

CHILDREN'S NATIONAL MEDICAL CENTER

Children's Research Institute
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PARTICIPATION IN A CLINICAL STUDY: Frequently Asked Questions for Participants and Parents

TITLE OF STUDY: Molecular Analysis of Samples from Patients
With Diffuse Intrinsic Pontine Glioma and
Brainstem Glioma

PRINCIPAL INVESTIGATOR: Javad Nazarian, PhD, Center for Genetic
Medicine

1. What is this study?

The aim of this study is to collect blood, urine, cerebrospinal fluid (CSF), brain tumor and normal brain tissue specimens from pediatric patients with diffuse intrinsic pontine glioma (DIPG) or brainstem glioma, either during therapy or postmortem, for investigation in the laboratory in order to learn more about brainstem glioma and work towards developing better treatments.

2. Why is this important?

High grade diffuse intrinsic pontine glioma (DIPG) accounts for approximately 80% of pediatric brainstem tumors and 10% of pediatric brain tumors, and is the most lethal form of brainstem gliomas in children. There is currently no effective therapy to treat these tumors. DIPGs and brainstem gliomas are rarely biopsied, making samples of the tumor unavailable for scientific study. Our goal is to characterize the genetic abnormalities that lead to tumor formation, which will help us identify therapeutic targets for designing more effective forms of treatment. In order to do this, we must have tumor tissue to examine in the laboratory. By participating in this study, you and your child would be giving a gift that would allow us to investigate these tumors and find better treatments for the children who suffer from them in the future.

3. Who can participate in this study?

Patients up to age 21 with clinical and radiologic diagnosis of diffuse intrinsic pontine glioma or brainstem glioma may participate in this study.

4. Who is conducting this study?

This study is led by a research team at Children's National Medical Center in the Center for Genetic Medicine. The principle investigator is Dr. Javad Nazarian, PhD, who works with scientists and physicians in the Departments of Neurosurgery, Neurology, and Neuro-oncology within the Children's Research Institute.

5. What does it mean for my child to enroll in this study?

You may elect to donate samples collected during the course of your their treatment, postmortem, or both.

a. Donating samples during the course of your child's treatment:

If child's doctor determines that during the course of treatment your child needs a procedure to obtain blood, urine, CSF or tumor tissue, a portion of this sample may be donated to our research laboratory for further study. Samples collected during the course of your child's treatment will not be collected for research purposes alone.

b. Donating samples post-mortem:

Brainstem glioma is a terrible disease, and one for which we do not yet have a cure. Sadly, for many children this is a terminal illness. If your child succumbs to his or her tumor, you may decide to donate samples for study upon your child's passing. This is a precious and invaluable gift that can help children in the future suffering from this terrible tumor by providing scientists a way to investigate it and develop potential treatments. You may elect for blood, CSF, tumor and brain tissue to be donated upon your child's passing through a post-mortem (autopsy) procedure.

6. Where do we go to participate in this study?

a. Donating Samples during treatment:

Children receiving care for their brainstem tumor at Children's National Medical Center can easily be enrolled in this study, and we will coordinate with your child's doctors for donation to Children's Research Institute upon sample collection. However, you do not need to be a patient at Children's National Medical Center to participate in this study. Study investigators can coordinate with your child's doctors ahead of time and will arrange shipment of specimens to Children's Research Institute upon their collection.

b. Donating samples post-mortem:

We understand that this is a very difficult time for your child and family, and if you would like to donate samples for study upon your child's passing we have a system in place to make this process as easy as possible. Children suffering from terminal illness may succumb to their disease unexpectedly. Therefore, families should work with their health care team to make any decisions and arrangements that are right for them at this difficult time.

Importantly, the choice to make a post mortem donation will not require families to amend their end of life planning, or change memorial or funeral services: we will work to coordinate the donation process around these arrangements.

At the time of enrollment in this study, we ask that you share your end of life plans with us. We can arrange transport to Children's National Medical Center or your local hospital for the post-mortem examination upon passing, followed by transport to the location of your choosing for any memorial services you may have planned. Samples collected at other institutions will be shipped to Children's Research Institute.

7. What samples are collected during my child's treatment and what is involved with each?

a. Urine and Blood

Your child's doctor may determine that blood or urine tests are needed for diagnosis or treatment. Collection will be performed in the usual fashion and only as determined necessary by your child's doctor. A portion of these samples can be donated to Children's Research Institute for further study.

b. Cerebrospinal Fluid (CSF) and Tumor Tissue

During the course of treatment your child's doctor may determine that surgery to take a sample (biopsy) or remove a portion or the entire tumor is necessary. If your child undergoes surgery, their neurosurgeon will give a sample of tissue to study in the laboratory. Your child's neurosurgeon may also collect cerebrospinal fluid (CSF) from around the brain and donate this sample for research study. Children with brainstem tumors who are not undergoing surgical biopsy or removal of their tumor, but are undergoing placement, revision, or clinical evaluation of a ventriculoperitoneal shunt, may also participate in the study. Your child's neurosurgeon may collect CSF from the shunt and donate a sample to study in the laboratory.

8. What samples are collected postmortem and what is involved with each?

Samples of **tumor**, normal **brain**, **cerebrospinal fluid** (CSF) and **blood** may be donated upon the patient's passing. This is called post-mortem collection of specimens, and it involves an autopsy procedure, also known as postmortem examination, performed by a specialized physician known as a pathologist.

During this procedure, the pathologist will collect blood from a blood vessel and cerebrospinal fluid from around the brain. The pathologist will also collect a portion of the brainstem which will include normal and tumor tissue. Lastly, the pathologist will collect a portion of normal brain tissue from the frontal lobe.

These tissue samples will be sent to the laboratory for further study.

In order to access the brainstem and CSF, the pathologist will make an incision at the base of the skull and open the cranial bone. The pathologist will remove the brain tissue and isolate the brainstem, brainstem tumor, and a portion of the frontal lobe. These samples will then immediately be sent to our laboratory for storage and study. Upon completion of the postmortem examination procedure, the opening in the cranial bone and skin incision will be closed. This incision will not be visible to observers during a funeral or memorial service.

9. What potential risks are involved?

Participation in this study does not require any experimental therapies or procedures. Participants will only undergo procedures deemed necessary by his or her physicians as part of the standard diagnosis and treatment of a child with a brainstem tumor, and only after the risks and benefits of these procedures are explained by your child's doctor and informed consent is obtained.

10. Are there additional treatments or tests required?

Participation in this study does not require additional evaluations, hospitalizations, doctor visits or treatments for your child. Your child will undergo

procedures and treatments only as determined by their physicians as part of the standard of care for their disease. Post-mortem donation does require an autopsy procedure, but this does not affect the treatment, course or prognosis of your child's disease.

11. Are there costs associated with participation in this study?

Because no additional treatments or procedures will be performed outside of the care already planned by your child's physicians, no additional costs will be incurred should you choose to donate samples to this study during your child's treatment. If you elect to donate samples through a post-mortem examination, all associated costs will be covered by this study at no additional cost to you.

12. What will happen to the samples my child donates?

Donated samples will immediately be sent to the Nazarian laboratory in the Children's Research Institute for processing and storage. Samples will enable scientists to perform a wide variety of studies. Blood, urine, CSF and tumor samples can be examined and compared to normal samples in order to identify markers such as proteins that are unique to brainstem gliomas. Genetic analysis will also be performed to identify potential genetic causes of the disease. These markers provide information about the behavior and make-up of the tumor, and can help improve diagnosis and develop targeted treatments. In addition, isolated tumor cells can be grown in a culture dish in order to observe their behavior and closely examine their genetic characteristics. By looking at tumor cell DNA, RNA and proteins, we can better understand how these tumors form and grow, and design therapies to kill tumor cells without affecting healthy brainstem tissue or creating terrible side effects. These tumor cells can then be used to grow tumors in animal models, such as mice, so that we can test the effectiveness of the drugs we design to treat them. In this way, donated samples will continue to provide scientists the ability to study this disease for years to come, in hopes of identifying more effective therapies for children with diffuse intrinsic pontine gliomas (DIPG) and other brainstem cancers, helping them live longer and suffer less from the treatment and progression of their disease.

13. Will my child's medical and personal information be kept private and protected?

We will keep the records of this study confidential. We will not tell anyone that participants are in the study. Only the people working on the study will know the participant's name. They will keep this information in case we have to find the participant later for medical reasons. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study and to make sure our results are correct. A child's medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

14. Will postmortem donation affect end of life care, funeral or bereavement plans?

We want to emphasize that understand that **the choice to make a post mortem donation will not require families to amend their end of life planning, or change memorial or funeral services: we will work to coordinate the donation process around these arrangements.** We will work closely with you and your child's health care team to coordinate donation in a respectful manner. Importantly, the postmortem examination does not leave any marks that would be visible during bereavement services.

15. What can we expect to happen when it is time for postmortem donation?

Upon your child's passing, participating families should notify Dr. Javad Nazarian and his research team at 202-423-6543. The team will contact transportation services for transport to the hospital where the postmortem examination is to take place, and notify the pathologist to perform the procedure. The autopsy procedure will be completed as soon as possible, often within 24 hours. Upon completion we will then arrange for transport of the body to the destination of the family's choosing.

16. If we have additional questions or concerns, who can we call?

We want study participants to ask questions about any part of this study at any time. If study participants have research or medical questions about this study, call the Principal Investigator Dr. Javad Nazarian, at 202-476-6022. If study participants believe they have been injured as a result of being in this study, they should call the Principal Investigator, Dr. Javad Nazarian, at 202-476-6022. If participants have any questions or concerns about their rights in this research study at any time, please call Children's Hospital's Manager of Customer Relations, at (202) 476-5000 or call the Chief Academic Officer of the Children's National Medical Center at (202) 476-5000.