Surgery-Anchored Immunotherapy for Glioblastoma: Extent of Resection as a Determinant of Benefit with Dendritic Cell Vaccines and Adoptive Cells

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BACKGROUND

- Cytoreduction reduces immunosuppressive tumor burden and can create a minimal-residual-disease state where immunotherapies may work best.
- Despite strong a biologic rationale, repeated neutral trials for upfront checkpoint blockade in GBM patients.
- Perioperative corticosteroids, which are often necessary for edema control, are a practical surgery-adjacent variable that can blunt immune activation and confound outcomes.
- Key effect modifiers include extent of resection, steroid exposure, and MGMT promoter methylation status.

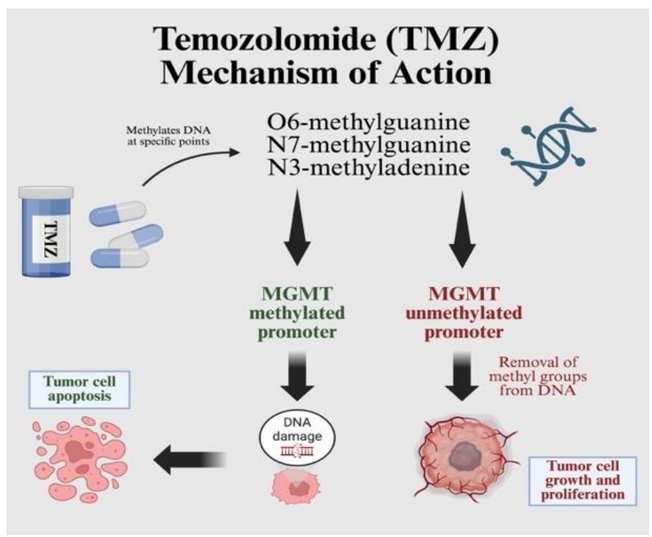
METHODS

- Qualitative systematic review conducted per PRISMA guidelines, targeting adult glioma/GBM trials with an adequate comparator arm.
- Databases: MEDLINE (PubMed), Embase, and Cochrane CENTRAL from January 1st, 2020 to August 10th, 2025.
- Included emerging immunomodulatory strategies; emphasis was placed on dendritic cell vaccines and adoptive cell therapies.
- Outcomes: OS and PFS (primary); landmark survival rates, duration of response, biomarkers/effect modifiers, and steroid prevalence (secondary).
- Safety: CTCAE grade 3 or higher adverse events and treatment-related mortality; extracted alongside operative-context modifiers (EOR, steroid exposure, and MGMT).

Results & Discussion

- 797 records identified; 13 trials included (9 newly diagnosed, 3 recurrent, and 1 mixed).
- Across included trials, extent of resection consistently tracked with better outcomes and larger apparent gains from vaccine/adoptive strategies. Supports aggressive-but-safe cytoreduction as an immunotherapy primer.
- Best supported surgery-adjacent signals came from DC vaccines and adoptive cells therapies, not upfront checkpoint blockade.
- DCVax-L trials: median OS 19.3 vs. 16.5 months (external controls) with improved long-term survival (5-yr OS 13.0% vs 5.7%).
- CIK cell therapy study: improved median OS (23.1 vs. 14.9 months) and PFS (8.1 vs. 5.5 months).
- Surgery is the enabling platform: (1) maximal safe resection amplifies immunotherapy by minimalizing residual disease, (2) reducing immunosuppressive mass effect, and (3) supplying antigen-rich tissue for vaccine manufacture.
- Steroid-sparing perioperative management is a major actionable takeaway: baseline corticosteroid use consistently attenuated immunotherapy benefit, making edema control strategies central to trial success and real-world translation.

A



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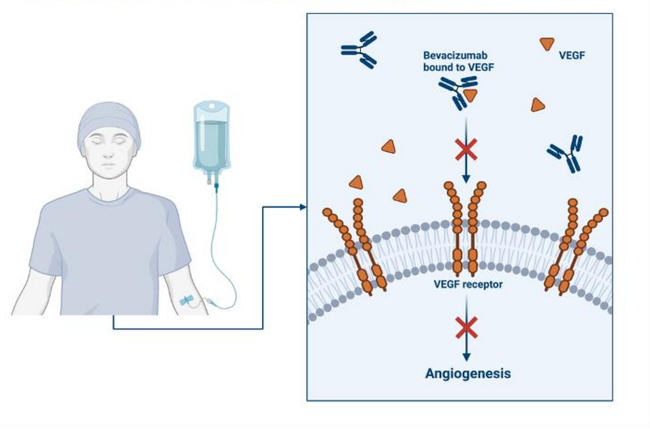

Figure 1. Current medications often used in the treatment of glioma.

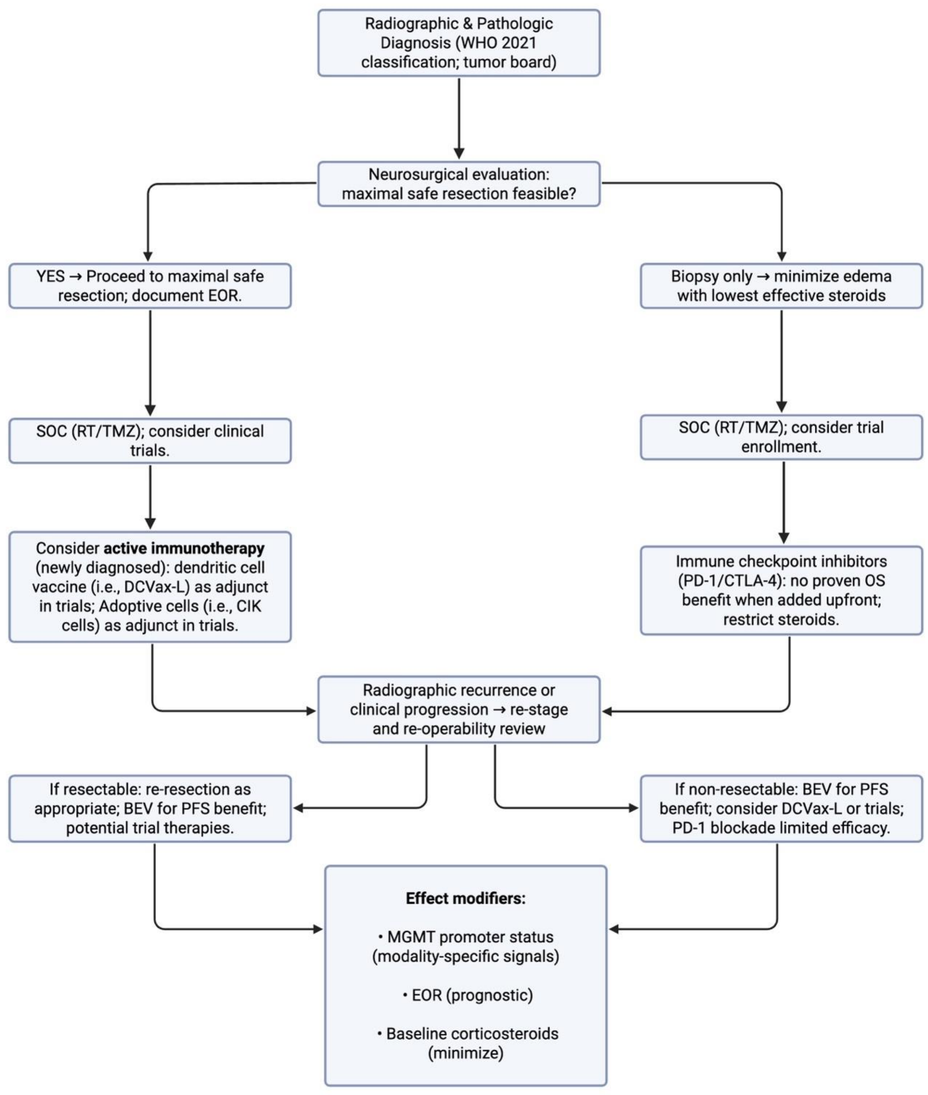

Figure 2. GBM clinical decision-making algorithm and potential implementation of adjunctive immunotherapy.

Modifier	Implications for Immunotherapy Use	Representative Evidence	Strength
MGMT Promoter Methylation	Patient-specific treatment considerations; PD-1 adds no benefit in methylated disease; interferon-α shows signal in unmethylated; DC vaccines may augment OS in methylated.	Lim et al. (2022); Liau et al. (2022); Guo et al. (2023)	Moderate
Extent of Resection (EOR)	Maximal safe resection likely enables vaccine benefit in minimal residual disease settings; verify EOR centrally.	Muragaki et al. (2023); Han et al. (2022)	Low-Moderate
Baseline Corticosteroids	Avoid or taper when possible; baseline dexamethasone associates with worse OS and muted immune checkpoint inhibitor activity.	Nayak et al. (2021); Lassman et al. (2025)	Moderate
Age (>65 years old)	Feasible and tolerable, but no efficacy signal with PD-1 in elderly; age alone should not exclude trials.	Sim et al. (2023)	Low
Exploratory Biomarkers	Interferon response signatures after DCVax-L + poly-ICLC correlate with improved outcomes; angiogenic markers (PIGF/sVEGFR1) track with poor immune checkpoint inhibitor overall survival.	Everson et al. (2024); Nayak et al. (2021)	Low-Moderate

Table 2. Effect modifiers and practical implications

CONCLUSION

- Comparator-trial evidence supports a surgery-anchored, steroid-sparing strategy when integrating active immunotherapies into GBM care.
- DC vaccines and adoptive/cellular therapies show the most consistent clinical signals (OS/PFS improvements and occasional durable survivors) compared with standard therapy.
- Routine upfront checkpoint blockade is not currently justified based on largely neutral first-line outcomes in the included evidence base.
- Future trials should prospectively stratify, or randomize within strata, by extent of resection and MGMT status.
- For operative practice: prioritize maximal safe resection, anticipate tissue for vaccines, and minimize baseline corticosteroids, if feasible.
- Takeaway: Optimize the surgical window (low residual disease + low steroids) to give immunotherapies the best chance of translating into meaningful survival gains in GBM patients.