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Timing of temozolomide in adult glioma: An exploratory study of an adaptive pre-radiotherapy approach in a mixed-grade cohort

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Abstract

Background

This exploratory study aimed to assess the impact of temozolomide (TMZ) timing—administered prior to radiotherapy (adaptive pre-RT TMZ) versus standard post-radiotherapy (post-RT TMZ)—on hematological toxicity and survival in adult patients with mixed-grade gliomas with unavoidable treatment delays.

Methods

A retrospective analysis was conducted on 134 patients with World Health Organization (WHO) grade 2–4 gliomas, Karnofsky performance status (KPS) ≥ 50 and residual disease. Cohorts received pre-RT TMZ (n = 39, ≥2 cycles) or post-RT TMZ (n = 95, ≥1 cycle). Progression-free survival (PFS), overall survival (OS), and toxicity were evaluated using multivariate Cox models and Fisher's exact tests.

Results

The median follow up was 88 months. The cohorts were well balanced. The adaptive pre-RT TMZ demonstrated a favorable safety profile; when censoring planned radiotherapy interruptions, severe toxicity-induced delays (> 4 weeks) were absent in the pre-RT arm compared to 11.6% in the post-RT arm (p = 0.033). While adaptive pre-RT TMZ was associated with longer unadjusted median OS (81 vs. 65 months) and PFS (47 vs. 37 months), multivariate analysis revealed no independent survival advantage (OS adjusted Hazard Ratio (aHR) 0.83, p = 0.520; PFS aHR 0.82, p = 0.420). A significant interaction was observed between TMZ timing and Isocitrate dehydrogenase-1 (IDH1) status (OS p = 0.046, PFS p = 0.055). In IDH1 wild-type tumors, adaptive pre-RT TMZ showed hypothesis-generating protective trends for PFS (aHR 0.50, p = 0.057) and OS (aHR 0.50, p = 0.074).

Conclusions

Adaptive pre-RT TMZ is a safe bridging strategy for RT delays, but confers no independent survival advantage in mixed-grade cohorts. Protective trends in IDH1 wild-type gliomas warrant prospective validation, particularly with O(6)-methylguanine-DNA methyltransferase (MGMT) promoter status profiling.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Subhash Gupta, upon reasonable request after data-anonymization.

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