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Martha Kruhm, MS, RAC
Head, Protocol and Information Office
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Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Executive Plaza North Room 730
Bethesda, MD 20892

Dear Ms. Kruhm,

Enclosed please find Amendment #8C to protocol **ACNS1723**, *A Phase 2 Study of Dabrafenib (NSC# 763760) with Trametinib (NSC# 763093) after Local Irradiation in Newly-Diagnosed BRAFV600-Mutant High-Grade Glioma (HGG) (IND#* [redacted]*).*

Amendment #8C is being submitted in response to the Updated CTEP Request for Rapid Amendment received on March 15, 2024. Section 6.1 of the protocol was revised to reflect updates made to the CAEPR. The condensed risk profile in the consent has been modified to include changes based on the updated Risk-List. Additionally, Section 6.1 of the protocol has been revised to reflect the new AURORA system in the Agent Ordering Section, and the previously used OAOP language has been removed.

Administrative changes have been made; specific changes are detailed in the Summary of Changes table below. Minor administrative updates (such as the correction of typographical errors, spelling, or updates to the numbers of referenced sections) are tracked in the protocol but not specified.

Please let me know if you have any questions or need additional information.

Sincerely,

Melina Chanthanouvong, Protocol Coordinator (for)
Rishi Lulla, MD, ACNS1723 Study Chair,
Maryam Fouladi, MD, CNS Committee Chair,
Sarah Leary, MD, CNS Committee Vice Chair, and
Douglas S. Hawkins, MD, COG Group Chair

A National Cancer Institute-funded group member of the National Clinical Trials Network

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SUMMARY OF CHANGES: INFORMED CONSENT

In accordance with the above discussion, the following specific revisions have been made to the consent. Additions are in **boldfaced** font and deletions in ~~strikethrough~~ font.

#	Section	Page(s)	Change
1.	General	All	Updated version date of consent to match the current version of the protocol.

2.	Possible Side Effects of Dabrafenib	7-8	In response to the Updated Request for Rapid Amendment (RRA) dated March 15, 2024, a revised risk-list for dabrafenib was inserted. Specific changes are listed as follows:
			• Added New Risk:
			  • Rare: Production of too many white cells that may cause failure of multiple organs; Heart failure which may cause shortness of breath, swelling of ankles, and tiredness
			• Provided Further Clarification:
			  • Changes in the eyes that may cause blurred vision or blindness (under Rare) is now reported as Vision loss (under Rare).
			  • Swelling and redness of the eye (under Rare) is now reported as Swelling and redness of the eye with a chance of blindness (under Rare).

This model informed consent form has been reviewed by the DCT/NCI and is the official consent document for this study. Institutions must use the sections of this document that are in bold type in their entirety. Editorial changes to these sections may be made as long as they do not change information or intent. If the local IRB insists on making deletions or more substantive modifications to any of the sections in bold type, they must be justified in writing by the investigator at the time of the institutional audit.

SAMPLE RESEARCH INFORMED CONSENT/PARENTAL PERMISSION FORM

ACNS1723: A Phase 2 Study of Dabrafenib (NSC# 763760) with Trametinib (NSC# 763093) after Local Irradiation in Newly Diagnosed *BRAF*^{V600}-Mutant High-Grade Glioma (HGG) (IND #[redacted])

Study Title for Participants:
A Study of the Drugs Dabrafenib and Trametinib after Radiation Therapy in Patients with Newly-Diagnosed High-Grade Glioma

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

Overview

You are being asked to take part in this research study because you have been diagnosed with high-grade glioma (HGG).

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive medical care.

The overall goal of this study is to see if using two drugs called dabrafenib and trametinib after radiation treatment will be better than treatments used in the past in helping to get rid of or shrink HGG.

The treatment involves cancer fighting medicines plus radiation. The treatment on this study takes a little over 2 years. It is divided into 2 phases of therapy.

All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer therapies can damage normal tissue and produce side effects.

Common side effects of cancer therapy include nausea and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea.

This study uses the investigational drugs dabrafenib and trametinib. Common side effects of dabrafenib are nausea, tiredness, fever, pain, headache, hair loss, and skin changes including rash. Some less common but notable side effects of dabrafenib are bleeding, developing a new skin cancer, and changes in the eyes that may cause blurred vision or blindness. Common side

effects of trametinib are diarrhea, nausea, tiredness, swelling of the body, and skin changes including rash and acne. Some less common but notable side effects of trametinib are changes in heart function and changes in the eyes (blood clot or retinal detachment) which may cause blindness. The full list of risks for dabrafenib and trametinib are available in the section **What side effects or risks can I expect from being in the study?**

You can ask your study doctor questions about side effects at any time.

We hope that this study will help you personally, but we do not know if it will. The potential benefits to you associated with participation in this study are described in the section **Are there benefits to taking part in the study?**

You have a choice between a standard treatment for HGG and this clinical trial.

The rest of this form provides detailed information about the study and what to expect should you decide to participate.

Why am I being invited to take part in this study?

You are being asked to take part in this research study because you have been newly-diagnosed with a type of cancer called high-grade glioma (HGG).

A glioma is a type of cancer that grows as a tumor in the brain. A glioma is considered “high-grade” when it is growing and spreading quickly.

You previously had pre-screening tests done on another study called APEC14B1 which you consented to. Those tests looked for genetic changes (called mutations) in your cancer cells such as *BRAF*^{V600}. The pre-screening tests confirmed that you have an HGG with a *BRAF*^{V600}-mutation. Because of this, the study doctors have determined that you are eligible for this study, ACNS1723. Please know that your eligibility for this trial may have been determined in part on the basis of a laboratory-developed test that has not been reviewed or approved by the FDA.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. This study is organized by Children’s Oncology Group (COG). COG is an international research group that conducts clinical trials for children with cancer. More than 200 hospitals in North America, Australia, New Zealand, and Europe are members of COG.

It is common to enroll children and adolescents with cancer in a clinical trial that seeks to improve cancer treatment over time. Clinical trials include only people who choose to take part. You have a choice between a standard treatment for HGG and this clinical trial.

Please take your time to make your decision. You may want to discuss it with your friends and family. We encourage parents to include their child in the discussion and decision to the extent that the child is able to understand and take part.

What is the current standard of treatment for this disease?

Standard treatment for HGG includes surgery to remove as much tumor as possible followed by radiation treatment (treatment with high-energy X-rays or high-energy protons) to kill cancer cells or stop them from growing back. Other commonly used treatments may include chemotherapy (anti-cancer drugs) given after radiation treatment.

Why is this study being done?

HGGs are hard to treat successfully. Study doctors want to find treatments that will be better at getting rid of or shrinking HGGs and stopping them from coming back. The pre-screening tests that you had done on APEC14B1 showed that you have an HGG with a *BRAF*^{V600}-mutation. This is important because previous studies have shown that patients who have the *BRAF*^{V600}-mutation in their cancer cells are most likely to benefit from a new type of treatment like the one we will test on this study. Two drugs that will be used on this study are dabrafenib and trametinib. This study will look at how well the combination of dabrafenib and trametinib works when given to children and young adults with HGGs after they receive radiation therapy. Although the combination of dabrafenib and trametinib is approved for adults by the Food and Drug Administration (FDA), the use of this combination to treat pediatric brain tumors is experimental.

The study doctors want to see if using dabrafenib and trametinib after radiation treatment will be better than treatments used in the past in helping to get rid of or shrink HGGs. Dabrafenib works by blocking a protein (a basic building block of the human body) called BRAF that lets cancer cells grow without stopping. Trametinib works similarly by blocking another protein called MEK that allows cancer cells to grow without stopping.

The overall goal of this study is to find out what effects, good and/or bad, dabrafenib and trametinib have on people with HGG.

What will happen on this study that is research?

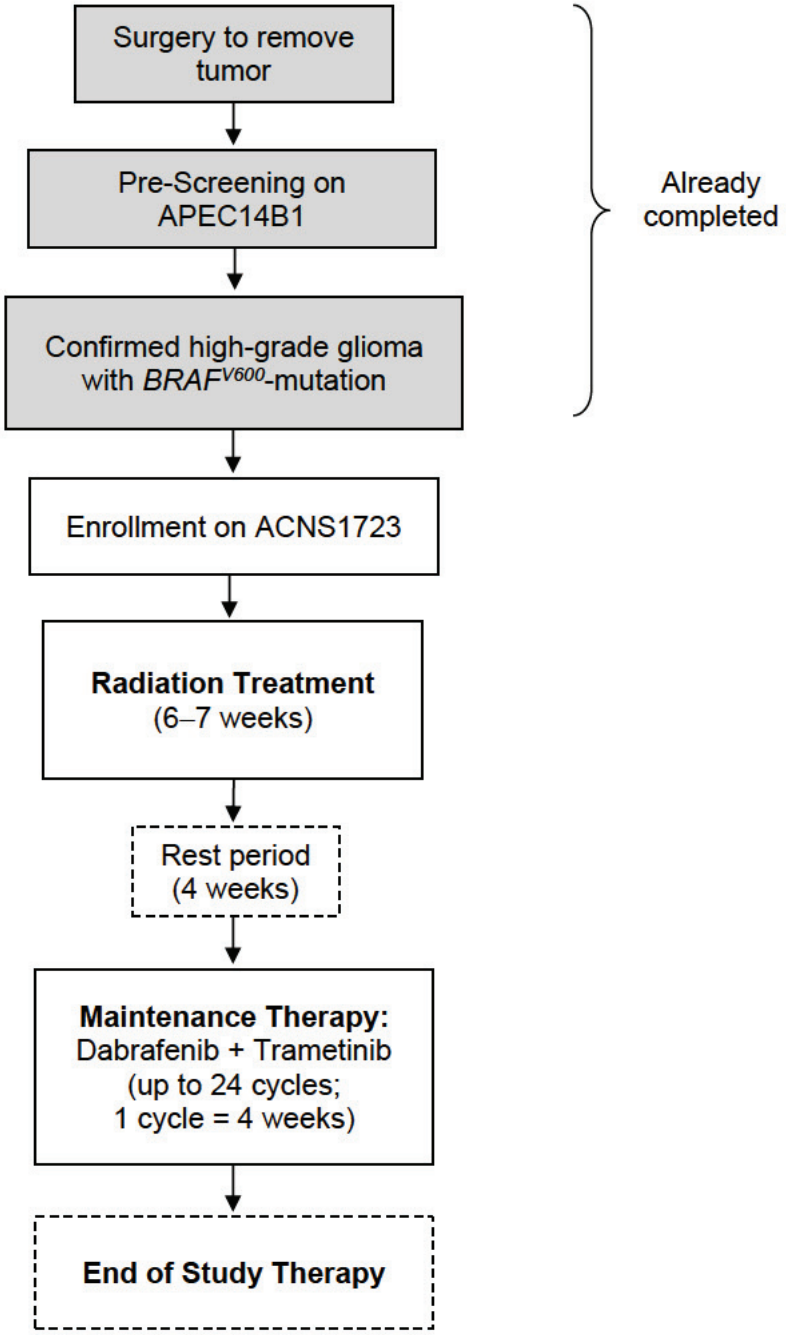
The study treatment involves cancer fighting medicine plus radiation therapy. The treatment on this study will last a little over 2 years. It is divided into two parts: radiation treatment followed by maintenance therapy (dabrafenib + trametinib). Radiation treatment will last 6–7 weeks. After radiation treatment, you will have a rest period during which you will not receive any treatment. After the rest period you will receive maintenance therapy. During maintenance therapy, you will receive treatment in “cycles.” Each cycle lasts 28 days. You will receive maintenance therapy for up to 24 cycles.

Radiation Treatment: X-rays used to kill cancer cells
Maintenance Therapy: Anti-cancer drugs dabrafenib + trametinib

The radiation treatment used in this study is standard or regular therapy for people with newly-diagnosed HGG. The treatment on this study is different from standard therapy because we are using the drugs dabrafenib and trametinib after the standard radiation therapy.

Diagram of Treatment

This chart shows treatment on this study.



Note: If your tumor gets bigger or if side effects are too severe, then you will stop study therapy and your doctor will discuss other options with you.

Methods for Giving Drugs

- **PO** - Drug is given by tablet, capsule or liquid swallowed through the mouth.

Treatment during Maintenance Therapy

Treatment during one 28-day cycle is described below. You may receive the treatment below for up to 24 cycles.

Drug	How the drug will be given	Days
Dabrafenib	PO, twice daily	1–28
Trametinib	PO, once daily	1–28

Research Study Tests and Procedures

The following tests will be done because you are part of this study. If you were not in the study you would probably not have these tests. Procedures that are common to all patients with HGG are described in **Attachment 1**.

Copies of the scans used to diagnose the cancer and determine the response to therapy will be sent to a central review center to help confirm findings. The results of these reviews will not be returned to you.

Optional Research Study Tests

Biobanking

We would like to take some samples for future research. This is called "specimen banking" or "tissue banking." A tissue bank is a lab where specimens (such as tumor, blood or bone marrow) are kept for use in future research studies.

You do not have to provide these samples if you do not want to. You can still be in the study if you do not want to provide these samples. At the end of this consent form, there is a place to record your decision about taking part in biobanking.

Tumor tissue: As part of your regular care, you had surgery to remove tumor tissue. If any of this tissue is left over and no longer needed for your medical care, we would like to keep some of this tissue. Obtaining these samples will not require extra surgery.

Blood: We would like to collect about 2 teaspoons of blood (10 mL) before you start treatment, during treatment when scans are being done (about 10 different times during treatment), at the end of treatment, and if the cancer comes back. The blood would be taken when blood is drawn for other standard tests and would not require any extra needle sticks.

Urine: We would like to collect about 4–10 teaspoons of urine (20–50 mL) before you start treatment, during treatment when scans are being done (about 10 different times during treatment), at the end of treatment, and if the cancer comes back.

CSF: We would also like to collect extra samples of cerebrospinal fluid (CSF) if available during your treatment. We will collect about 1 teaspoon (5 mL) of CSF each time it is drawn for other standard tests. Obtaining these samples would not require any extra procedures.

What side effects or risks can I expect from being in the study?

Treatment Risks
All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer therapies can damage normal tissue and produce side effects.

The risks of individual drugs given on this study are listed below. The risks of radiation therapy which is given on this study are listed in Attachment 2.

Common side effects of cancer therapy include nausea and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea.

Side effects can be increased when drugs are combined.

Risks of Study
The use of dabrafenib and trametinib after radiation treatment may cause more complications.

The dabrafenib and trametinib treatment that is being studied could be less effective than the current standard treatment.

You may lose time at school, work, or home and spend more time in the hospital or doctor's office than usual. You may be asked sensitive or private questions which you normally do not discuss.

The treatment used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health

There is also a risk that you could have side effects from the study drugs/study approach. Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

You can ask your study doctor questions about side effects at any time.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drugs.

The table(s) below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Dabrafenib

COMMON, SOME MAY BE SERIOUS In 100 people receiving dabrafenib (GSK2118436B), more than 20 and up to 100 may have:
• Nausea • Tiredness • Fever *(Fever and complications of fever are more frequent and severe when dabrafenib is used together with trametinib dimethyl sulfoxide.)* • Pain • Headache • Hair loss • Skin changes including rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dabrafenib (GSK2118436B), from 4 to 20 may have:
• Anemia which may require blood transfusion. • Constipation, diarrhea, vomiting • Chills • Swelling of arms, legs • Flu-like symptoms including body aches. • Cold symptoms such as stuffy nose, sneezing, sore throat • Bleeding *(The risk of bleeding is increased when dabrafenib is used together with trametinib dimethyl sulfoxide.)* • Infection, especially when white blood cell count is low • Loss of appetite • A new skin cancer resulting from treatment of earlier cancer • Wart • Dizziness • Cough • Dry skin • Change in hair • Increased sweating • Redness, pain or peeling of palms and soles • Itching • High blood pressure which may cause headaches, dizziness, blurred vision • Blood clot which may cause swelling, pain, shortness of breath *(The risk is increased when dabrafenib is used together with trametinib dimethyl sulfoxide.)*

RARE, AND SERIOUS In 100 people receiving dabrafenib (GSK2118436B), 3 or fewer may have:

- Heart failure which may cause shortness of breath, swelling of ankles, and tiredness.
- Swelling and redness of the eye with a chance of blindness
- Visual loss
- A tear or hole in the bowels that may require surgery
- Pain in belly (pancreas) that may require hospitalization
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat.
- Production of too many white cells that may cause failure of multiple organs
- Fainting
- Kidney damage which may require dialysis *(The risk is increased when dabrafenib is used together with trametinib dimethyl sulfoxide.)*
- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure.
- Swelling and redness of the skin
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Trametinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), more than 20 and up to 100 may have:
• **Diarrhea, nausea** • **Tiredness** • **Swelling of the body** • **Skin changes including rash, acne**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Abnormal heartbeat** • **Blurred vision or other visual disturbances** • **Dry eye, mouth, skin** • **Swelling of the eye** • **Pain** • **Constipation, heartburn, vomiting** • **Sores in the mouth which may cause difficulty swallowing** • **Chills, fever** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Infection** • **Change in heart function** • **Loss of appetite, dehydration** • **Dizziness, headache** • **Cough, shortness of breath** • **Hair loss, itching** • **Change in or loss of some or all of the finger or toenails** • **High blood pressure which may cause headaches, dizziness, blurred vision** • **Bleeding**

RARE, AND SERIOUS In 100 people receiving trametinib dimethyl sulfoxide (GSK1120212B), 3 or fewer may have:
• **Heart failure which may cause shortness of breath, swelling of ankles, and tiredness** • **Changes in the eyes (blood clot or retinal detachment) which may cause blindness** • **Blood clot which may cause swelling, pain, shortness of breath** • **A tear or hole in the bowels that may require surgery** • **Damage to muscle which may cause muscle pain, dark red urine** • **Damage to the lungs which may cause shortness of breath** • **Redness, pain or peeling of palms and soles** • **Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure** • **Severe skin rash with blisters and peeling which can involve mouth and other parts of the body**

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Reproductive risks

Women should not become pregnant and men should not father a baby while on this study because the drug(s) in this study can be bad for an unborn baby. If you or your partner can get pregnant, it is important for you to use birth control or not have sex while on this study and for 4 months after the last dose of study therapy. Check with your study doctor about what kind of birth control methods to use and how long to use them.

Some birth control methods might not be approved for use in this study. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. Men (including those that have had a vasectomy) taking the dabrafenib and trametinib combination therapy must use a condom during sex and for 16 weeks after stopping treatment, and should not father a child during these periods. Women should not breastfeed a baby while on this study. Also check with your doctor about how long you should not breastfeed after you stop the study treatment(s).

Are there benefits to taking part in the study?

We hope that this study will help you personally, but we do not know if it will.

Potential benefits to you could include:

- getting rid of your cancer for a long time

With any cancer treatment, sometimes treatment does not make the cancer go away. Or, sometimes treatment makes the cancer go away for a while but the cancer comes back later.

We expect that the information learned from this study will benefit other patients in the future.

What other options are there?

Instead of being in this study, you have these options:

- **Current standard therapy even if you do not take part in a study. Standard therapy is described in Attachment 1.**
- **Taking part in another study.**

Please talk to your doctor about these and other options.

How many people will take part in the study?

The total number of people enrolled on this study is expected to be 58.

How long is the study?

People in this clinical trial are expected to receive treatment on this study for about 2 years. After treatment, you will have follow-up examinations and medical tests.

We would like to continue to find out about your health for about 5 years after you enter this study. By keeping in touch with you for a while after you complete treatment, we can better understand the long-term effects of the study treatments.

You can stop taking part in the study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first. They will help you stop safely.

Your doctor or the study doctor may decide to take you off this study:

- if he/she believes that it is in your best interest
- if you become pregnant
- if your disease comes back during treatment
- if you experience side effects from the treatment that are considered too severe
- if new information becomes available that shows that another treatment would be better for you

What about privacy?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. Information about the certificate is included in **Attachment 3**.

Organizations that may look at and/or copy your research or medical records for research, quality assurance and data analysis include groups such as:

- **Children's Oncology Group,**
- **The NCI's National Clinical Trials Network and the groups it works with to conduct research including the Imaging and Radiation Oncology Core (IROC)**
- **Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. and international governmental regulatory agencies involved in overseeing research,**
- **The Institutional Review Board of this hospital,**
- **Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute**
- **Any drug company supporting the study or their designated reviewers.**

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.

- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

What are the costs?

Taking part in this study may lead to added costs to you or your insurance company. There are no plans for the study to pay for standard medical treatment. Please ask about any expected added costs or insurance problems. Staff will be able to assist you with this.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury. However by signing this form, you are not giving up any legal rights to seek to obtain compensation for injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

You will not be charged for the optional biobanking on this study.

The NCI will supply dabrafenib and trametinib at no charge while you take part in this study. The NCI does not cover the cost of getting dabrafenib and trametinib ready and giving it to you, so you or your insurance company may have to pay for this.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide dabrafenib and trametinib to the NCI for some reason. If this does happen, other possible options are:

- You might be able to get dabrafenib and trametinib from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.

- If there is no dabrafenib and trametinib available at all, no one will be able to get more and the study would close.

If a problem with getting dabrafenib and trametinib occurs, your study doctor will talk to you about these options.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

Funding support

If you choose to enroll on this study, this institution will receive some money from the Children's Oncology Group to do the research. There are no plans to pay you for taking part in this study.

This study includes providing specimens to the researcher, there are no plans for you to profit from any new product developed from research done on your specimens.

What are my rights as a participant?

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive medical care.

You can decide to stop being in the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your doctor will still take care of you.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. A committee outside of COG closely monitors study reports and notifies COG if changes must be made to the study. Members of COG meet twice a year to discuss results of treatment and to plan new treatments.

During your follow-up visits after treatment, you may ask to be given a summary of the study results, which will only be available after the study is fully completed. *A summary of the study results will also be posted on the Children's Oncology Group website (http://www.childrensoncologygroup.org/)*. To receive the results, you may either (1) go to the COG website to check if results are available or (2) register your information with the COG on its web site and have an email sent to you when the results are available. Your pediatric oncology team from your hospital can give you additional instructions on how to do this. Please note, that the summary of results may not be available until several years after treatment for all people on the study is completed, and not only when you complete treatment.

Whom do I call if I have questions or problems?

For questions about the study or if you have a research related problem or if you think you have been injured in this study, you may contact Dr. *XXXX* or your doctor at *XXXX*.

If you have any questions about your rights as a research participant or any problems that you feel you cannot discuss with the investigators, you may call *XXXX* IRB Administrator at *XXXX*.

If you have any questions or concerns that you feel you would like to discuss with someone who is not on the research team, you may also call the Patient Advocate at *XXXX*.

Where can I get more information?

The COG Family Handbook for Children with Cancer has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at https://www.childrensoncologygroup.org/index.php/cog-family-handbook.

Visit the NCI's Web site at http://www.cancer.gov.

If you are in the United States, you may call the NCI's *Cancer Information Service* at: 1-800-4-CANCER (1-800-422-6237).

Information about long term follow-up after cancer treatment can be found at: http://www.survivorshipguidelines.org/.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You will get a copy of this form. You may also ask for a copy of the protocol (full study plan).

Specimens for Optional Biobanking

If you agree to Biobanking, your sample will be stored in the *Biopathology Center at Nationwide Children's Hospital, in a locked freezer*. The Biopathology Center is supported by the NCI. The samples will be kept until they are used up, unless you request that they be destroyed. Some information from your medical record will also be kept in secure databases at the Biobank and updated from time to time. The information and samples will be kept under a code, not your name.

This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. Qualified researchers can submit a request to use the materials stored in the Biobank. The research may be about your type of cancer, about other cancers, or even about conditions unrelated to cancer. A science committee at the Children's Oncology Group, and/or the National Cancer Institute, will review each request. The goal of this is to make more research possible that may improve people's health. Researchers will not be given your name or any other information that could directly identify you. Your sample will not be sold to third parties. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples, unless something is discovered that could directly affect your health. If that happens your study doctor will be notified and will decide whether and how to contact you.

Right now, we don't know what research may be done in the future using your samples. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers

understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

Some of your genetic and health information may be placed in central databases that may be made available to qualified researchers, along with information from many other people. Information that could directly identify you will not be included.

Even without your name or other identifiers, your genetic information is unique to you. If you agree to Biobanking, there is a risk of a data security breach and that someone could trace the genetic information in a central database back to you. Although this has never happened in real life and we have many safeguards in place to prevent it from happening, the risk may change in the future as people come up with new ways of tracing information. There are laws against the misuse of genetic information, but they may not give full protection. In some cases, misuse of the information could be used to make it harder for you to get or keep a job or insurance.

There can also be risks in learning about your own genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. Sometimes this is upsetting to families or they wish they didn't know the information. We encourage you to discuss this study with your relatives before you decide whether to participate in the Biobanking part.

If you want to learn more about tissue research with banked specimens, the NCI website has an information sheet called "Providing Your Tissue For Research: What You Need To Know." This sheet can be found at: https://www.cancer.gov/publications/patient-education/providing-tissue.

Please read the information below and think about your choices. After making your decisions, check "Yes" or "No", then add your initials and the date after your answer. If you have any questions, please talk to your doctor or nurse, or call our research review board at the IRB's phone number included in this consent.

1) Check YES if you agree to have tissue, blood, urine, and CSF samples kept (banked) for use in research to learn about, prevent, or treat cancer or other health problems (for example: diabetes, Alzheimer's disease, or heart disease). Check NO if you do not want samples banked.

Yes_____ No_____ _____ / _____
Initials Date

Signature

I have been given a copy of all _____ pages of this form. The form includes three (3) attachments.

I have reviewed the information and have had my questions answered.
I agree to take part in this study.

Participant_____Date _____

Parent/Guardian_____Date _____

Parent/Guardian_____Date _____

Physician/PNP obtaining consent_____Date _____

Attachment 1

Treatment and Procedures Common to all Patients with High-Grade Glioma

Methods for Giving Drugs

Various methods will be used to give drugs:

- **PO** - Drug is given by tablet (Trametinib) and capsule (Dabrafenib) or liquid swallowed through the mouth.

Standard Radiation Therapy for Subjects on All Treatment Arms

All subjects will receive standard radiation therapy while on this study. Standard radiation therapy for high-grade glioma is radiation therapy to the brain 5 days a week for approximately 6 weeks. The amount of radiation you receive on this study will be the standard amount used to treat newly diagnosed high-grade glioma. The risks of standard radiation therapy are shown in **Attachment 2**.

Standard Tests and Procedures

The following tests and procedures are part of regular cancer care and may be done even if you do not join the study.

- Frequent labs to monitor your blood counts and blood chemistries.
- Urine tests to measure how your kidneys are functioning.
- Pregnancy test for females of childbearing age before treatment begins.
- MRI scans to monitor your response to treatment.
- Tests to monitor your liver function.

Attachment 2

Risks of Radiation Used to Treat High-Grade Glioma

Possible Side Effects of Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, more than 20 and up to 100 may have:
• **Reddening, tanning, or peeling of the skin** • **Mild pain** • **Hair loss** • **Tiredness** • **Diarrhea, nausea** • **Anemia, which may require transfusion** • **Infection, especially when white blood cell count is low**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, from 4 to 20 may have:
• **Thickening and numbness of the skin** • **Sores or ulcers on the skin or near the cancer location** • **Permanent hair loss** • **Bleeding from the skin** • **Sores in mouth which may cause difficulty swallowing**

RARE, AND SERIOUS In 100 people receiving radiation therapy, 3 or fewer may have:
• **Damage to internal organs** • **Abnormal opening in internal organs which may cause pain and bleeding**

Attachment 3

Certificate of Confidentiality

The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.