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# Integrated clinical and molecular landscape of disseminated pediatric low-grade glioma

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## Abstract

**Background:** Pediatric-type low-grade gliomas (PLGG) are the most common central nervous system (CNS) tumor in children. Many are indolent and have excellent outcomes, however some inexplicably spread throughout the CNS leading to increased morbidity and mortality.

**Methods:** To better understand this rare and difficult-to-treat entity, as well as the features associated with dissemination in CNS tumors, we assembled a large international cohort (n = 269) of patients with disseminated PLGG with detailed clinical and molecular characterization, including DNA sequencing and methylome profiling.

**Results:** We identified three subgroups of patients based on the temporal and spatial distribution of dissemination. Tumors with diffuse leptomeningeal spread without a primary tumor mass and those occurring in infants had the worst clinical outcomes. The genetics overlapped substantially with that of non-disseminated PLGG, suggesting that non-genetic mechanisms are an important contributor to dissemination. Therapeutically, targeted RAS/MAPK-pathway inhibition was more effective than conventional chemotherapy as first or second-line treatment.

**Conclusion:** In sum, this cohort increases our clinical and biological understanding of this rare disease, provides insights for improving patient care, and directs future clinical trials and basic science

research.

**Keywords:** CNS tumours; cancer metastasis; liquid biopsy; low-grade glioma; methylation; next generation sequencing; pediatric cancer; pediatric neuro-oncology; targeted therapy.