Chart audit in pediatric low-grade glioma: molecular testing and treatment patterns

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Introduction

- Pediatric low-grade gliomas (pLGGs) are the most common brain tumors of childhood:[1]
  - Although pLGGs tend to be less aggressive than high-grade tumors with 10-year survival rates exceeding 90%, disease progression after first-line surgery or chemotherapy means that ~50% may require additional lines of therapy
- Genomic alterations of *BRAF*, which encodes a component of the mitogen-activated protein kinase/extracellular-signal-regulated kinase (MAPK/ERK) pathway, are the most common oncogenic drivers in pLGG,[2] leading to the investigation of MAPK pathway-targeted agents in this setting[3-5]

Objective

- Given the increasing importance of the genomic profiling of tumors to inform selection of the most appropriate therapeutic agents, a retrospective chart audit study was conducted to assess molecular testing and treatment patterns in a real-world population of patients with pLGG

Methods

- US-based physicians with a primary or secondary medical specialty in pediatric oncology, who had been in practice for 3–30 years and had treated ≥3 patients with relapsed/refractory pLGG in the previous 24 months, were recruited
- Participants completed an online survey in May 2022 and provided information from medical charts for a random sample of 3–10 patients with relapsed/refractory pLGG who were representative of their typical treatment patterns
- Patients included in the chart audit were:
  - ≤25 years of age
  - Originally diagnosed with pLGG before 15 years of age
  - To have either started or completed second-line systemic treatment, following at least one line of prior systemic therapy, and were to have received their most recent dose of systemic treatment on/after April 1, 2020 (~within the previous 2 years)

Results

Patients

- 27 participating pediatric oncologists provided chart data from 163 patients
- Patient demographics and baseline clinical characteristics are summarized in **Table 1**:
  - Most patients were white (58%), were most recently on second-line (86%) systemic therapy, and pilocytic astrocytoma (47%) was the most common pLGG histology
- 107 (66%) patients had tumors that had undergone resection at some point, with inoperable/high risk tumor location being the main reason why resection had not been attempted (**Figure 1**)

Genomic testing

- Tumors had been biopsied and/or resected in 138 (85%) patients; of those, tumors from 93 (67%) patients underwent genomic testing (first surgical procedure), were not tested in 29 (21%) patients; testing status was unknown in 16 (12%) patients (**Figure 2**):
  - Genomic testing was most commonly performed when tumors were totally or partially resected. Of the tumors from 96 patients that underwent genomic testing at any time, 81 (84%) were tested for *BRAF* mutations, and 70 (73%) for *BRAF* fusions (**Figure 3**)
  - The most common reasons for not conducting genomic testing (**Figure 4**) were prohibitive cost of biopsy/tissue testing or no insurance coverage (31%), testing not relevant for initial treatment (21%), and tissue being poor quality (21%) or insufficient (17%)
  - Chemotherapy and/or radiation were the treatments of choice for those patients whose tumors were not tested

Systemic treatment

- Chemotherapy was the most common treatment administered to patients first-line (n=119, 73%) (**Figures 5 and 6**):
  - 45 (28%) patients received targeted therapy, with MEK inhibitors the most frequently administered class of targeted agents overall (n=26, 16%)
  - 32 (20%) patients received MAPK pathway-targeted agents
  - 32 (20%) patients received radiation therapy, most commonly in combination with chemotherapy
- Targeted agents were administered to a greater proportion of patients second-line (n=91, 56%):
  - 66 (40%) patients received MAPK pathway-targeted agents
  - MEK inhibitors were the most frequently administered class of targeted agents (n=48, 29%)
  - 14 (9%) patients received radiation, including 2 in combination with MAPK-targeted agents and one with chemotherapy

Table 1. Baseline characteristics

Characteristic	N=163
Gender, n (%)	
Male	87 (53)
Female	76 (47)
Ethnicity, n (%)	
White	94 (58)
Black	27 (17)
Hispanic/Latino	16 (10)
Asian	11 (7)
Native American	2 (1)
Not known	13 (8)
Age, years	
Median, range	12 (1–24)
Most recent line of systemic treatment, n (%)	
Second-line	140 (86)
Third-line	19 (12)
Fourth-line	4 (2)
Tumor type, n (%)	
Pilocytic astrocytoma	76 (47)
Oligodendroglioma	41 (25)
Ganglioglioma	26 (16)
Mixed glioma (oligoastrocytoma)	18 (11)
Other*	2 (1)
Insurance status	
Private	99 (61)
Medicaid	31 (19)
Medicare	9 (6)
No insurance/cash paying	7 (4)
Not known	17 (10)

Data are n (%) unless otherwise stated; *Optic glioma

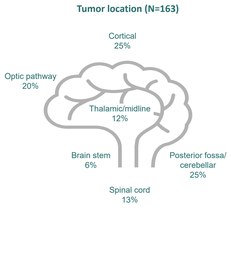


Figure 1. Surgical outcomes

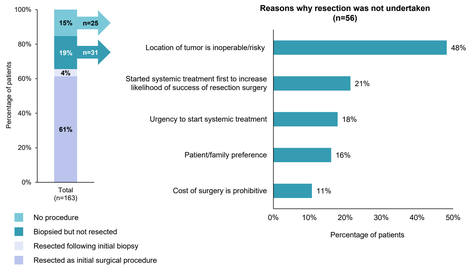


Figure 2. Genomic testing in pLGG

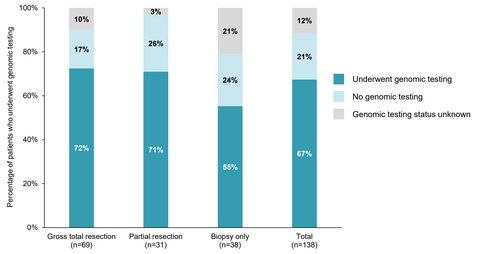
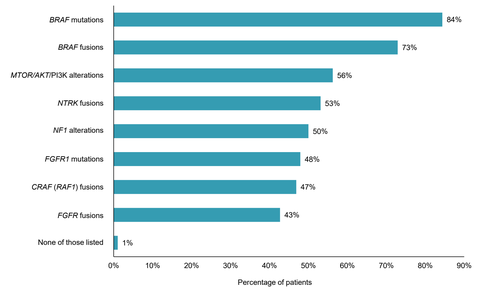
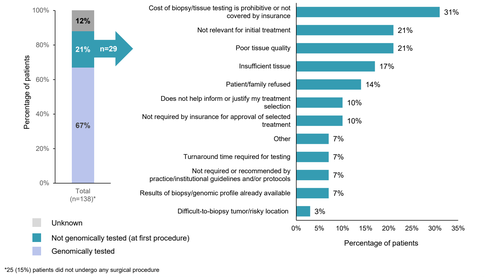


Figure 3. Genomic alterations tested for*



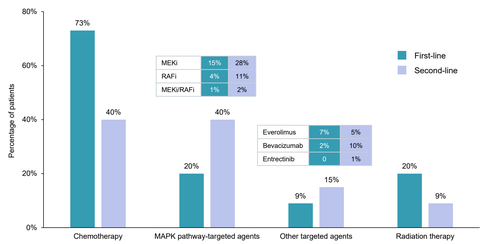
*At any time

Figure 4. Reasons for not performing genomic testing



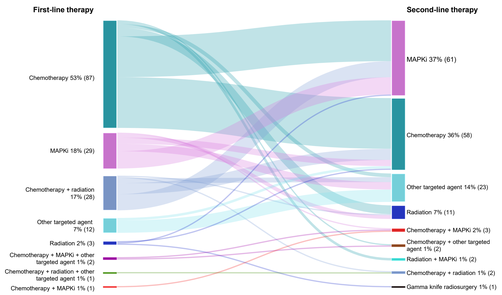
*25 (15%) patients did not undergo any surgical procedure

Figure 5. First- and second-line systemic treatment



MAPK, mitogen-activated protein kinase; MEKi, MEK inhibitor(s); MEKi/RAFi, MEK inhibitor combined with RAF inhibitor; RAFi, RAF inhibitor(s)

Figure 6. First- to second-line treatment progression



Data are percentage (n). Other targeted agents administered included everolimus, bevacizumab and entrectinib
MAPKi, mitogen-activated protein kinase pathway inhibitors

Conclusions

- While genomic testing of tumors is common in patients with relapsed/refractory pLGG, not everyone gets tested
  - *BRAF* mutations and *BRAF* fusions were the genomic alterations most frequently tested for
  - Barriers to testing included cost and lack insurance coverage and poor quality or insufficient tissue
  - Patients whose tumors did not undergo testing were primarily treated with chemotherapy and radiation
- Chemotherapy remains the most common first-line systemic treatment in patients with pLGG:
  - 47% of patients who received chemotherapy in the first-line were retreated with chemotherapy in second-line
  - Targeted therapies were used more frequently in the second-line setting
  - MEK inhibitors were the most common type of targeted agents used in both first- and second-line settings

References

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Acknowledgments

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