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Title: Comparative Effectiveness of Temozolomide versus Immunotherapy in Elderly Glioblastoma Patients: A Systematic Review and Meta-Analysis

Publication Type

Review (Systematic Review and Meta-Analysis)

Year of Publication

2024

Patient Demographics

- **Age Group**: 60+ years (studies included patients aged 60-85)
- **Total Patients Analyzed**: 1,847 patients across 12 clinical trials
- **Condition**: Newly diagnosed or recurrent glioblastoma
- **Geographic Distribution**: Studies from North America (5), Europe (5), Asia (2)
- **Study Period**: 2018-2024

Disease Focus

Glioblastoma multiforme treatment outcomes comparing standard chemotherapy versus immune checkpoint inhibitors in geriatric oncology populations

Treatment Discussed

Temozolomide Regimen (8 studies, n=1,203): Standard dosing: 75 mg/m² concurrent with radiotherapy, followed by adjuvant 150-200 mg/m² (days 1-5 of 28-day cycles) for up to 12 cycles.

Immunotherapy Regimen (4 studies, n=644): Anti-PD-1/PD-L1 agents (nivolumab, pembrolizumab) at standard doses (240-480 mg every 2-4 weeks) as monotherapy or combination therapy.

Study Outcome Summary

Overall Survival Meta-Analysis: - Temozolomide: Pooled median OS = 13.8 months (95% CI: 12.6-15.1) - Immunotherapy: Pooled median OS = 10.2 months (95% CI: 8.7-11.9) - Hazard ratio: 0.78 favoring TMZ (95% CI: 0.69-0.89, p<0.001)

Progression-Free Survival: - Temozolomide: Pooled median PFS = 6.5 months (95% CI: 5.9-7.2) - Immunotherapy: Pooled median PFS = 3.1 months (95% CI: 2.6-3.8) - Hazard ratio: 0.64 favoring TMZ (95% CI: 0.56-0.74, p<0.001)

Response Rates: - Temozolomide objective response rate: 31.2% (95% CI: 27.8-34.8%) - Immunotherapy objective response rate: 11.4% (95% CI: 8.2-15.3%)

Subgroup Analysis (Age-Specific): - Age 60-69 years: TMZ vs Immunotherapy HR = 0.74 (p=0.002) - Age 70+ years: TMZ vs Immunotherapy HR = 0.82 (p=0.011)

MGMT Methylation Impact: - MGMT-methylated tumors with TMZ: median OS 18.2 months - MGMT-unmethylated tumors with TMZ: median OS 11.4 months - MGMT status showed no correlation with immunotherapy response

Quality of Life: Both treatments showed similar impact on quality of life scores. Temozolomide associated with higher rates of hematologic toxicity, while immunotherapy showed more immune-related adverse events but potentially better cognitive function preservation.

Safety Comparison: - Grade 3/4 adverse events: TMZ 31.2% vs Immunotherapy 15.7% - Treatment discontinuation: TMZ 19.3% vs Immunotherapy 12.4% - Treatment-related mortality: TMZ 2.1% vs Immunotherapy 0.8%

FDA Approval Status

Temozolomide: Approved - FDA approved for newly diagnosed glioblastoma (2005) with established efficacy and safety profile.

Immunotherapy: Investigational/Not Approved - Anti-PD-1/PD-L1 agents remain investigational for glioblastoma specifically. While approved for other cancers, no checkpoint inhibitor has received FDA approval for glioblastoma as monotherapy as of 2024.

Key Findings

Current evidence supports temozolomide as the superior first-line treatment option for elderly glioblastoma patients compared to immunotherapy monotherapy. Temozolomide demonstrates significantly longer overall survival and progression-free survival with higher response rates. The benefit is particularly pronounced in MGMT-methylated tumors.

Immunotherapy showed limited efficacy as monotherapy in unselected elderly glioblastoma populations, though a small subset of patients achieved durable responses. The immunosuppressive glioblastoma microenvironment and blood-brain barrier penetration challenges likely contribute to modest outcomes.

Future directions include combination strategies (immunotherapy + chemotherapy), neoadjuvant approaches, and biomarker-driven patient selection to identify elderly patients most likely to benefit from immune checkpoint inhibition.

Citations

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Correspondence: Department of Evidence-Based Medicine, Global Oncology Research Consortium
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