Immune checkpoint inhibitors in combination with standard of care treatment versus standard treatment alone for newly diagnosed glioblastoma: a systematic review and meta-analysis

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Aims and scope →

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Abstract

Introduction

The standard treatment for patients with newly diagnosed glioblastoma is based on surgical resection associated with radiotherapy (RT) and temozolomide (TMZ). However, the effectiveness of this approach is limited by the intratumoral heterogeneity and by the enzyme MGMT (O6-methylguanine-DNA methyltransferase) activity itself. Immune checkpoint inhibitors (ICIs) emerge as a compelling therapeutic strategy combined with RT and TMZ for these patients.

Methods

A systematic review and meta-analysis of English-language studies from PubMed, Embase, and ICTRP was conducted to assess the efficacy and safety of ICIs in combination with the standard treatment for newly diagnosed glioblastoma. The primary outcomes were overall survival (OS), progression-free survival (PFS), and treatment-related adverse events. Secondary endpoints were OS and PFS according to extent of surgical resection (ESR), and adverse events for grade 3 or above. Hazard ratios (HRs) with 95% confidence intervals (CIs) were pooled. Quality assessment and risk of bias were evaluated.

Results

Three randomized controlled trials (RCTs) with 938 patients were included, 506 (54%) of whom had been administered ICI + TMZ + RT. OS (HR: 1.06, 95% CI: 0.92–1.21; $p = 0.41$; $I^2 = 0\%$) and PFS (HR: 1.05, 95% CI: 0.94–1.17; $p = 0.35$; $I^2 = 44\%$) were not significantly different between the ICIs and the standard treatment alone groups. Nivolacbe, as an adverse event, occurred significantly more frequently in the ICI group (HR: 1.58, 95% CI: 1.06–2.42; $p = 0.03$; $I^2 = 0\%$). Other adverse events showed no significant differences between the groups. No subgroup analysis – neither OS nor PFS stratified by ESR – demonstrated significant differences between treatment groups.

Conclusion

This meta-analysis demonstrates the addition of ICIs to TMZ plus RT does not confer statistically significant survival benefits in newly diagnosed glioblastoma and glioblastoma are significantly associated with an increased incidence of headache when compared to the standard treatment alone. This signal was not accompanied by a significant rise in other adverse events, suggesting the overall safety remains manageable.

Data availability

No new datasets were generated; existing data were analyzed.

Abbreviations

RT: radiotherapy

TMZ: Temozolomide

OS: overall survival

MGMT: O6-methylguanine-DNA methyltransferase

ICI: immune-checkpoint inhibitor

PFS: progression-free survival

HR: hazard ratio

OR: odds ratio

RCT: randomized controlled trial

ESR: extent of surgical resection

IDH1: isocitrate dehydrogenase

KPS: karnofsky performance status

ECOG: Eastern Cooperative Oncology Group

CI: confidence interval

GTR: gross total resection

STR: subtotal resection

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Contributions

All authors contributed significantly to the study's conception and design. V.A.F.N. developed the methodology for the article. The comprehensive literature search was conducted by M.L.E.G. and J.C.A.F., L.E.S.R., and J.H.N.A., ensuring a thorough review of relevant studies. Data extraction was performed by J.H.N.A., L.C.M., and V.A.F.N., who ensured the accuracy and completeness of the data collected. V.A.F.N. conducted the statistical analysis. The first draft of the manuscript was crafted by J.C.A.F. The manuscript was critically reviewed by V.A.F.N., J.H.N.A., L.C.M., and H.R.S. and offered valuable feedback and revisions to enhance the quality and clarity of the work. All authors have read and approved the final manuscript, demonstrating their collective agreement on the study's findings and conclusions.

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Ethics declarations

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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