CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

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

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Martha Kruhm, MS, RAC
Head, Protocol and Information Office
Operations and Informatics Branch
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 #5A to protocol **AREN1721**, *A Randomized Phase 2 Trial of Axitinib/Nivolumab Combination Therapy vs. Single Agent Nivolumab for the Treatment of TFE/Translocation Renal Cell Carcinoma (tRCC) Across All Age Groups*.

This amendment is being done to include proposed language from a stipulation in the PedCIRB's Continuing Review of AREN1721.

Minor administrative updates have been made; specific changes are detailed in the Summary of Changes table below.

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

Sincerely,

Kathryn Franklin Protocol Coordinator (for)
James Geller, MD, AREN1721 Study Chair,
Jeff Dome, Interim Renal Committee Chair, and
Douglas S. Hawkins, MD, COG Group Chair

AREN1721 SUMMARY OF CHANGES: INFORMED CONSENT DOCUMENT 2 (applicable to patients enrolled after Amendment 2A)

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.	Why is this study being done?	2	Text regarding the overall goal of the study has been revised to provide greater clarity at the request of the PedCIRB during their Continuing Review of the study.

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

Study Title for Study Participants: A Study to Compare Treatments for a Type of Kidney Cancer called TFE/Translocation Renal Cell Carcinoma (tRCC)

AREN1721: A Randomized Phase 2 Trial of Axitinib/Nivolumab Combination Therapy vs. Single Agent Nivolumab for the Treatment of TFE/Translocation Renal Cell Carcinoma (tRCC) Across All Age Groups

NOTE TO SITES: THIS CONSENT FORM ONLY APPLIES TO PATIENTS ENROLLED AFTER AMENDMENT #2A.

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.

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 diagnosed with TFE/translocation renal cell carcinoma. TFE stands for 'transcription factor E', a gene and protein that activates other genes and proteins, providing multiple 'signals' within the cancer cells that can promote tumor growth. Renal cell carcinoma (RCC) is a type of cancer that occurs in the kidneys. TFE/translocation renal cell carcinoma (tRCC) is a subtype of RCC that is more common in children and young adults but can be found in all age groups.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This trial is part of the national NCI Clinical Trials Network (NCTN) program which is sponsored by the National Cancer Institute (NCI). The trial will be conducted by the network of NCTN researchers, led by the 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, adolescents, and adults 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 another treatment for tRCC 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?

At this time, there is no treatment that is standard or typical for patients with tRCC. Treatment options might include treatments that are used for other forms of renal cell carcinoma, such as surgery to remove the tumor, chemotherapy (cancer fighting medicine), or immunotherapy (treatments that help your body's immune system to fight cancer).

Why is this study being done?

In this study, we are interested in learning more about how to treat tRCC. To do this, we will test 2 drugs (axitinib and nivolumab) given together or one drug (nivolumab) given alone.

The drugs axitinib and nivolumab have been used to treat adults and children with different types of cancer, including RCC. Axitinib is a chemotherapy drug that works by stopping the growth of new blood vessels to cancer cells, which (if left untreated) would feed the cancer cells and allow them to grow. Nivolumab is an immunotherapy that works by helping the body's immune system (your body's own defense system) to recognize and attack the cancer cells.

Both axitinib and nivolumab have been approved by the FDA for treating RCC. However, using these 2 drugs together is considered experimental. Also, this will be the first study of treatments specifically for tRCC. We would like to know if using these drugs alone or together for the treatment of tRCC will be well-tolerated in subjects. Subjects are people who are agree to take part in this study.

The study is being conducted to determine which of 2 treatment regimens, axitinib and nivolumab in combination or nivolumab alone, provides better disease control and survival.

What will happen on this study that is research?

The treatment involves the drugs axitinib and nivolumab given together or nivolumab given alone. You may receive treatment on this study for up to 2 years depending on your response to therapy. The treatment on this study is experimental for tRCC.

Summary of Study Treatments
In this study you will get 1 of 2 treatment plans. The 2 treatment plans are called Arm A and Arm C, as follows:

- **Arm A:** Axitinib and Nivolumab
- **Arm C:** Nivolumab only

Random Assignment
You will receive 1 of 2 different treatment plans. The treatment plan that you receive is decided by a process called randomization. Randomization means that the treatment is assigned based

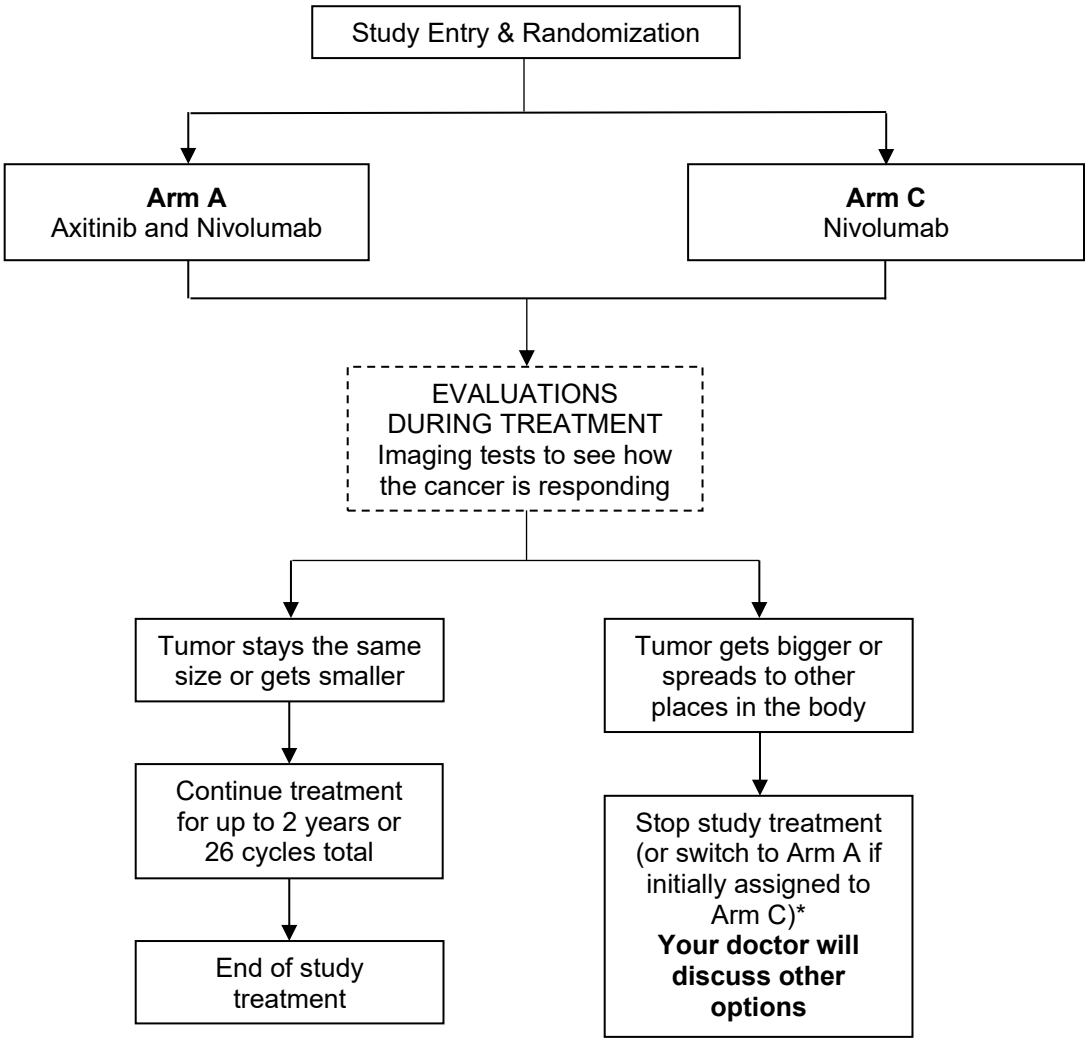
on chance. It is a lot like flipping a coin, except that it is done by computer. You and your doctor will not pick which treatment you get. The randomization process is described in the COG Family Handbook for Children with Cancer.

Some subjects will be randomized to receive treatment on Arm A; some will be randomized to receive treatment on Arm C. There is a 50:50 chance that you will be randomized to Arm A or Arm C.

If you are randomized to Arm C and your cancer gets worse while you are receiving treatment on Arm C, you may have the option to switch to receiving treatment on Arm A. You must have had no more than 21 cycles of Arm C therapy to be eligible to switch to Arm A. Your doctor will guide you as to how to safely change therapy.

Note: If you completed study treatment on Arm C prior to September 2021 then you would not have the option to switch to treatment on Arm A.

Diagram of Treatment
This chart shows the treatments on this study.



*This is only an option if you have had no more than 21 cycles of therapy on Arm C.

Treatment that is Research

Methods for Giving Drugs

Drugs that are part of the treatment in this study are given in different ways. The ways that they are given are:

- **PO** - Drug is given by tablet swallowed through the mouth.
- **IV** - Drug is given using a needle or tubing inserted into a vein.

Central Line

Your doctor may recommend that you get a special kind of IV called a "central line." This is a kind of IV placed into a big vein in your body, usually in the chest, that can stay in for a long time. The risks connected with central lines will be explained to you and all of your questions will be answered. If you are to have a central line inserted, you will be given a separate informed consent document to read and sign for this procedure. A description of the types of central lines is in the COG Family Handbook for Children with Cancer.

On this study, treatment will be given in cycles that last 28 days (4 weeks) each. The tables below describe 1 cycle for each of the different treatment plans.

Treatment for subjects who are on Arm A

Drug	How the drug will be given	Days
Axitinib	PO (by mouth)	1 - 28
Nivolumab	IV over 30 minutes or per institutional guidelines	For patients younger than 18: Days 1 and 15 For patients 18 years of age and older: full dose on Day 1 only OR dose split and given on Days 1 and 15

Treatment for subjects who are on Arm C

Drug	How the drug will be given	Days
Nivolumab	IV over 30 minutes or per institutional guidelines	For patients younger than 18: Days 1 and 15 For patients 18 years of age and older: full dose on Day 1 only OR dose split and given on Days 1 and 15

Whether you are on Arm A or Arm C, you will also have evaluations (imaging tests) during treatment to see how the cancer is responding. These evaluations will happen at the end of Cycles 2, 4, 6, 9, 12, and then every 4 cycles after that. If your tumor has not gotten bigger or spread to other places in the body, and you do not have bad side effects, your doctor may suggest that you continue with the study treatment. If this happens, you may receive up to 2 years or 26 cycles of treatment, whichever comes first.

If your tumor gets bigger or spreads to other places in the body at any time during treatment, or if the side effects from the treatment are too severe, you will stop getting treatment on this study. If that happens, your doctor will discuss other treatment options with you. If you are randomized to Arm C and your tumor gets bigger or spreads to other places in the body at any time during treatment, you may have the option to switch to receiving treatment on Arm A. If this

happens, you still may receive up to a total of 2 years or 26 cycles of treatment, whichever comes first, and this will include the time that you received treatment on Arm C.

Potential Axitinib Dose Increase
If you are randomized to Arm A, which includes Axitinib, or you switch to be treated on Arm A your doctor may decide to increase your Axitinib dose. Patients eligible for dose increase must meet specific safety criteria which your doctor can discuss with you. Axitinib dose increases have been well studied in adult patients. However, this has not been studied in pediatric patients. The possible risks and side effects of Axitinib may be increased if your dose is increased.

Research Study Tests and Procedures
Some of the tissue already taken and used to diagnose the cancer will be sent to a central review center as part of COG quality control. The results of these reviews will not be returned to you.

Required Research Study Tests

Pharmacokinetic Studies
These samples are required for subjects in Arm A (or subjects transferred to Arm A after receiving treatment on Arm C) who are less than 18 years of age.

During treatment, blood samples will be collected to see how much axitinib is in your blood at certain timepoints. This is known as a pharmacokinetic study. We will collect 2 mL (~1/2 teaspoon) of blood at the following times:

- Cycle 1, Day 1: a sample will be collected at 2, 4, and 6 hours after you receive axitinib.
- Cycle 2, Day 1: a sample will be collected before you receive axitinib.
- Cycle 3, Day 1: a sample will be collected before you receive axitinib.

If you switch from Arm C to Arm A, these samples will be collected on Day 1 of the first three cycles during which you receive both drugs per Arm A therapy.

Optional Research Study Tests
We would also like to do some tests called biologic studies. These tests are important to help us learn more about axitinib and nivolumab and may help people who receive these drugs in the future. The information learned would not change the way you are treated, and the results of these tests will not be given to you. You do not have to do these tests if you do not want to. You can still be in the study if you do not want to do these tests. At the end of this consent form, there is a place to record your decision about taking part in each test.

Tumor Tissue Collection for Biomarker Testing
As part of your regular care, your doctor may have removed some tumor tissue. During the study, you may have surgery to remove more tumor and you may have tumor tissue removed if the tumor gets bigger or comes back. We would like to test some of the tissue from each time you have tumor removed. These tests will help us learn more about biomarkers in tRCC tumors. Biomarkers are molecules in the body that might help us to predict how a certain type of cancer might respond to different treatments. Obtaining these samples will not require extra surgery since the tumor tissue can be obtained at the same time as regularly scheduled surgeries.

Blood Collection for Biomarker Testing
Study doctors would like to examine biomarkers in your blood to learn how your body's immune system is changing during treatment. This might help them to predict if someone will benefit

from the treatment. About 1 tablespoon (15-20 mL) of blood will be collected before the start of therapy, before Cycles 2, 3, and 9 of therapy, and at the end of therapy. Obtaining these samples should not require extra blood draws since they can be obtained at the same time as other routine blood tests.

Banking
We would like to take some of your tumor, blood, and urine for future research. This is called "specimen banking" or "tissue banking." A tissue bank is a lab where specimens (such as tumor, blood, or urine) are kept for use in future research studies. Obtaining these samples will not require extra surgery or blood draws since the samples can be obtained at the same time as regularly scheduled procedures.

Research on the banked specimens is **very unlikely** to discover results that are important to your current or future health. However, if it does, COG will try to contact your doctor about what the research tests might mean. Only the doctor will be notified and the information will not become part of your medical record. Your doctor will decide whether to discuss the results with you. Your doctor may recommend repeat testing, meeting with a genetic counselor, or no further action.

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

Side effects can be increased when drugs are combined.

The most common serious side effect from cancer treatment is lowering of the number of blood cells resulting in anemia, increased chance of infection, and bleeding tendency. Low blood counts are described in the COG Family Handbook for Children with Cancer. Parents will be taught more about caring for their child when his or her blood counts are low.

Risks of Study
The use of nivolumab alone, or axitinib and nivolumab together may cause complications. Getting axitinib and nivolumab together may cause more complications than getting nivolumab only.

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. You might not be able to take part in future studies.

The therapy 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.

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 Axitinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving axitinib (AG-013736), more than 20 and up to 100 may have:
• **Anemia which may require blood transfusion** • **Pain** • **Diarrhea, nausea, vomiting** • **Tiredness** • **Bruising, bleeding** • **Weight loss, loss of appetite** • **Changes in voice** • **Redness, pain or peeling of palms and soles** • **High blood pressure which may cause headaches, dizziness, blurred vision**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving axitinib (AG-013736), from 4 to 20 may have:
• **Constipation, heartburn** • **Sores in the mouth which may cause difficulty swallowing** • **Infection, especially when white blood cell count is low** • **Dehydration** • **A new cancer resulting from treatment of earlier cancer** • **Dizziness, headache** • **Changes in taste** • **Cough, shortness of breath** • **Rash**

RARE, AND SERIOUS In 100 people receiving axitinib (AG-013736), 3 or fewer may have:
• **Heart failure which may cause shortness of breath, swelling of ankles, and tiredness**

- **A tear or hole in internal organs that may require surgery**
- **Bleeding from multiple sites including nose**
- **Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood or blood in urine**
- **Non-healing surgical site**
- **Bleeding in the brain which may cause confusion**
- **Brain damage which may cause headache, seizure, blindness (known as Reversible Posterior Leukoencephalopathy Syndrome)**
- **Blood clot in artery which may cause swelling, pain, shortness of breath or change of color in extremity**
- **Blood clot which may cause swelling, pain, shortness of breath**
- **Weakening of artery which may cause bleeding**

Possible Side Effects of Nivolumab

Special precautions
Side effects of nivolumab may happen anytime during treatment or even after your treatment has ended. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, more than 20 and up to 100 may have:

- **Tiredness**

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, from 4 to 20 may have:

- **Anemia which may require blood transfusion**
- **Swelling and redness of the eye**
- **Pain**
- **Diarrhea, nausea**
- **Dry mouth**
- **Fever**
- **Swelling and redness at the site of the medication injection**
- **Bruising, bleeding**
- **Pain or swelling of the joints**
- **Loss of appetite**
- **Reaction during or following a drug infusion which may cause fever, chills, rash**

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- **Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.**
- **Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving nivolumab, from 4 to 20 may have:
• **Skin: itching; rash, blisters including inside the mouth; loss of skin pigment** • **Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.** • **Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urination; dizziness or fainting.**

RARE, AND SERIOUS In 100 people receiving nivolumab, 3 or fewer may have:
• **Dry eyes** • **Sores in the mouth which may cause difficulty swallowing** • **A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause blurred vision, ringing in the ears, changes in hair or hair loss** • **Swelling of the bowels** **Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:** • **Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness** • **A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma** • **Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.** • **Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.** • **Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine** • **Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck, confusion, sleepiness, seizures or injury to the brain which may cause headache, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)** • **Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and**

can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

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 at least 5 months after stopping treatment for women or for at least 7 months after stopping treatment for men. 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. Women should not breastfeed a baby for at least 5 months after stopping treatment. 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 or for the rest of your life,
- extending your life,
- lessening symptoms, such as pain, that are caused by the cancer.

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:

- **Getting treatment for your cancer without being in a study.**

- **Taking part in another study.**

- **Getting comfort care, also called palliative care.** This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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 about 40.

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 every year 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 your disease comes back during treatment
- if you become pregnant
- 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 2.

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, Alliance for Clinical Trials in Oncology, ECOG-ACRIN Cancer Research Group, NRG Oncology and SWOG**
- **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.**

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 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.

The NCI will supply the axitinib and/or nivolumab at no charge while you take part in this study. The NCI does not cover the cost of getting the axitinib and/or nivolumab 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 manufacturers may not continue to provide axitinib and nivolumab to the NCI for some reason. If this does happen, other possible options are:

- You might be able to get the axitinib and/or nivolumab from the manufacturers or your pharmacy but you or your insurance company may have to pay for it.
- If there is no axitinib and/or nivolumab available at all, no one will be able to get more and the study would close.

If a problem with getting axitinib or nivolumab 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 research tests

The choice to let us use specimens for research is up to you. No matter what you decide to do, it will not affect your care. You can still be a part of the main study even if you say 'No' to taking part in any of these optional research studies.

If you decide now that your specimens can be used for research and banking, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens. Then, any specimens that we have will be destroyed.

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 My tumor tissue may be collected and studied to look for biomarkers that may be used to predict how a person will respond to therapy.

Yes_____ No_____ _____ / _____
Initials Date

#2 My blood may be collected and studied to look for biomarkers that may be used to predict how a person will respond to therapy.

Yes_____ No_____ _____ / _____
Initials Date

If you agree to Biobanking, your sample will be stored *in the Biopathology Center at Nationwide Children's Hospital, in a locked freezer*. 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.

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. 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.

Some of the research on your samples may be about genes. Genes carry information about features that are found in you and in people who are related to you. 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 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 any new samples banked.

Yes_____ No_____ _____ / _____
Initials Date

Signature

I have been given a copy of all ____ pages of this form. The form includes two (2) 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

Procedures Common to all Patients with tRC*C*

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.
- X-rays and scans to monitor your response to treatment.
- Tests to monitor your heart and lung function.

Attachment 2

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.