



Editorial

Bridging Consensus and Precision: Interpreting the Chinese Pediatric Low-grade Glioma Guidelines



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Pediatric low-grade gliomas (pLGGs) are the most common brain tumors in children, accounting for approximately 25–40% of all pediatric central nervous system neoplasms.¹ Although their overall prognosis is substantially better than that of high-grade gliomas, their management remains uniquely challenging because treatment must balance durable tumor control with the long-term preservation of cognitive, endocrine, neurological, and psychosocial function. Over the past decade, pLGG management has increasingly shifted from an approach based mainly on anatomical location and histopathology toward one guided by molecular biology and precision therapeutics. Within this evolving context, the newly published Guidelines for the Diagnosis and Treatment of Pediatric Low-Grade Gliomas in China (2024) represent a major milestone for pediatric neuro-oncology in China and beyond.² The guidelines were developed in 2024 and formally published in 2026. In our view, their greatest contribution lies not merely in standardizing clinical practice but in providing a practical roadmap for integrating molecular biology into routine pediatric neuro-oncology care.

The 2021 World Health Organization (WHO) Classification of Central Nervous System Tumors reshaped glioma taxonomy by distinguishing pediatric-type diffuse gliomas from adult gliomas and formally integrating molecular alterations into diagnostic criteria.³ In parallel, advances in the molecular biology of pLGGs, including KIAA1549-BRAF fusions, BRAF V600E mutations, FGFR1 alterations, and other RAS/MAPK pathway events, have moved the field toward molecularly stratified risk assessment and targeted therapy.^{4,5} Whereas the WHO classification primarily provides a molecular framework for tumor taxonomy, the value of the Chinese guidelines lies in translating this evolving framework into a clinically actionable pathway that integrates diagnosis, molecular testing, surgery, systemic therapy, radiotherapy, and long-term follow-up.² At the same time, the guidelines also highlight a broader evidence gap in China: China-specific molecular epidemiology and long-term outcome data remain limited, leaving many risk-stratification strategies dependent on international cohorts.

A major strength of these guidelines is that they move beyond isolated recommendations and provide a coherent clinical frame-

work that integrates diagnosis, treatment, and long-term management without losing sight of practical applicability.

Perhaps the most important advance is the explicit integration of molecular diagnostics into routine clinical decision-making. The guidelines strongly advocate combining histopathological evaluation with molecular genetic testing, in alignment with the WHO 5th edition classification system.³ Importantly, the recommendations are not merely theoretical; they provide practical workflows for detecting KIAA1549-BRAF fusions, MYB/MYBL1 alterations, and other key biomarkers across institutions with varying technical capacities.² By endorsing stepwise testing strategies and allowing the use of “NOS (not otherwise specified)” and “NEC (not elsewhere classified)” designations when comprehensive profiling is unavailable, the guidelines balance precision medicine aspirations with implementation feasibility. Nevertheless, unequal access to advanced molecular diagnostics across China remains a major implementation challenge, particularly between tertiary academic centers and smaller regional hospitals.

Another major strength is the guidelines’ nuanced approach to surgery. Gross total resection remains appropriately recognized as the most important prognostic factor when safely achievable. However, the recommendations avoid equating surgical aggressiveness with surgical success. For infiltrative tumors or lesions located in eloquent regions, surgery is framed not solely as a curative intervention but also as a tool for decompression, symptom relief, hydrocephalus management, and acquisition of tissue for molecular diagnosis. This reflects one of the most important conceptual advances in contemporary pediatric neuro-oncology: maximal safe resection must always be balanced against long-term neurological preservation.

The guidelines appropriately emphasize treatment de-escalation, especially the delay or avoidance of radiotherapy in children younger than three years old because of the long-term neurocognitive and endocrine consequences of radiation exposure during brain development.² At the same time, they preserve necessary clinical flexibility by recognizing that selected high-risk tumors, such as diffuse astrocytomas or tumors involving the thalamus and midbrain, may still require earlier or more intensive treatment.

Targeted therapy is another area where molecular precision is essential. Dabrafenib combined with trametinib has demonstrated efficacy and is now an established targeted approach for BRAF V600E-mutant pediatric gliomas,⁶ but this strategy should not be extrapolated to BRAF-fusion-driven tumors. First-generation BRAF inhibitors may paradoxically activate the MAPK path-

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way in BRAF-fusion tumors and can potentially accelerate tumor growth rather than suppress it.^{7,8} In contrast, tovorafenib, a type II RAF inhibitor, has emerged as an important option for relapsed or refractory BRAF-altered pLGG, with FIREFLY-1 reporting an overall response rate of 51% and a median duration of response of 13.8 months.^{9,10} The ongoing FIREFLY-2/LOGGIC trial is further evaluating tovorafenib as frontline therapy for newly diagnosed BRAF-altered pLGG.¹¹ These distinctions highlight why molecular subtype, rather than histology alone, should guide targeted therapy selection. Beyond BRAF-directed therapy, the guidelines also incorporate mTOR inhibitors for tuberous sclerosis complex-associated subependymal giant cell astrocytoma and TRK inhibitors for NTRK fusion-positive tumors.²

When compared with international frameworks such as the WHO CNS5 (Central Nervous System Tumor Classification, 5th edition) classification, Response Assessment in Pediatric Neuro-oncology response criteria, and Children's Oncology Group recommendations, the Chinese guidelines offer several distinctive contributions. Rather than focusing on a single aspect of care, they integrate diagnosis, molecular testing, surgery, systemic therapy, radiotherapy, and longitudinal follow-up into a unified clinical framework. A particular strength is the guidelines' emphasis on implementation within resource-variable healthcare settings. While the WHO classification provides a molecular framework for tumor taxonomy, it does not address how molecular diagnostics should be incorporated in regions with limited technical capacity. In contrast, the Chinese guidelines adopt a tiered testing strategy that balances precision medicine with real-world feasibility. The guidelines also place strong emphasis on developmental preservation and long-term survivorship, highlighting neurocognitive, endocrine, and psychosocial consequences of treatment. At the same time, unequal access to advanced molecular diagnostics, limited China-specific multicenter data, high costs of targeted therapies, and shortages of specialized pediatric neuro-oncology resources may hinder equitable adoption across different regions. These challenges do not diminish the value of the guidelines; rather, they define important priorities for future clinical infrastructure development and collaborative research.

Future progress should focus on several practical priorities. First, molecularly stratified prospective clinical trials are needed so that targeted therapies can be matched to specific molecular alterations rather than guided solely by histology-based treatment paradigms. Second, successful implementation of precision medicine will require a national molecular testing network supported by regional reference laboratories, standardized diagnostic platforms, and quality-control systems to improve equitable access to molecular diagnostics. Third, prospective national registries should link molecular characteristics with treatment responses and long-term functional outcomes, thereby generating China-specific evidence and refining future iterations of the guidelines. Finally, long-term neurocognitive, endocrine, educational, behavioral, and psychosocial outcomes should become integral components of both clinical trials and routine survivorship care. Together, these efforts would help translate molecular precision into equitable and developmentally informed pediatric neuro-oncology practice.

In summary, the 2024 Chinese Guidelines for Pediatric Low-Grade Gliomas represent a major achievement in the standardization and modernization of pediatric neuro-oncology care. By integrating molecular diagnostics, risk-adapted therapeutics, and age-adapted treatment strategies into a unified framework, these recommendations provide a clinically practical model for precision medicine in resource-variable settings. However, the gap

between guideline aspiration and real-world implementation remains substantial. Addressing disparities in molecular testing access, building national data infrastructure, controlling the costs of targeted therapies, and supporting smaller hospitals in guideline adoption are essential next steps. Ultimately, the success of modern pLGG care should be measured not only by survival but also by whether children are able to grow, learn, and live well beyond their disease.

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The authors declare that they have no competing interests or conflicts of interest related to this manuscript.

Author contributions

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References

- [1] Ostrom QT, de Blank PM, Kruchko C, Petersen CM, Liao P, Finlay JL, *et al.* Alex's Lemonade Stand Foundation Infant and Childhood Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2007-2011. *Neuro Oncol* 2015;16(Suppl 10):x1-x36. doi:10.1093/neuonc/nou327, PMID:25542864.
- [2] Zhang L, Wan F, Zhang J, Du S, Qiu X, Li H, *et al.* Guidelines for the Diagnosis and Treatment of Pediatric Low-Grade Gliomas in China (2024). *Neurosurgical Subspecialties* 2026;2(1):1-14. doi:10.14218/NSSS.2026.00004.
- [3] Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, *et al.* The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol* 2021;23(8):1231-1251. doi:10.1093/neuonc/noab106, PMID:34185076.
- [4] Ryall S, Tabori U, Hawkins C. Pediatric low-grade glioma in the era of molecular diagnostics. *Acta Neuropathol Commun* 2020;8(1):30. doi:10.1186/s40478-020-00902-z, PMID:32164789.
- [5] Ryall S, Zapotocky M, Fukuoka K, Nobre L, Guerreiro Stucklin A, Bennett J, *et al.* Integrated Molecular and Clinical Analysis of 1,000 Pediatric Low-Grade Gliomas. *Cancer Cell* 2020;37(4):569-583.e5. doi:10.1016/j.ccell.2020.03.011, PMID:32289278.
- [6] Bouffet E, Hansford JR, Garré ML, Hara J, Plant-Fox A, Aerts I, *et al.* Dabrafenib plus Trametinib in Pediatric Glioma with BRAF V600 Mutations. *N Engl J Med* 2023;389(12):1108-1120. doi:10.1056/NEJMoa2303815, PMID:37733309.
- [7] Sievert AJ, Lang SS, Boucher KL, Madsen PJ, Slaunwhite E, Choudhari N, *et al.* Paradoxical activation and RAF inhibitor resistance of BRAF protein kinase fusions characterizing pediatric astrocytomas. *Proc Natl Acad Sci U S A* 2013;110(15):5957-5962. doi:10.1073/pnas.1219232110, PMID:23533272.
- [8] Jain P, Fierst TM, Han HJ, Smith TE, Vakili A, Storm PB, *et al.* CRAF gene

- fusions in pediatric low-grade gliomas define a distinct drug response based on dimerization profiles. *Oncogene* 2017;36(45):6348–6358. doi:10.1038/onc.2017.276, PMID:28806393.
- [9] Singh S, Bradford D, Chatterjee S, Li X, Aungst SL, Skinner AM, *et al.* FDA Approval Summary: Tovorafenib for Relapsed or Refractory BRAF-Altered Pediatric Low-Grade Glioma. *Clin Cancer Res* 2025;31(8):1383–1389. doi:10.1158/1078-0432.CCR-24-3439, PMID:39808502.
- [10] Kilburn LB, Khuong-Quang DA, Hansford JR, Landi D, van der Lugt J, Leary SES, *et al.* The type II RAF inhibitor tovorafenib in relapsed/refractory pediatric low-grade glioma: the phase 2 FIREFLY-1 trial. *Nat Med* 2024;30(1):207–217. doi:10.1038/s41591-023-02668-y, PMID:37978284.
- [11] van Tilburg CM, Kilburn LB, Perreault S, Schmidt R, Azizi AA, Cruz-Martínez O, *et al.* LOGGIC/FIREFLY-2: a phase 3, randomized trial of tovorafenib vs. chemotherapy in pediatric and young adult patients with newly diagnosed low-grade glioma harboring an activating RAF alteration. *BMC Cancer* 2024;24(1):147. doi:10.1186/s12885-024-11820-x, PMID:38291372.