

Impact of PD-1 inhibitor immunotherapy on survival in patients with newly diagnosed and recurrent glioblastoma: a systematic review of comparative evidence

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Abstract

Introduction: Glioblastoma (GBM) is the most common and aggressive primary malignant brain tumor. PD-1 inhibitors have shown potential use in GBM. There is some evidence to suggest that programmed death-1 (PD-1) inhibitors may be effective in treating GBM. However, the results of clinical trials conducted to date have been inconclusive, which has led to questions regarding the efficacy of PD-1 inhibitors in this context.

Aim: This systematic review aimed to evaluate whether PD-1 inhibitors provide a survival advantage over the standard regimens in GBM.

Materials and methods: This review followed the PRISMA guidelines. Comprehensive searches were conducted in PubMed, Scopus, and the Cochrane Library from 2015 to 2025. The extracted data included the study design, sample characteristics, interventions, comparators, and reported survival outcomes. The risk of bias was assessed using the Cochrane RoB 2 tool.

Results: Four trials were included in this review. In newly diagnosed GBM, PD-1 inhibitors plus radiotherapy showed an inferior overall survival (OS) rate compared to standard regimens (median OS [mOS] 13.4 vs. 14.9 months, HR 1.31 [95% CI: 1.09-1.58]). PD-1 inhibitors as an adjuvant to temozolomide-based therapy also showed no statistically significant improvement in OS (mOS 11.6 vs. 11.8 months, HR 0.85 [95% CI 0.54-1.33]) or progression-free survival (PFS) (median PFS [mPFS] 7.4 vs. 5.9 months, HR 0.77 [95% CI 0.49-1.19]) compared to placebo. For recurrent GBM, there was no significant difference in OS between nivolumab and bevacizumab (mOS 11.6 vs. 10.0 months, HR 1.04 [95% CI: 0.83-1.3]). Consistently, PD-1 inhibitors did not demonstrate a survival advantage in either newly diagnosed or recurrent glioblastoma.

Conclusion: PD-1 inhibitors showed no statistically significant improvement in OS and PFS in patients with GBM.

Keywords

PD-1 inhibitor, immunotherapy, glioblastoma

Introduction

Glioblastoma (GBM) is the most common and aggressive

primary malignant brain tumor in adults, characterized by rapid proliferation, diffuse infiltration, and profound resistance to conventional therapies.^[1] Despite maximal surgical resection followed by radiotherapy and temozolo-

mide—commonly known as the Stupp regimen—clinical outcomes remain poor, thus exhibiting a high recurrence rate.^[2,3] In recent years, immunotherapy has emerged as a promising therapeutic strategy for the treatment of various solid tumors. Among these, immune checkpoint inhibitors (ICIs), particularly agents targeting the programmed cell death-1 (PD-1) receptor, have demonstrated significant survival benefits in melanoma, non-small cell lung cancer, and other malignancies, including emerging new breakthrough clinical trial in treating newly diagnosed or recurrent glioblastomas.^[4]

Several early-phase clinical trials have evaluated different PD-1 inhibitors, such as nivolumab, bevacizumab, and pembrolizumab, in GBM. However, the results are varied. Therefore, a systematic synthesis of current literature is essential.

Aim

This review aims to evaluate whether PD-1 inhibitors provide a survival advantage over standard regimens in patients with GBM. By critically examining the existing clinical evidence, this study seeks to clarify their clinical utility, identify gaps in knowledge, and inform future research and therapeutic strategies.

Material and methods

Searching strategies

This study was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. This systematic review was not registered in PROSPERO because data extraction had commenced prior to protocol submission. However, the protocol was developed a priori and adhered to PRISMA 2020 guidelines.

A literature search was conducted to identify the effects

of PD-1 inhibitor immunotherapy on overall survival in patients with GBM. The literature search was conducted using a predefined set of keywords from three primary databases: PubMed, Scopus, and CENTRAL, as shown in **Table 1**.

Following the removal of duplicate entries, titles and abstracts were independently screened by two reviewers (TMLSW, FH). Full-text versions of these studies were retrieved and assessed in detail to determine eligibility for inclusion. Each stage of the search and selection process was performed independently to reduce the risk of selection bias.

Study eligibility criteria

Studies were included if they met the following criteria: 1) primary research (clinical trials, cohort, or single-arm study) focusing on PD-1 inhibitors as the treatment group; 2) assessment of overall survival rate or progression-free survival rate in GBM; and 3) publications between 2015 and 2025. Studies were excluded if they met any of the following criteria: 1) focus on another drug tested with PD-1 as an adjuvant or pretreatment; 2) limited to narrative or literature reviews; 3) not published in English; or 4) full text was unavailable.

Data extraction and risk of bias assessment

The following data were extracted from each eligible study: (1) the first author, study name or abbreviation, and year of publication; (2) study-level characteristics, including geographic location, study design, and sample size; and (3) details of the intervention and comparator. OS was designated as the primary endpoint, whereas PFS and event-free survival (EFS) were collected as secondary endpoints when available. The risk of bias in the studies was evaluated using a revised Cochrane risk-of-bias tool for randomized trials (RoB2) by three reviewers (TMLSW, FH, MH). Assessments were performed independently by the investigators, and any disagreements were resolved through consensus-based discussions including the senior reviewer (RAA).

Table 1. Keywords used for literature search in each database

Database	Keyword
PubMed	((“PD-1 inhibitor” OR “anti PD-1” OR “nivolumab” OR “pembrolizumab”) AND (“glioblastoma” OR “glioblastoma multiforme” OR “recurrent glioblastoma” OR “GBM”) AND (“survival” OR “death” OR “progression free” OR “overall survival” OR “event free”))
Scopus	(TITLE-ABS-KEY (“PD-1 inhibitor” OR “anti PD-1” OR “nivolumab” OR “pembrolizumab”) AND (“glioblastoma” OR “glioblastoma multiforme” OR “recurrent glioblastoma” OR “GBM”) AND (“survival” OR “death” OR “progression free” OR “overall survival” OR “event free”))
CENTRAL	(“PD-1 inhibitor” OR “anti PD-1” OR “nivolumab” OR “pembrolizumab”) AND (“glioblastoma” OR “glioblastoma multiforme” OR “recurrent glioblastoma” OR “GBM”) AND (“survival” OR “death” OR “progression free” OR “overall survival” OR “event free”)

Results

Study flow and characteristics

A systematic search of three electronic databases conducted on November 23rd, 2025, identified 380 records. After removing duplicates, 286 records were screened based on their titles and abstracts. Of these, 234 were excluded for not meeting the inclusion criteria. The full texts of the remaining 52 articles were sought for retrieval, and six full texts were unable to be obtained because the data were secured for ongoing clinical trials. The full texts of the remaining 46 reports were assessed for eligibility, resulting

in the exclusion of 42 studies, with reasons documented in the PRISMA flow diagram (Fig. 1). Four studies fulfilled the eligibility criteria and were included in the final synthesis.

Four studies, all of which were randomized controlled trials (RCTs), were published between 2020 and 2023. All studies included were multicenter, international, and registered studies with varied sample sizes ranging from 103 to 716 participants. The patient characteristics of all studies assessed GBM patients, with one study focusing solely on recurrent GBM. The characteristics of all studies included in this systematic review are presented in Table 2. The treatment regimens, dosing schedules, and outcome measures are summarized in Table 3.

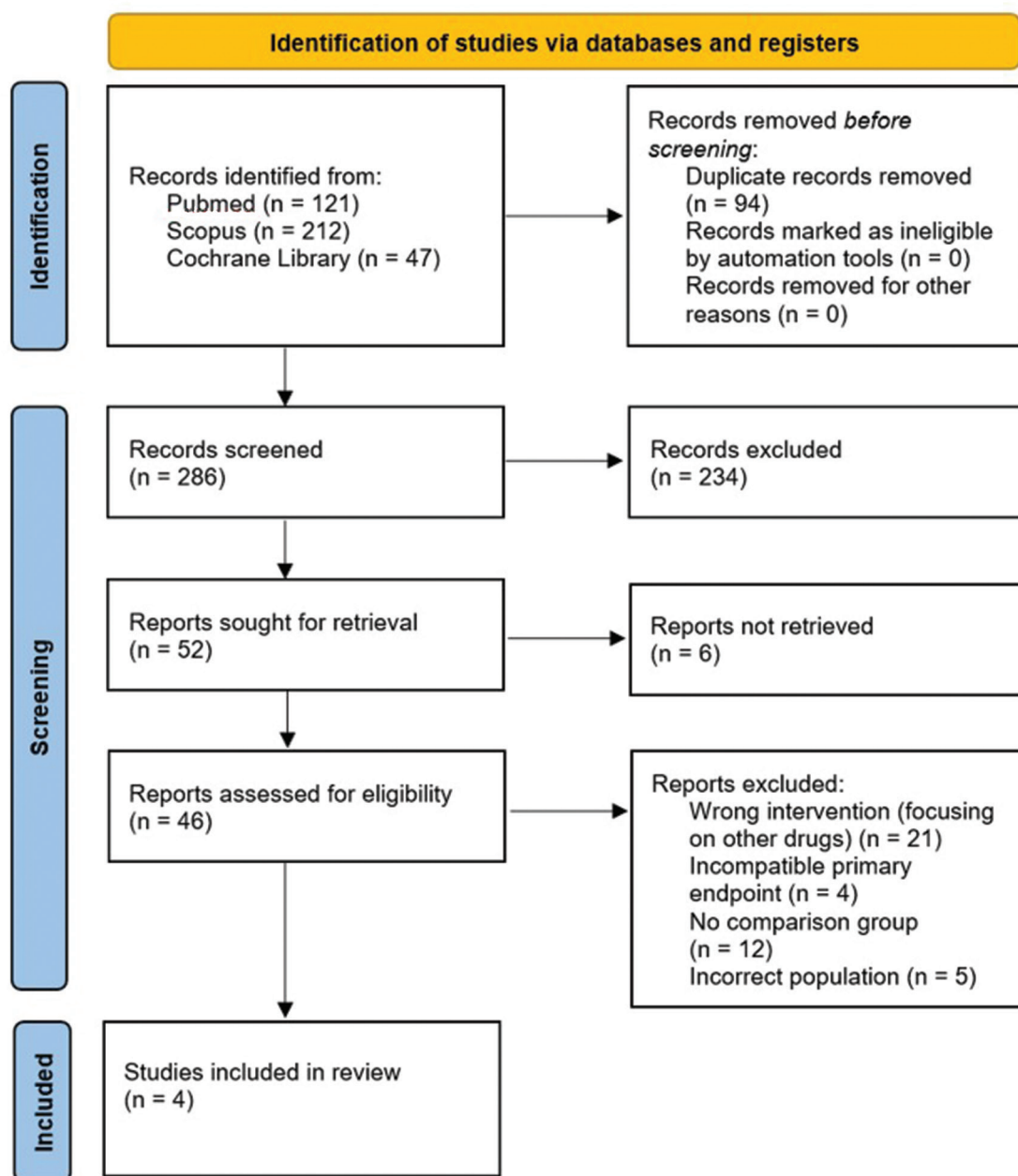


Figure 1. The PRISMA flow diagram for this systematic review.

Table 2. Included studies characteristics

No	Author (year)	Type of study	Location	Sample characteristics	
				Patients characteristics	Sample population (n)
1	Omuro et al. (2023) ^[4]	RCT	125 locations from 19 countries (United States, Australia, Europe, Japan, Russia)	Patients with newly diagnosed, histologically confirmed, supratentorial glioblastoma (GBM) with unmethylated MGMT promoter Median age of 59.5 (treatment group) and 56 (control group), with a range of 18-83 years	n=560 Treatment group (n=280) Control group (n=280)
2	Sim et al. (2023) ^[5]	RCT	Australia and United States	Elderly patients (aged >65 years) with newly diagnosed glioblastoma Median age of 73 with a range of 65-81 years	n=103 Treatment group (n=69) Control group (n=34)
3	Lim et al. (2022) ^[6]	RCT	123 locations from 19 countries (United States, Australia, Europe, Japan, Russia)	Patients with newly diagnosed, histologically confirmed supratentorial glioblastoma who had not received any treatment aside from surgery, with methylated MGMT promoter Median age of 60 with a range of 18-81 years	n=716 Treatment group (n=358) Control group (n=358)
4	Reardon et al. (2020) ^[7]	RCT	112 locations from 12 countries (United states, Australia, and Europe)	Patients with histologically confirmed grade IV recurrent glioblastoma after temozolomide + radiotherapy treatment. Median age of 55.5 (treatment group) and 55 (control group), with a range of 22-77 years	n=369 Treatment group (n=184) Control group (n=185)

The risk of bias for the included studies was assessed using the Cochrane RoB 2 tool for analyzing RCTs). A key methodological concern was the absence of a control or comparator group in four of the six studies, which may introduce confounding and increase the risk of selection bias. Additionally, one study reported missing outcome data affecting more than 5% of the participants, indicating a potential risk of attrition bias. Despite these limitations, all studies demonstrated adequate alignment between the prespecified analysis plans and the reported outcomes. A visual summary of the risk of bias across all assessed domains is provided in **Fig. 2**.

Impact on newly diagnosed glioblastoma

Overall survival rate

Omuro et al.^[4] compared nivolumab combined with radiotherapy to temozolomide combined with radiotherapy. The median OS in the nivolumab group was 13.4 months (95% CI: 12.6–14.3) versus 14.9 months (95% CI: 13.3–16.1) with the hazard ratio (HR) of 1.31 (95% CI: 1.09–1.58; $p=0.0037$), indicating a statistically significant survival advantage for the temozolomide group. The 24-month OS rate was also higher in the control group (21.2%, 95% CI: 16.4–26.5) than in the nivolumab group (10.3%, 95% CI: 6.8–14.6).

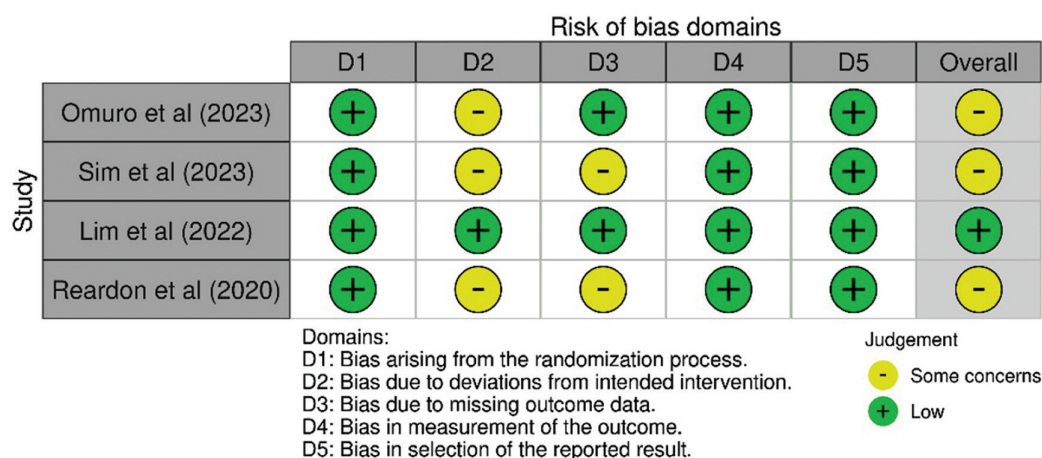
**Figure 2.** Risk of bias assessment for all included studies using the Cochrane RoB 2 tool.^[11]

Table 3. Study result measurements and outcomes

No	Author (year)	Group Treatment	Control	Result measurement	Outcome
1	Omuro et al. (2023) ^[4]	Nivolumab 240 mg every 2 weeks for eight cycles, then 480 mg every 4 weeks +Radiotherapy	Temozolomide 75 mg/m ² daily during radiotherapy and 150–200 mg/m ² /day 5 each 28 days during maintenance +Radiotherapy	HR of median OS rate was 1.31 (95% CI: 1.09–1.58, <i>p</i> =0.0037) mOS of treatment group was 13.4 months (95% CI: 12.6–14.3) mOS of control group was 14.9 months (95% CI: 13.3–16.1) HR of median PFS rate was 1.38 (95% CI: 1.15–1.65) mPFS of treatment group was 6 months (95% CI: 5.7–6.2) mPFS of control group was 6.2 months (95% CI: 5.9–6.7) 24-month OS rate of treatment group was 10.3% (95% CI: 6.8–14.6) vs. control group 21.2% (95% CI: 16.4–26.5) 18-month PFS rate of treatment group was 3% (95% CI: 1.3–5.8) vs. control group 8.1% (95% CI: 5.1–11.9)	Temozolomide (standard regimen) appeared as a superior line of treatment with a significantly higher median and 24-month OS rate compared to anti-PD1 (nivolumab). Temozolomide also showed superior impact on progression-free survival compared to nivolumab.
2	Sim et al. (2023) ^[5]	Nivolumab 240 mg once daily on days 1 and 15 every 28 days for cycles 1–4, then 480 mg once daily on day 1 and every 28 days for cycles 5–6 Hypofractionated chemoradiation, followed by a 4-week treatment break, followed with 6 cycles of nivolumab + temozolomide	Temozolomide only Hypofraction chemo-radiation, followed by a 4-week treatment break, followed by up to 6 cycles of temozolomide	HR of median OS rate was 0.85 (95% CI: 0.54–1.33) mOS of treatment group was 11.6 months (95% CI: 9.7–13.4) mOS of control group was 11.8 months (95% CI: 8.3–14.8) HR of median PFS rate was 0.77 (95% CI: 0.49–1.19) mPFS of treatment group was 7.4 months (95% CI: 6.3–8.7) mPFS of control group was 5.9 months (95% CI: 3.6–8.2)	Although nivolumab as an adjuvant showed a superior PFS rate compared to the standard regimen alone, there was no statistically significant impact on the PFS rate, as well as the OS rate, of adding nivolumab to the standard regimen of chemoradiotherapy + temozolomide.
3	Lim et al. (2022) ^[6]	Nivolumab 240 mg every 2 weeks for eight cycles, then 480 mg every 4 weeks +Temozolomide +Radiotherapy	Placebo +Temozolomide +Radiotherapy	HR of median OS rate was 1.1 (95% CI: 0.9–1.13) mOS of treatment group was 28.9 months (95% CI: 24.4–31.6) mOS of control group was 32.1 months (95% CI: 29.4–33.8) HR of median PFS rate was 1.1 (95% CI: 0.9–1.3) mPFS of treatment group was 10.6 months (95% CI: 8.9–11.8) mPFS of control group was 10.3 months (95% CI: 9.7–12.5) 24-month OS rate of treatment group was 60.9% (95% CI: 54.4–66.8) vs. control group 67.1% (95% CI: 61–72.6)	There was no statistically significant impact on the overall survival and progression-free survival rate of adding nivolumab to the standard regimen of radiotherapy + temozolomide.
4	Reardon et al. (2020) ^[7]	Nivolumab 3 mg/kg every 2 weeks Patients have finished radiotherapy + temozolomide standard treatment.	Bevacizumab (anti- VEGF agent) 10 mg/kg every 2 weeks Patients have finished radiotherapy + temozolomide standard treatment	HR of median OS rate was 1.04 (95% CI: 0.83–1.30, <i>p</i> =0.76) mOS of treatment group was 9.8 months (95% CI: 8.2–11.8) mOS of control group was 10 months (95% CI: 9–11.8) HR of median PFS rate was 1.97 (95% CI: 1.57–2.48, <i>p</i> <0.001) mPFS of treatment group was 1.5 months (95% CI: 1.5–1.6) mPFS of control group was 3.5 months (95% CI: 2.9–4.6) 18-month OS rate of treatment group was 21.7% (95% CI: 16.1–27.9) vs. control group 21.6% (95% CI: 15.8–28) 18-month PFS rate of treatment group was 5.8% (95% CI: 3.0–11.0) vs. control group 8.9% (95% CI: 5.1–14.1)	There was no statistically significant impact on overall survival rate between anti PD-1 and anti-VEGF therapy after the standard regimen of radiotherapy + temozolomide. However, bevacizumab showed a higher median PFS rate compared to nivolumab.

In Lim et al.^[6], nivolumab was added to standard radiotherapy and temozolomide and compared with placebo plus standard therapy. The median OS was 28.9 months (95% CI: 24.4–31.6) in the nivolumab group and 32.1 months (95% CI: 29.4–33.8) in the placebo group. The hazard ratio for OS was 1.10 (95% CI: 0.90–1.13), demonstrating no statistically significant improvement in survival with nivolumab addition. The 24-month OS rate was 60.9% (95% CI: 54.4–66.8) in the nivolumab group versus 67.1% (95% CI: 61.0–72.6) in the control group.

In elderly patients receiving hypofractionated chemoradiotherapy^[5], adjuvant nivolumab plus temozolomide yielded a median OS of 11.6 months (95% CI: 9.7–13.4), compared with 11.8 months (95% CI: 8.3–14.8) in the temozolomide-only group. The hazard ratio for OS was 0.85 (95% CI: 0.54–1.33), indicating no statistically significant survival benefit with nivolumab.

Progression-free survival rate

In Omuro et al.^[4], the median PFS was 6.0 months (95% CI: 5.7–6.2) in the nivolumab group compared to 6.2 months (95% CI: 5.9–6.7) in the temozolomide group, with a hazard ratio of 1.38 (95% CI: 1.15–1.65). The 18-month PFS rate was 3.0% (95% CI: 1.3–5.8) in the nivolumab group and 8.1% (95% CI: 5.1–11.9) in the control group, demonstrating inferior disease control with nivolumab than with chemotherapy.

However, a study by Lim et al.^[6] showed that the median PFS was 10.6 months (95% CI: 8.9–11.8) in the nivolumab group and 10.3 months (95% CI: 9.7–12.5) in the placebo group, with a hazard ratio of 1.10 (95% CI: 0.90–1.30), indicating no significant difference between groups.

Sim et al.^[5] also reported a median PFS of 7.4 months (95% CI: 6.3–8.7) in the nivolumab group and 5.9 months (95% CI: 3.6–8.2) in the control group, with a hazard ratio of 0.77 (95% CI: 0.49–1.19). Despite a numerically longer PFS with nivolumab, the difference was not significant.

Impact on recurrent glioblastoma

Overall survival rate

In the recurrent setting^[7], nivolumab was compared with bevacizumab following radiotherapy and temozolomide. The median OS was 9.8 months (95% CI: 8.2–11.8) in the nivolumab group and 10.0 months (95% CI: 9.0–11.8) in the bevacizumab group. The hazard ratio for OS was 1.04 (95% CI: 0.83–1.30; $p=0.76$), indicating no statistically significant difference in overall survival between the two treatments. The 18-month OS rates were 21.7% (95% CI: 16.1–27.9) for nivolumab and 21.6% (95% CI: 15.8–28.0) for bevacizumab.

Progression-free survival rate

According to Reardon et al.^[7], the PFS difference between nivolumab and bevacizumab was significantly different. The median PFS was shorter in the nivolumab group at 1.5 months (95% CI: 1.5–1.6) compared with 3.5 months (95%

CI: 2.9–4.6) in the bevacizumab group, with a hazard ratio of 1.97 (95% CI: 1.57–2.48; $p<0.001$). The 18-month PFS rates were 5.8% (95% CI: 3.0–11.0) for nivolumab and 8.9% (95% CI: 5.1–14.1) for bevacizumab.

Discussion

Despite the initial promise of immune checkpoint inhibitors in various malignancies, clinical trials investigating PD-1 inhibitors in glioblastoma have largely failed to demonstrate significant improvements in overall survival. In newly diagnosed glioblastoma, PD-1 inhibitors showed no statistically significant improvement compared to standard temozolomide-based chemoradiotherapy alone, either in the general population or in the geriatric setting.^[5,6] Moreover, PD-1 inhibitors as a single agent yielded poorer median overall survival than standard temozolomide, with a statistically significant hazard ratio that was not markedly elevated.^[4] This consistent lack of efficacy across treatment settings contrasts sharply with the substantial survival advantages observed with PD-1 inhibition in other cancer types, underscoring the unique immunological challenges posed by the GBM microenvironment, which may render the tumor less susceptible to traditional immune checkpoint blockade.^[8] The lack of survival benefit with PD-1 inhibitors in recurrent GBM was further corroborated by analyses indicating comparable median OS between nivolumab and bevacizumab.^[7] PD-1 inhibitors have also shown minimal to no benefit for PFS in GBM patients.^[5–7]

This may be attributable to the distinct tumor microenvironment of GBM compared with that of other malignancies. GBM is characterized by a highly immunosuppressive tumor microenvironment, featuring dense infiltration of myeloid-derived suppressor cells and tumor-associated macrophages that actively suppress anti-tumor immune responses.^[9] In contrast, an RCT of PD-1 inhibitors in melanoma has demonstrated significant survival benefits, underscoring the differential immune landscapes of these cancers.^[10] Similar efficacy has been observed in other malignancies, such as non-small cell lung cancer, where pembrolizumab improves overall survival rates.^[11] The failure of PD-1 inhibition in GBM likely stems from the tumor's unique immunosuppressive mechanisms, including PD-L1 expression on GBM cells, which induces T-cell anergy and exhaustion.^[12]

However, PD-1 therapy in GBM may still have a beneficial impact on specific patient subsets or when combined with other therapeutic strategies. The administration of pembrolizumab followed by continued adjuvant therapy post-surgery has shown promise in increasing patients' OS and enhancing both local and systemic immune responses in patients with recurrent GBM, as shown in the Cloughesy et al. study.^[13] Further research is needed to elucidate the optimal combination strategies and patient selection criteria to maximize the therapeutic potential of PD-1 inhibitors in this challenging disease.

Study limitation

This study systematically reviewed the current literature on PD-1 inhibitors' impact on GBM cases, both primary and recurrent GBM. By assessing the risk of bias within included studies, a potential bias within studies is addressed, which is essential for clinical implications. However, some limitations must be addressed. As this is limited to a systematic review only and lacks meta-analysis, a pooled effect of PD-1 inhibitors in GBM in comparison to standard regimens is not evaluated. The heterogeneity of the results across studies is not identified, which can be done with meta-analysis. Publication bias analysis is not done as well. Lack of meta-analysis in this study due to an insufficient number of studies: 3 studies compared with standard of care, and 1 study comparing a different regimen of PD-1 inhibitors. As the comparator of most studies is not unified, the ineffectiveness of PD-1 inhibitor administration is probably not limited to standard therapy. Thus, the interaction between PD-1 inhibitors and symptomatic therapy—such as corticosteroids—is not explored, which may be responsible for the ineffectiveness of PD-1 inhibitors.

Future directions

Further research is essential, particularly through rigorously designed, high-quality randomized controlled trials that address the limitations identified in the current evidence. Future investigations should focus on optimized combination strategies, such as pairing PD-1 inhibitors with neo-adjuvant administration, personalized immunotherapeutic approaches, or rational combinations with agents targeting the GBM immune microenvironment. Such studies should also clearly define and stratify patient subgroups, molecular profiles, and adjuvant therapy protocols to better determine which populations may benefit from these treatments. Advancing the therapeutic potential of PD-1 inhibition in GBM will require strategic trial designs that overcome the tumor's immunosuppressive barriers and refine the role of combination adjuvant regimens.

Conclusion

This systematic review does not confer a survival advantage in patients with newly diagnosed or recurrent GBM compared with standard-of-care treatment.

Despite the known efficacy of PD-1 inhibitors in other malignancies, current comparative evidence does not support a meaningful survival benefit of PD-1 inhibitor therapy in patients with glioblastoma.

References

1. Kanderi T, Munakomi S, Gupta V. Glioblastoma multiforme. In: Stat-Pearls. StatPearls Publishing; 2025. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK558954/> (Accessed December 6, 2025).
2. Kotecha R, Odia Y, Khosla AA, et al. Key clinical principles in the management of glioblastoma. *JCO Oncol Pract* 2023; 19(4):180–9. doi: 10.1200/OP.22.00476
3. Loebel F, Sánchez CV, Alvarez LB, et al. Profiles of survival prediction in glioblastoma. *Brain Spine* 2025; 5:104324. doi: 10.1016/j.bas.2025.104324
4. Omuro A, Brandes AA, Carpentier AF, et al. Radiotherapy combined with nivolumab or temozolomide for newly diagnosed glioblastoma with unmethylated MGMT promoter: An international randomized phase III trial. *Neuro-Oncol* 2023; 25(1):123–34. doi: 10.1093/neuonc/noac099
5. Sim HW, Wachsmuth L, Barnes EH, et al. NUTMEG: A randomized phase II study of nivolumab and temozolomide versus temozolomide alone in newly diagnosed older patients with glioblastoma. *Neuro-Oncol Adv* 2023; 5(1):vdad124. doi: 10.1093/noonjnl/vdad124
6. Lim M, Weller M, Idbaih A, et al. Phase III trial of chemoradiotherapy with temozolomide plus nivolumab or placebo for newly diagnosed glioblastoma with methylated MGMT promoter. *Neuro-Oncol* 2022; 24(11):1935–49. doi: 10.1093/neuonc/noac116
7. Reardon DA, Brandes AA, Omuro A, et al. Effect of nivolumab vs bevacizumab in patients with recurrent glioblastoma: The CheckMate 143 Phase 3 Randomized Clinical Trial. *JAMA Oncol* 2020; 6(7):1003. doi: 10.1001/jamaoncol.2020.1024
8. Filley AC, Henriquez M, Dey M. Recurrent glioma clinical trial, CheckMate-143: the game is not over yet. *Oncotarget* 2017; 8(53):91779–94. doi: 10.18632/oncotarget.21586
9. Baskaran AB, Kozel OA, Venkatesh O, et al. Immune checkpoint inhibitors in glioblastoma IDHwt treatment: a systematic review. *Cancers* 2024; 16(24):4148. doi: 10.3390/cancers16244148
10. Yasinjan F, Xing Y, Geng H, et al. Immunotherapy: a promising approach for glioma treatment. *Front Immunol* 2023; 14:1255611. (Accessed December 7, 2025). Available from <https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2023.1255611/full>
11. Marei HE, Hasan A, Pozzoli G, et al. Cancer immunotherapy with immune checkpoint inhibitors (ICIs): potential, mechanisms of resistance, and strategies for reinvigorating T cell responsiveness when resistance is acquired. *Cancer Cell Int* 2023; 23(1):64. doi: 10.1186/s12935-023-02902-0
12. Kreatsoulas D, Bolyard C, Wu BX, et al. Translational landscape of glioblastoma immunotherapy for physicians: guiding clinical practice with basic scientific evidence. *J Hematol Oncol* 2022; 15(1):80. doi: 10.1186/s13045-022-01298-0
13. Cloughesy TF, Mochizuki AY, Orpilla JR, et al. Neoadjuvant anti-PD-1 immunotherapy promotes a survival benefit with intratumoral and systemic immune responses in recurrent glioblastoma. *Nat Med* 2019; 25(3):477–86. doi: 10.1038/s41591-018-0337-7

Additional information

Ethical statement

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

Conflict of interest

The authors have declared that no competing interests exist.

Artificial Intelligence (AI) use

The authors accept full responsibility for the content of the manuscript, including the disclosure of any use of AI. No AI tools were used in the preparation of this manuscript.

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Data availability

All of the data that support the findings of this study are available in the main text.