 1/2: 52.2%) - Proteinuria (Grade 3: 4.5%, Grade 1/2: 23.9%) - Thromboembolic events (Grade 3/4: 8.2%) - DVT (n=6), PE (n=5) - Hemorrhage (Grade 3: 3.0%) - intracranial hemorrhage (n=4) - Wound healing complications: 6.0% - GI perforation: 1.5% (n=2, both fatal)

Treatment Discontinuation: - Disease progression: 71.6% - Adverse events: 13.4% - Clinical deterioration: 11.9% - Patient preference: 3.0%

Prognostic Factors: Favorable prognostic factors included: - KPS ≥80 (HR 0.58, $p<0.001$) - Time to first recurrence >12 months (HR 0.65, $p=0.003$) - Lower corticosteroid requirement (HR 0.71, $p=0.018$) - Smaller tumor volume at recurrence (HR 0.67, $p=0.009$)

FDA Approval Status

Approved - Bevacizumab (Avastin) received accelerated FDA approval in 2009 for recurrent glioblastoma based on radiographic response rates. However, confirmatory trials did not demonstrate overall survival benefit in newly diagnosed glioblastoma, limiting its use primarily to recurrent disease. Approval remains valid for recurrent GBM despite ongoing debate about clinical benefit versus radiographic response.

Key Findings

Bevacizumab monotherapy in elderly patients with recurrent glioblastoma demonstrated radiographic response rates consistent with prior clinical trials, though overall survival remained limited. The treatment provided meaningful clinical benefits including corticosteroid reduction and symptom control in over half of patients.

The radiographic response may not fully reflect true anti-tumor activity due to reduction in vascular permeability rather than tumor cytoreduction. Clinicians should interpret imaging carefully and incorporate clinical assessment when evaluating treatment efficacy.

Safety profile in the elderly population showed manageable toxicity, though thromboembolic events and hemorrhage risk require vigilant monitoring. Elderly patients with good performance status derived similar benefits as younger populations in historical comparisons.

Bevacizumab remains a reasonable therapeutic option for recurrent glioblastoma in elderly patients, particularly for those requiring corticosteroid reduction or experiencing symptomatic mass effect. Patient selection based on performance status and comorbidity assessment is critical.

Citations

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Data Source: Electronic health records from 12 participating institutions
Statistical Analysis: Kaplan-Meier survival analysis, Cox proportional hazards modeling
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