Navigating pediatric low-grade glioma (pLGG)

Your guide in understanding and managing the disease

Aiyden, lives with pLGG.
Lives for basketball.

Day One
BIOPHARMACEUTICALS

What is pLGG?
Understanding tumor growth
Setting goals
Treatment options
Targeted therapies
Your care team
pLGG community

Introduction

This guide was put together to inform and empower you and your family at every step.

Because pediatric low-grade glioma (pLGG) is a rare disease, finding resources and knowing what to expect isn't always so simple.

We hope this brochure brings confidence in your conversations and decision-making along the way.

Explore the guide

What is pLGG?

pLGG is the most common type of central nervous system (CNS) brain tumor diagnosed in children, accounting for about 30% of tumors.

Gliomas are graded based on how quickly they grow—the slower the growth, the lower the grade. Because pLGG is a low-grade chronic disease, doctors focus on how the child is functioning in their day-to-day life.

You may hear this type of tumor described as:

- **benign:** less dangerous than malignant tumors
- **non-cancerous brain tumor:** grows slowly and typically doesn't spread to other parts of the body
- **low-grade brain tumor:** slow growing and less aggressive

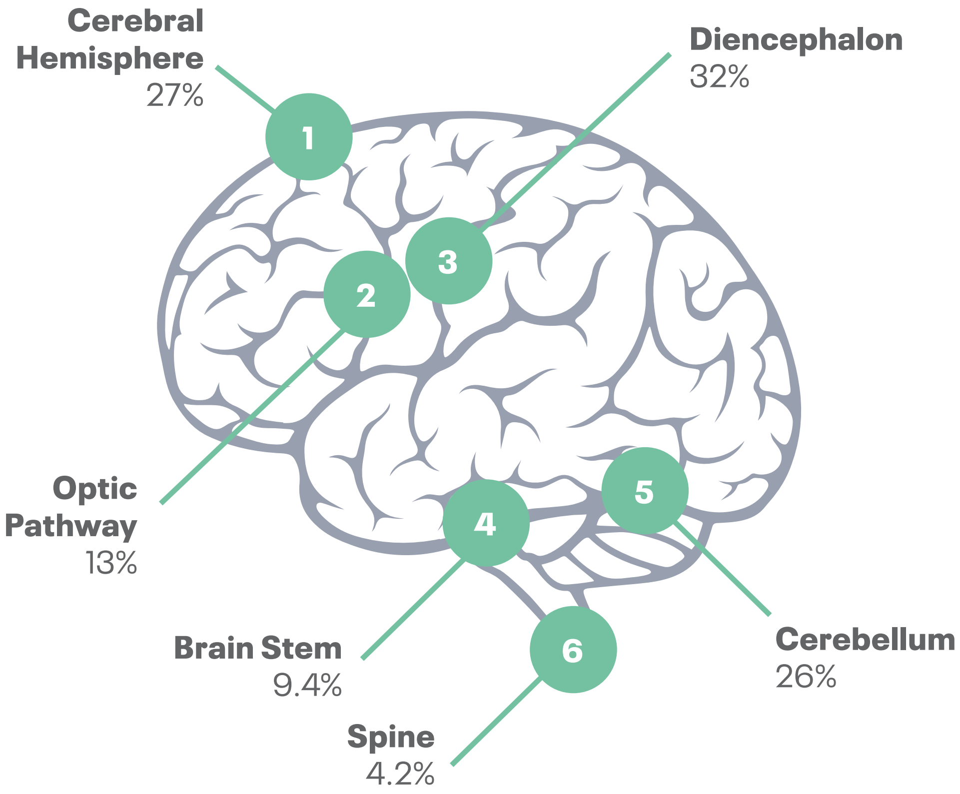
Low-grade doesn't mean low impact

pLGG is different from many other tumors because of its slow growth and high survival rate. But it's important to remember that it can still affect a child's life in a major way.

Every child's journey with pLGG is unique

The tumor's location in the brain plays a major role in what symptoms appear, how daily life is affected, and how the disease is managed.

Common pLGG tumor locations and the symptoms they may cause:



1 **CEREBRAL HEMISPHERE**
Might cause headaches, seizures, nausea, vomiting, or changes in personality or behavior

2 **OPTIC PATHWAY**
May affect vision or hormone function, including metabolism, growth, and mood

3 **DIENCEPHALON**
May cause weakness or paralysis, vision loss, difficulty maintaining or gaining weight (also known as "failure to thrive"), and slowed growth

4 **BRAIN STEM**
Can cause paralysis, weakness, numbness, loss of balance, sleep difficulties, and difficulty swallowing

5 **CEREBELLUM**
Could impact coordination, balance, fine motor skills, sensory difficulties, and learning disabilities

6 **SPINE**
Might cause more general symptoms, including pain, nausea, vomiting, constipation, vision changes, numbness, headaches and seizures

Depending on the location of the tumor, doctors will determine if it can be removed with surgery, which plays a role in how the child's life will be impacted by pLGG.

These are not all the possible symptoms of pLGG. You know your child best, so if you notice any changes in behavior or if something concerns you, speak with a doctor.

Living with pLGG

pLGG is not a one-time event. It is a chronic condition. Children often live with this type of cancer into adulthood. Due to pLGG's slow-growing nature, treatment can span across years.

Managing pLGG often cycles between stretches of active treatment and periods of close monitoring, sometimes known as a "watch and wait" approach.

With this approach, doctors hold back on treatment unless the cancer progresses or new symptoms develop.

It's important to note that tumors return or even progress in about 50% of children after an initial treatment.

50%

Your family may need to consider, discuss, and navigate:

- **Multiple rounds of treatment**
  Adjustments may be needed as the tumor or symptoms change.
- **Ongoing scans and appointments**
  Regular check-ins that help track progress and catch changes early.
- **Daily life disruptions**
  Fatigue, school absences, and emotional stress, which can affect the whole family.
- **Long-term effects**
  Some treatments may have side effects that appear years later, making ongoing follow-up care and monitoring important.

Because of so many factors to consider, goals may change, and that's okay.

Talk to your care team at any point to address needs and concerns big or small. They are here for you.

Understanding tumor growth

Understanding more about the tumor can help figure out its behavior, which may lead to choosing the most appropriate treatment.

This may be helpful to your child's care team in discovering how the tumor behaves and what treatments may be best to discuss with you.

Genomic testing is typically done via biopsy. However, it's important to note that not all doctors recommend this procedure due to reasons such as tumor size, location or other factors.

Ask your care team if genomic testing could be an option for your child.

Recent scientific advances show that the MAPK pathway plays a key role in driving tumor growth in pLGG.

The MAPK pathway

Normal cells in the body have proteins that work together to relay information and control cell growth.

Like a factory line, each protein has a specific job to do before passing it down the line (signaling). Together, they build and coordinate their unique machinery (cell growth).

In pLGG, a signal in the MAPK pathway can malfunction, causing uncontrolled cell growth.

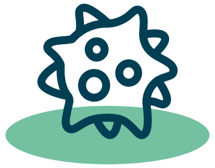
SCAN HERE

or visit rethinkplgg.com/inside-pLGG to see how the MAPK pathway works.

Common gene changes in pLGG

Gene changes can lead to multiple cell function changes.

A gene change, also known as an “alteration” or “mutation,” can lead to multiple cell function changes, including how cells grow.



Learning if your child has a gene change and understanding the role it may play in tumor growth can help you and your care team make more informed decisions.

75%

Up to 75% of children with pLGG have some type of *BRAF* change

What is the *BRAF* gene?

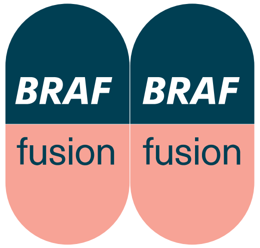
BRAF is a gene that makes a protein involved in sending signals in cells and in cell growth.

Mutated forms of the *BRAF* gene and protein have been found in many types of cancer. These changes can increase the growth and spread of cancer cells.

2 common changes in the *BRAF* gene include:

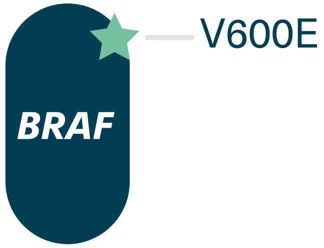
***BRAF* FUSION**

When the *BRAF* gene joins another gene



***BRAF* POINT MUTATION**

A specific change in the *BRAF* gene. The most common point mutation is the V600E mutation



In addition, NF1 and FGFR1 are other common changes to ask your child’s doctor about.

Setting goals and choosing treatment

Treatment goals are not just about the tumor, but also the overall well-being of the child.

Doctors consider many goals when evaluating options— to help stabilize the tumor and symptoms, preserve neurological (brain) function, limit side effect impact, protect quality of life, and support academic and social achievements so that kids can be kids.

Recommending treatment

When doctors recommend starting, continuing, or changing treatment, they look at both clinical and family factors.

Clinical factors include things such as tumor behavior, previous treatments, side effects, and the overall health of the child physically and neurologically.

Family or lifestyle factors are more about how treatment fits into your family's routine, and if your child is acting like themselves.

It also means thinking about how much time it can take away from school and their interests.

How tumor response is evaluated

All of these factors help doctors know how the tumor is responding so they can better recommend next steps.

They may refer to the following when describing how your child's tumor is responding to treatment:

- **Complete response**
  No evidence of the tumor
- **Partial response**
  Signifies a decrease in the size of a tumor. Not complete disappearance, no more than 50%
- **Stable disease**
  The tumor neither shrinks nor grows a lot during treatment. Specifically, no more than 25%
- **Progressive disease**
  The tumor has increased in size by more than 25%, or physical symptoms have worsened

pLGG treatment options

Your child may need more than one type of treatment along the way, at different points.

Doctors will also consider the child's age and overall development. They will also weigh benefits and risks based on the needs of each patient.

Every option comes with risks. Make sure to speak with your care team about the pros and cons of each approach.

SURGERY

The treatment choice most used for patients when tumor removal is feasible. However, this may not be possible depending on the tumor's location or if the disease has spread.

Even with surgery, there is a chance your child may need additional treatments—especially if not all of the tumor could be removed or if it comes back.

CHEMOTHERAPY

Often used after surgery or if surgery is not an option for a specific tumor.

Chemotherapy can cause harsh side effects. Toxicity and tolerability are concerns, especially for infants and young children. It also often requires an uncomfortable port or IV.

RADIATION

Generally reserved for a specific type of patient who may not have as many treatment options.

While radiation can be effective, it's often avoided due to potential risks such as the development of secondary cancers and cognitive decline.

TARGETED THERAPY

This treatment type targets and attacks tumor cells with certain genetic characteristics.

Targeted therapies have unique side effects that are distinct from conventional chemotherapies used in pLGG management.

Targeted therapies

Thanks to ongoing research in helping to understand the biology behind pLGG, targeted treatments are constantly being developed.

This class of therapies works differently from traditional treatments, and includes inhibitors that can affect tumor growth.

TARGETED THERAPY

Treatments that work by interfering with messages sent in the cell pathways that are common in pLGG. Targeted therapies are often used to treat newly diagnosed tumors or tumors that have come back or worsened.

Current targeted therapies:

MEK INHIBITOR

Inhibits MEK, a key protein in the MAPK pathway that impacts cell growth.

BRAF INHIBITOR

Type I inhibits MAPK signaling for primarily V600E point mutations, whereas **Type II** inhibits BRAF fusions and mutations in the MAPK pathway.

Evaluating approaches can feel overwhelming. Ask your care team about all options and if a targeted therapy may be right.

The importance of your care team

Various therapies have been shown to help support children living with pLGG. Throughout the journey, families may work with many types of specialists at different points.

Depending on the needs of your family, and your child's treatment plan, each member plays a special role.

Members of your care team may include:

- Pediatric neuro-oncology team
- Radiologist
- Neurosurgeon
- Family pediatrician
- Ophthalmologist
- Audiologist
- Endocrinologist

- Psychologist
- Therapist
- Child life specialist
- Physical therapist
- Occupational therapist
- Social worker

- Teacher
- School administrator
- Transition education specialist

If you have questions, concerns, or need specific recommendations, speak up. Communication is key.

How to start the conversation

Your child may be the one living with pLGG, but everyone who loves them is impacted. Consider what each treatment approach has to offer and how it fits into your family's life and best supports your child.

The following questions may help lead the discussion:

DIAGNOSIS AND UNDERSTANDING THE TUMOR

- What type of pLGG does my child have?
- Where is the tumor located, and how does that affect my child's overall health or development?
- Is it operable?
- Is the tumor growing or considered stable right now?
- Is genomic testing recommended? What can it tell us?

KNOWING OPTIONS, NARROWING DOWN APPROACH

- What treatment options are available to us at this point?
- What is the goal of treatment—tumor shrinkage, stability, or symptom management?
- Are there any clinical trials my child may be eligible for?
- Is surgery an option? If so, what are the risks and benefits?

LOOKING AHEAD—PROGNOSIS, MONITORING, AND LIFE ON TREATMENT

- What is the expected outlook of these treatments?
- What does success look like?
- How will we monitor the tumor's response?
- How might treatment impact my child's daily life, development, or schooling?
- What signs or symptoms should we watch for that might require urgent attention?
- What can we do to help ensure we are always prepared with a plan for what might happen next?

The pLGG community

With the right support and appropriate treatment in place, your child can have the best chance to achieve their best outcome. Engaging with the community and using available resources are great ways to gain support and knowledge.

A few patient organizations include:

Momcology®

momcology.org

TEAM JACK FOUNDATION

teamjackfoundation.org

Pediatric Brain Tumor FOUNDATION

curethekids.org

The Lilabean Foundation

lilabeanfoundation.com

CBTF CHILDREN'S BRAIN TUMOR FOUNDATION
RESEARCH · COMMUNITY · COMPANIONSHIP

cbtf.org

Some of these organizations run private social media groups for families on platforms like Facebook.

Building connections with others going through the same things and talking in a safe space can be helpful. You are not alone.

No matter where you are in your journey, you're now armed with knowledge and resources.

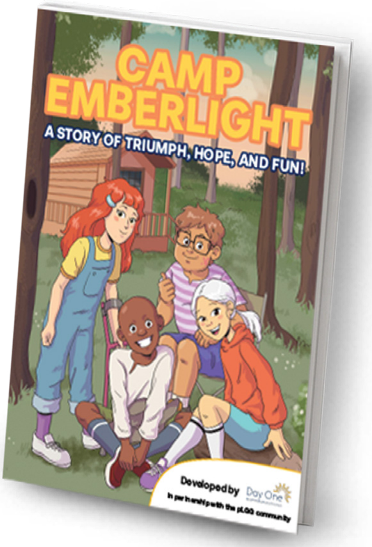
What matters most is being confident in a shared decision between your family and your care team.

rethinkpLGG
from Day One Biopharmaceuticals

Scan this code or visit rethinkplgg.com, where you will find additional information about the disease, patient videos, and other educational resources.

Our Children's Book is also available, written for and about children navigating pLGG.

And while the story celebrates their unique traits and powerful resiliency, it's something the whole family can enjoy reading together.



Scan this code or visit rethinkplgg.com/book-signup to sign up and enjoy the book!

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