Neurooncol Pract. 2023 Oct 27;11(2):171-177. doi: 10.1093/nop/npad065. eCollection 2024 Apr.

# Switch to generic formulation of temozolomide results in statistically significant increase in grade 3 and 4 bone marrow toxicity in glioma patients in the province of Alberta

Egiroh Omene [1 2], Omar Abdel-Rahman [1 2], Eugene Batuyong [3 4], Samir Patel [1 2], Roland Coppens [1], Jacob Easaw [1 2], Kelvin Young [1 2]

Affiliations

PMID: 38496912 PMCID: PMC10940820 (available on 2024-10-27) DOI: 10.1093/nop/npad065

## Abstract

**Background:** Temozolomide (TMZ) is an oral, systemic chemotherapy used chiefly for treating high-grade glioma. Due to the rising costs of systemic chemotherapy, many jurisdictions have replaced brand name with generic formulations. The aim of this study was to determine whether or not there was difference in the incidence of grade 3 or 4 bone marrow toxicity and median overall survival in patients treated with brand name versus generic TMZ in the province of Alberta, Canada. The province suspended the use of generic TMZ based on preliminary data pointing to excess toxicity.

**Methods:** This multicenter, retrospective study included data from patients with newly diagnosed high-grade glioma that received treatment with TMZ in Alberta. Multivariate logistic regression analysis was performed to determine the association between grade 3 or 4 toxicity to generic versus brand name TMZ exposure, ECOG score, and age. Kaplan-Meier survival estimates and log-rank testing were used to determine differences in overall survival between the brand name and generic TMZ cohorts, as well as the cytopenic versus non-cytopenic patients. Furthermore, a screening analysis for grade 3 or 4 bone marrow toxicity was conducted on all de novo glioma patients treated with brand name TMZ after Alberta preemptively stopped generic TMZ.

**Results:** Grade 3 or 4 neutropenia and thrombocytopenia were observed in 15% and 19% of patients treated with generic TMZ ($n$ = 156) as compared to 3% and 5% of patients ($n$ = 100) treated with brand name TMZ-treated patients; $P$= .003 and .001. A trend toward increased median overall survival in glioblastoma patients treated with generic TMZ (13.7 months) versus brand name (15.8 months, $P$ = .178.) was also observed through meeting statistical significance. Based on these results, the province stopped the use of generic TMZ and reverted to the Merck TMZ. An initial review of all new glioma patients ($n$ = 89) treated with Merck TMZ since the province stopped the generic drug demonstrated 3.4% and 10.1% grade 3 or 4 neutropenia, respectively.

**Conclusions:** The statistically significant difference in toxicity profile has prompted the province of Alberta to replace generic TMZ with brand name TMZ in high-grade glioma patients pending more detailed analysis. Our study provides evidence supporting the importance of conducting prospective studies on long-term safety for generic chemotherapies.

**Keywords:** TMZ; brand-name formulation; cytopenia; generic formulation; high-grade glioma.