

Rare gliomas: standard treatment approaches and new target therapies

Summarize the findings: Bruno F, Pellerino A, Pronello E, Rudà R. Rare gliomas: standard treatment approaches and new target therapies. Curr Opin Neurol. 2025 Sep 25. doi: 10.1097/WCO.0000000000001428. PMID: 40990677.

Here is a structured summary of the key points and findings from Bruno et al. (2025), *Rare gliomas: standard treatment approaches and new target therapies* [PubMed](#)

Background & Scope

- “Rare gliomas” refer to less common CNS gliomas such as circumscribed astrocytic, glioneuronal, and neuronal tumors, which are heterogeneous and for which high-level evidence is limited. [PubMed](#)
 - Historically, treatment has relied on surgery and radiotherapy, with chemotherapy used more sparingly, owing to modest benefit. [PubMed](#)
 - The advent and increasing accessibility of molecular profiling has revealed potentially actionable genetic or signaling alterations in subsets of these tumors, motivating a reassessment of therapeutic strategies. [PubMed](#)
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Standard (Conventional) Treatments

Surgery

- **Gross total resection** is emphasized as the cornerstone of therapy, when feasible, to maximize tumor control and symptom relief. [PubMed](#)
- Extent of resection remains a strong prognostic factor, as in other glioma types. (Implicitly, residual tumor burden is associated with worse outcomes.)

Radiotherapy

- Postoperative radiotherapy is often used when resection is incomplete or in recurrent disease, particularly in WHO grade 3 rare gliomas. [PubMed](#)
- Radiotherapy helps in local tumor control and delaying progression.

Chemotherapy

- Conventional cytotoxic chemotherapy has limited efficacy in rare gliomas and is generally reserved for refractory or progressive disease. [PubMed](#)
 - Use is selective and often tailored to individual cases, rather than standard-of-care for most.
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Emerging & Targeted Therapies

Because molecular profiling has revealed alterations in various signaling pathways, the authors review the emerging use of targeted agents. Key points:

- A meaningful subset of rare gliomas harbor **actionable molecular alterations** (e.g., in BRAF/MAPK pathway, NTRK fusions, FGFR, mTOR) that may be therapeutically exploited. [PubMed](#)
 - Examples of promising targeted agents:
 - **BRAF / MAPK pathway inhibitors** (e.g. dabrafenib + trametinib, tovorafenib)
 - **NTRK inhibitors** (e.g. larotrectinib, entrectinib)
 - **FGFR inhibitors** (e.g. erdafitinib, pemigatinib)
 - **mTOR inhibitors** (e.g. everolimus)
 - These have shown clinical activity in selected patients with the corresponding molecular alterations. [PubMed](#)
 - The authors advocate for integration of **precision oncology** into the management of rare gliomas, ideally via **multidisciplinary molecular tumor boards** to guide selection of targeted therapies. [PubMed](#)
 - Challenges remain: determining the optimal **timing** of targeted therapy (first line vs at recurrence), **combination strategies** (with radiotherapy / chemotherapy), mechanisms of **resistance**, and need for **biomarkers** and **liquid biopsy tools** to monitor response. [PubMed](#)
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Conclusions & Future Directions

- The therapeutic landscape for rare gliomas is evolving: **precision medicine is poised to play an increasing role**, beyond the historical reliance on surgery and radiotherapy. [PubMed](#)
- To fully realize this shift, further research is needed to:
 1. **Refine patient selection** via biomarkers (including circulating / liquid biopsy markers)
 2. **Optimize sequencing and combinations** of standard and targeted therapies
 3. **Understand and overcome resistance mechanisms**

4. **Design clinical trials** specific to rare glioma subtypes, given the low incidence

- The authors suggest that in the near future, targeted therapies may move earlier in treatment algorithms, rather than being reserved for salvage therapy only. [PubMed](#)
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If you like, I can also compare how this review's recommendations align (or conflict) with other recent reviews, or extract a "take-home" summary for clinicians or researchers. Do you want me to do that?

Yes

Great — here's a compact, evidence-backed comparison of Bruno et al. (2025) with other recent reviews, followed by a short, practical **take-home summary** for clinicians and for researchers.

Quick comparison with recent literature

Major points of agreement

- **Surgery remains foundational.** Bruno et al. and other recent reviews all emphasize gross-total resection when feasible as the primary, prognostically important intervention. [PubMed+1](#)
- **Molecular profiling is essential.** Multiple recent papers echo Bruno's call to routinely perform broad genomic profiling in rare gliomas because a meaningful fraction harbor actionable drivers (BRAF, NTRK fusions, FGFR, mTOR/PI3K pathway, IDH, etc.). [PubMed+1](#)
- **Targeted agents show real, subtype-specific activity.** Reviews and trial summaries consistently report clinical responses for targeted drugs in molecularly selected patients (e.g., BRAF±MEK inhibitors in BRAF-mutant gliomas; NTRK inhibitors for NTRK-fused tumors). Bruno's survey of these agents aligns with other syntheses. [PubMed+1](#)

Additions / emphasis in other reviews

- **Evidence quantification & trial results:** Recent papers provide more trial-level outcome data and response rates (and note variable CNS penetration and durability). Some multicenter profiling/targeted-therapy series quantify disease control rates and PFS benefits with molecularly guided therapy—useful context beyond Bruno's conceptual review. [Nature+1](#)
- **Practical obstacles highlighted elsewhere:** Other reviews emphasize blood-brain barrier penetrance, intracranial activity heterogeneity, mechanisms of resistance, and the lack of randomized data — echoing Bruno but placing stronger emphasis on these translational gaps. [BioMed Central+1](#)

Points of uncertainty / where interpretations vary

- **When to use targeted therapy (up-front vs at relapse):** Bruno argues these agents *may* move earlier in treatment algorithms; other reviews are more cautious, recommending targeted agents primarily for refractory disease or within trials until more comparative evidence exists. [PubMed+1](#)

- **How broadly to test:** There's consensus on broad panels for most adults, but pediatric-focused reviews stress particular genes/fusions and note different prevalence patterns (e.g., BRAF fusions vs V600E) — meaning age/diagnosis-tailored panels may be optimal. [PMC+1](#)

Take-home summary (actionable)

For clinicians (practical checklist)

1. **Do comprehensive molecular profiling** (large NGS panel ± RNA fusion testing) for nearly all rare gliomas at diagnosis or at first progression. This identifies potential matches for targeted agents. [PubMed+1](#)
2. **Aim for maximal safe resection** when possible — extent of resection remains a dominant prognostic factor. [PubMed](#)
3. **Use targeted therapy when an actionable driver is present**, ideally guided by multidisciplinary molecular tumor board and—when possible—based on evidence of intracranial activity for the chosen agent (e.g., BRAF±MEK for BRAF-V600E, NTRK inhibitors for NTRK fusions). If evidence is limited, prefer trial enrollment. [PMC+1](#)
4. **Be cautious about drug delivery / BBB issues:** check available data on CNS penetration and documented intracranial responses for the agent you consider. [BioMed Central](#)
5. **Prioritize clinical-trial enrollment** for patients without clear actionable targets or when sequencing (up-front vs salvage) is uncertain. [PMC](#)

For researchers (priority agenda)

1. **Biomarker-stratified trials:** design multi-institutional, histology-agnostic but biomarker-driven trials to generate level-1 evidence for targeted approaches in rare glioma subsets. [Nature](#)
2. **Study combination strategies & timing:** randomized or well-controlled studies should test targeted agents alone vs combined with RT/chemo or given up-front vs at relapse. [PMC](#)
3. **Investigate resistance mechanisms and longitudinal liquid biopsies** (cfDNA, CSF assays) to detect resistance and guide next lines of therapy. [Nature](#)
4. **Preclinical focus on BBB and intracranial efficacy:** prioritize models and PK/PD studies that predict clinical CNS penetration and activity. [BioMed Central](#)

Short clinician-facing “one-liner”

“Maximal safe surgery + routine broad molecular profiling; when an actionable CNS-active target is found, preferentially use a targeted agent (ideally in a trial or after tumor-board review) — and study combinations/timing prospectively.” [PubMed+1](#)

If you want, I can now:

- extract a 1-page pocket guide (one-paragraph decision pathway) for tumor boards, or
- produce a short slide deck (3–5 slides) summarizing recommended workflow and selected actionable targets + drugs.

Which of those would help you most?

Extract a 1-page pocket guide

Here’s a **1-page pocket guide** (clinician-ready format) synthesizing the key takeaways from **Bruno et al., 2025 (Curr Opin Neurol)** and recent consensus reviews on **rare gliomas**.

Rare Gliomas — 2025 Pocket Guide

Standard care & emerging targeted options

1 Definition & Scope

- Encompasses **rare circumscribed astrocytic, glioneuronal, neuronal**, and other uncommon gliomas (non-diffuse IDH-mutant / H3-mutant).
- Heterogeneous biology; outcomes hinge on **surgical resection** and **molecular subtype**.
- Evidence base: limited randomized data → rely on precision-guided, case-based management.

2 Core Principles of Management

Step	Practical guidance
Diagnosis	MRI + neuropathology + broad NGS panel ± RNA fusion testing (BRAF, FGFR, NTRK, mTOR/PI3K, IDH, MYB, etc.)
Multidisciplinary board	Review histology, molecular results, imaging, functional mapping, and clinical status
Surgery	Aim for maximal safe resection — single most important prognostic factor
Radiotherapy	Consider adjuvant RT for incomplete resection, recurrence, or WHO grade 3 lesions
Chemotherapy	Limited benefit; use selectively (e.g., temozolomide) if no actionable target

3 Molecularly Targeted Therapies

Alteration / Pathway	Representative agents	Key notes
BRAF V600E / MAPK	dabrafenib + trametinib, tovorafenib	Documented intracranial responses
NTRK fusions	larotrectinib, entrectinib	Durable responses across ages

Alteration / Pathway	Representative agents	Key notes
FGFR alterations	erdafitinib, pemigatinib	CNS activity emerging
mTOR / PI3K	everolimus, sirolimus	Used mainly in SEGA or TSC-related tumors
IDH-mutant	ivosidenib, vorasidenib (under study)	Early data; may move up-front
Others (MYB, MYBL1, ROS1)	Trial enrollment recommended	Evidence still early

 Use only if actionable alteration present and CNS penetration documented; prioritize clinical-trial access.

4 When to Use Targeted Therapy

- **Relapse / progression:** Current default outside trials.
- **Up-front use:** Consider in select, molecularly-driven, low-grade cases or when standard therapy offers low benefit.
- **Always** involve molecular tumor board review and confirm tissue/blood testing quality.

5 Follow-Up & Research Priorities

- Serial MRI every 3–6 mo × 2 y, then 6–12 mo.
- Incorporate **liquid biopsy / cfDNA** when available for resistance tracking.
- Encourage registry participation and basket-trial enrollment.

6 “At-a-Glance Algorithm”

- 1 Diagnosis → Histopathology + NGS/fusion panel
- 2 Tumor board: decide on resectability & adjuvant need
- 3 Maximal safe surgery
- 4 If residual or grade 3 → RT ± chemo
- 5 If actionable alteration → targeted agent (prefer trial)
- 6 Monitor → MRI ± liquid biopsy → adjust / switch at progression

Key message:

“Maximal safe surgery plus routine molecular profiling.

If an actionable, CNS-penetrant target exists — use or trial a targeted agent; otherwise, standard local therapy and close follow-up.”

[10 Oct 2025]