NCI Community Oncology Research Program – Kansas City (NCORP-KC)

ARST1321

ICD for Subjects in the Non-Standard Chemotherapy Group

Arm C and Arm D, Part 2 Only

Part 2 for the non-standard chemotherapy group is closed as of October 12, 2017. As of Amendment #6, no additional updates will be made to the content of this consent.

Study Title for Study Participants: Testing the addition of the drug pazopanib to radiation in people with non-rhabdomyosarcoma soft tissue sarcoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Pazopanib Neoadjuvunt Trial on Non-Rhabdomyosarcoma Soft Tissue Sarcomas (PAZNTIS): A Phase II/III Randomized Trial of Preoperative Chemoradiation or Preoperative Radiation Plus or Minus Pazopanib (NSC# 737754, IND# 118613)

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.

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) and NRG Oncology.

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 a standard treatment for non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) and this clinical trial.

What is the usual approach to the type of cancer I have?

You are being asked to take part in this research study because you have a type of cancer called non-rhabdomyosarcoma soft tissue sarcoma (NRSTS). This study is for people with intermediate or high risk NRSTS that cannot be removed by surgery at the time of diagnosis. The term risk refers to the chance of the cancer coming back after treatment.

Patients with intermediate or high risk NRSTS are commonly treated with surgery to remove the tumor, chemotherapy (cancer fighting medicine) and/or radiation therapy (high energy X-rays). The chemotherapy drugs commonly used in NRSTS are ifosfamide and doxorubicin. However, not all patients receive chemotherapy.

You are being given this informed consent form because you have decided to proceed with radiation treatment and surgery without chemotherapy based on your discussion with your treating physician. You are in the non-standard chemotherapy group Part 2 of this study.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available

Please talk to your doctor about these and other options.

Why is this study being done?

In this study, researchers want to find out if we can improve the treatment for subjects (people who agree to take part in this study) with intermediate and high risk NRSTS by adding an experimental drug called pazopanib to standard therapy.

In adults with certain types of NRSTS pazopanib has been shown to have anti-tumor activity and it is FDA approved for use in adults with certain diseases, including advanced soft tissue sarcoma. Pazopanib has also been used in a small study in children with cancer. Although pazopanib is experimental for use in intermediate and high risk NRSTS, it has been shown to be well tolerated in children and adults. Pazopanib is approved in adults with certain diseases but is considered investigational in children and certain adults.

The addition of pazopanib to standard therapy could cause tumor cells to die but it could also cause side effects. This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To be better, the study drug should cause more tumor cells to die and improve survival compared to the usual approach.

Only some of the subjects in this group will receive the experimental drug pazopanib.

The goal of this study is:

- **To find out what effects (good and/or bad) pazopanib given with radiation therapy has on people with intermediate and high risk NRSTS.**

In addition to the treatment goal, we would like to answer some biology and imaging research questions that might benefit future patients. These studies are described in detail later in this form.

There will be about 200 people taking part in this study.

What will happen on this study?

There are 2 parts to this study. The only difference in treatment between the 2 parts is that some subjects treated in Part 1 will receive a different dose of pazopanib than the subjects treated in Part 2. You have been assigned to Part 2 of this study.

Part 1
We will find out the highest dose of pazopanib that can be given in combination with the standard therapy (radiation) without causing side effects that are too severe. This dose is called the maximum tolerated dose (MTD). Different doses of pazopanib will be given to groups of study subjects. The first dose to be examined is called dose level 1. If the therapy does not have too many side effects then the pazopanib dose for the next group of subjects will be increased. But, if the therapy at dose level 1 causes too many side effects then the pazopanib dose for the next group of subjects will be lowered.

We will determine the MTD for subjects aged less than 18 years and the MTD for subjects aged 18 years or older.

Once we have determined the MTD of pazopanib to give with standard therapy, we will move on to Part 2 of the study.

Part 2
All patients who enroll in Part 2 and are assigned to receive pazopanib will be given the drug at the MTD found in Part 1. We will treat more subjects to find out how effective the MTD of pazopanib is against NRSTS, when it is given in combination with standard therapy (radiation).

What are the study plans?

This non-chemotherapy group contains 2 treatment plans and you will get 1 of the 2 treatment plans. One treatment plan includes the experimental drug, pazopanib, and the other does not. The 2 treatment plans for the non-chemotherapy group are called Arm C and Arm D, as follows:

- Arm C (Experimental): Subjects receive standard radiation therapy and surgery (if possible) plus the drug pazopanib.

- Arm D (Standard): Subjects receive standard radiation therapy and surgery (if possible).

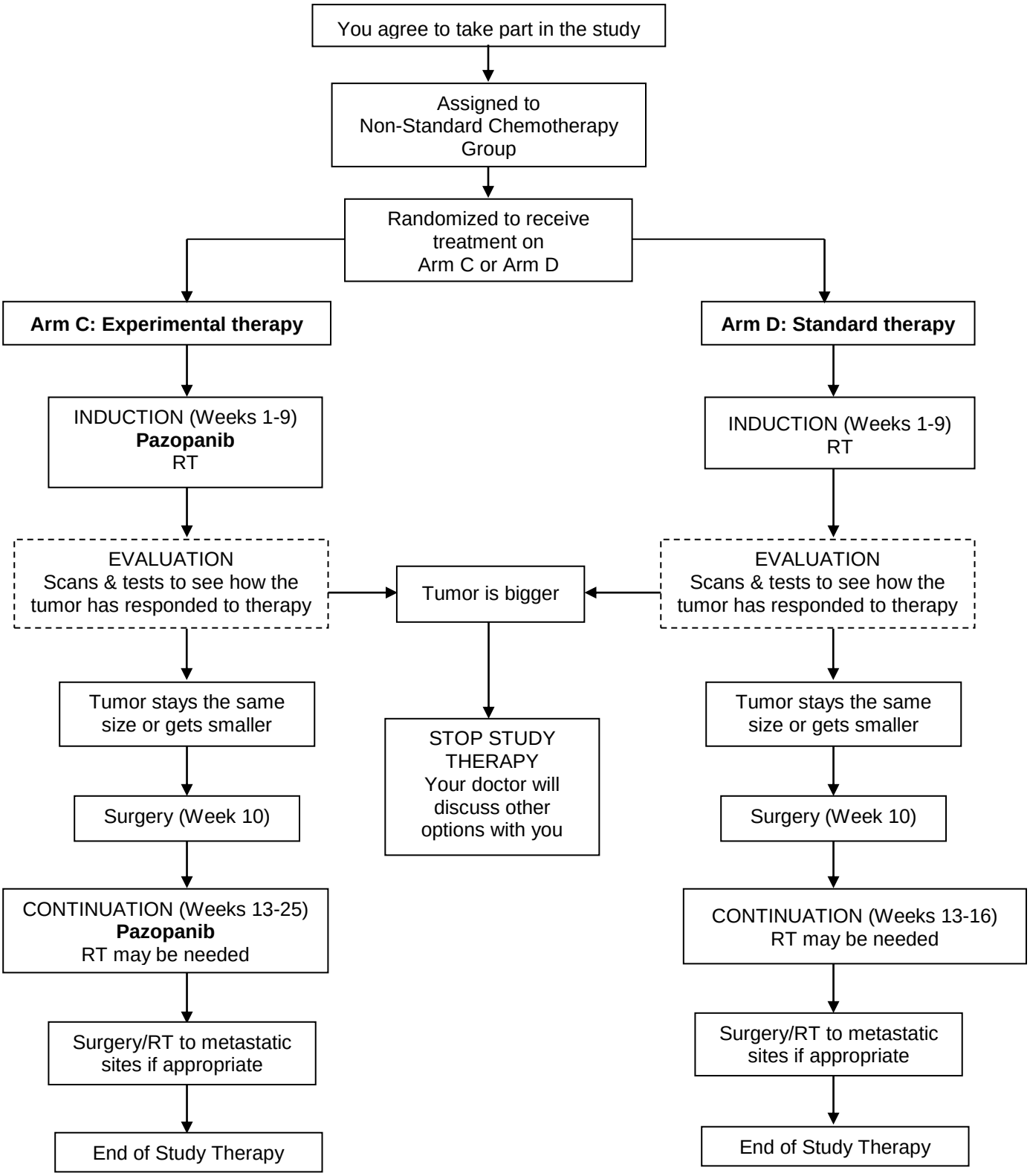
Random Assignment

In this study some subjects will receive pazopanib (Arm C) and some will not (Arm D). 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.

Standard treatment is divided into 3 stages, called Induction, Local Control, and Continuation. Treatment that is standard is described in Attachment #1.

A diagram of the study treatment is shown below.

Diagram of Treatments for the Non-Chemotherapy Group



RT = Radiation therapy. In Induction, RT will start at Week 1. If given during Continuation, RT will start at Week 13. RT will not be given every day during Induction or Continuation.

Treatment that is Research

Treatment for subjects who are on Arm C (Experimental)

An overview of the complete treatment follows:

Arm C, Non-Standard Chemotherapy Group with Pazopanib							
Induction Phase			**Local Control**	**Continuation Phase**			
Week 1	Week 4	Week 7	Week 10	Week 13	Week 16	Week 19	Weeks 22- 25
Pazopanib Weeks 1-9			Surgery	Pazopanib Weeks 13-25			
Radiotherapy				Radiotherapy may be needed			

During Induction and Continuation, subjects will be given the experimental drug, pazopanib, along with the standard treatment. Pazopanib tablets are to be swallowed whole every day during Weeks 1-9 and Weeks 13-25. Pazopanib will not be given for at least 7 days before surgery and for at least 14 days after surgery. To allow for that, you may not be given pazopanib for a full 7 days in Weeks 9 or 25.The standard therapy that will be given is described in Attachment #1.

The dose of radiation treatment is different than previously used in similar patients and may be less or more for children or adults because of the treatment with pazopanib.

You will be given a Patient Medication Diary at the beginning of each cycle of Pazopanib. Use the diary to record the date and time you take the drug, the number of tablets taken, side effects you experience and any other medications you are taking. The diary should be returned to the clinic before starting the next cycle. This will help us to know how much of the drug you take and how it made you feel.

Treatment for subjects who are on Arm D (Standard):
The standard therapy is described in Attachment #1.

How long will I be in this study?

People in this clinical trial who receive pazopanib (Arm C) are expected to receive treatment on this study for around 25 weeks (around 6 months). People in this clinical trial who receive standard radiotherapy alone (Arm D) are expected to receive treatment on this study for around 16 weeks (around 4 months).

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.

What extra tests and procedures will I have if I take part in this study?

A number of tests will be performed that are part of regular cancer care and may be done even if you do not decide to take part in this study. Examples of regular tests are included in Attachment #1. These include labs to monitor blood counts and blood chemistries, and scans to monitor your response to therapy.

Some blood tests will be done more frequently because you are taking part in this study. We will perform blood tests as often as every week during therapy.

If you are to receive pazopanib (Arm C) and you are aged less than 18 years, we will take x-rays of your knees before treatment begins and possibly again at the end of the treatment.

Some of the tissue already taken and copies of the scans used to diagnose the cancer will be sent to a central review center as part of COG quality control.

Required Research Study Test

If you choose to participate in this study, we will examine tumor tissue and blood to look for changes in genes (mutations) that may impact how an NRSTS tumor responds to therapy with pazopanib. We hope that in the future we may be able to direct therapy against tumor cells that carry certain mutations. The information learned would not change the way you are treated, and the results of these tests will not be given to you.

Tissue was removed in order to diagnose the cancer. We will use some of that tissue for this research test. In addition, we will collect blood samples from each subject. We will collect 7½ mL (around 1½ teaspoons) before you start treatment. This blood can be taken at the time of a routine blood test and will not require an extra needle stick.

If any tumor tissue or blood is left over from the research study described above, we would like to keep it for future medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”. Biobanking is discussed *in the section on optional studies* later in this consent form.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the *tumor tissue and blood* that will be used for this research study.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work, school 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 risks of the standard surgery and radiation therapy apply to all subjects in this study and are listed in Attachment #2.

The risks of taking pazopanib apply to subjects on Arm C only.

The study approach with pazopanib may not be better, and could possibly be worse, than the usual approach for your cancer.

The addition of pazopanib to standard treatment (radiation) may cause more complications.

The *pazopanib* 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 drug/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 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. For children enrolled on this study information about low blood counts can be found 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.

The tables below show the most common and the most serious side effects that researchers know about pazopanib. 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 risks and side effects related to pazopanib include those which are:

COMMON, SOME MAY BE SERIOUS In 100 people receiving pazopanib, more than 20 and up to 100 may have:
• **Diarrhea, nausea, vomiting** • **Tiredness** • **Bruising, bleeding** • **Infection, especially when white blood cell count is low** • **Loss of appetite** • **Changes in hair color** • **High blood pressure which may cause blurred vision**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pazopanib, from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Abnormal heartbeat** • **Pain** • **Constipation, heartburn** • **Sores in the mouth which may cause difficulty swallowing** • **Swelling of the arms, legs** • **Fever** • **Weight loss** • **Dehydration** • **Dizziness, headache** • **Changes in taste** • **Cough, shortness of breath** • **Internal bleeding, which may cause coughing up blood, black tarry stool, blood in vomit, or blood in urine** • **Bleeding from multiple sites including the nose or vagina** • **Hair loss, rash, skin changes** • **Redness, pain or peeling of palms and soles**

RARE, AND SERIOUS In 100 people receiving pazopanib, 3 or fewer may have:
• **Anemia, kidney problems which may require dialysis** • **Blood clot which may cause confusion, paralysis, swelling, pain, or shortness of breath** • **Heart failure or heart attack which may cause shortness of breath, swelling of ankles, and tiredness** • **Bleeding of the eye which may cause blurred vision with a chance of blindness** • **A tear or hole in internal organs that may require surgery** • **Liver damage which may cause yellowing of eyes and skin, swelling** • **Change in heart function** • **Change in the heart rhythm** • **Bleeding in the brain** • **Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)** • **Kidney damage which may require dialysis** • **Damage to the lungs which may cause shortness of breath**

Some drugs, food, and supplements may interact with <u>pazopanib</u>. Examples include:

Drugs that may interact with pazopanib*

• Antibiotics
  • Ciprofloxacin, levofloxacin, moxifloxacin, clarithromycin, erythromycin, nafcillin, rifabutin, rifampin, telithromycin
• Antidepressants and antipsychotics
  • Aripiprazole, citalopram, escitalopram, nefazodone, quetiapine
• Antifungals

- Fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole
- Arthritis medications
  - Leflunomide, tofacitinib
- Anti-rejection medications
  - Cyclosporine, sirolimus, tacrolimus
- Antiretrovirals and antivirals
  - Atazanavir, boceprevir, darunavir, delaviridine, efavirenz, etravirine, fosamprenavir, indinavir, lopinavir, nelfinavir, nevirapine, rilpivirine, ritonavir, saquinavir, Stribild, telaprevir, tipranavir
- Anti-seizure medications
  - Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone
- Heart medications
  - Amiodarone, amlodipine, dronedenarone, verapamil
- Some chemotherapy (be sure to talk to your doctor about this)
- Many other drugs, including the following:
  - Aprepitant, deferasirox, ivacaftor, lomitapide, mifepristone, natalizumab, warfarin

Food and supplements that may interact with pazopanib**

- Echinacea
- St. John's Wort
- Grapefruit, grapefruit juice, Seville oranges, star fruit

**Sometimes these drugs are used with pazopanib on purpose. Discuss all drugs with your doctor.*

***Supplements may come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided.*

The list above does not include everything that may interact with your chemotherapy. Talk to your doctor before starting any new medications, over-the-counter medicines, or herbal supplements and before making a significant change in your diet.

An information sheet with further details of things that may interact with pazopanib is provided in Attachment #3.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks

Women should not become pregnant because the drug(s) in this study can be bad for an unborn baby. If you or your partner could become pregnant, it is important for you to use birth control or not have sex while on this study and for at least 1 month after the last dose of pazopanib. 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. Women should not breastfeed a baby while on this study and for at least 1 month after the last dose of pazopanib. Also check with your doctor about how long you should not breastfeed after you stop the study treatment(s).

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study approach with pazopanib is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

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.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

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. The 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.

For questions about your rights while in this study, call the Central Institutional Review Board at 888-657-3711.

What are the costs of taking part in this study?

You will not be paid for taking part in this study.

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

company may have to pay for this. It is possible that the pazopanib may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of *treating* your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for. 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.

If you choose to enroll on this study, this institution will receive some money from the National Cancer Institute through the Children's Oncology Group, NRG Oncology or other NCI Cooperative Group within the NCTN to do the research.

The drug company that makes pazopanib is also providing money to the Children's Oncology Group and NRG Oncology to do some biology research.

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 happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors *will not* offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

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 #4.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- **Children's Oncology Group**
- **NRG Oncology**
- **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 (IRB) of this hospital. IRB is a group of people who review the research with the goal of protecting the people who take part in the study**
- **Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute**
- **The drug company that makes the drug, pazopanib, or their designated reviewers.**

Where can I get more information?

For children enrolled on this study, 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.

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

Information about long term follow-up after treatment for childhood, adolescent, and young adult cancers 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 anytime.

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

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ at _____ .

ADDITIONAL STUDIES SECTION: Optional Research Studies

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue and blood. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

1. Optional Sample Collections for Laboratory Studies and Biobanking for Possible Future Studies

If you choose to take part in this treatment study, we would like to collect tissue and blood for research on ways that might improve treatment for NRSTS in the future. We want to do laboratory studies:

i) We hope to find out if the presence or absence of certain genetic differences within tumor tissue can be linked with response to therapy. If there is a link, we may be able to identify targets for therapy in the future.
ii) Researchers think that certain biologic factors may help to predict how a tumor will respond to therapy. These cell factors are called "biomarkers". For example, the amount of tumor DNA present in blood may be a possible biomarker. In this study we want to examine possible biomarkers in tumor tissue and in blood.

The results of these laboratory studies *will not* be added to your medical records and you or your study doctor *will not* know the results.

If any tumor tissue or blood is left over from the research studies described above, we would like to keep it for future medical research. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by the COG and supported by the National Cancer Institute.

Future 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 IS INVOLVED?

If you agree to take part, here is what will happen next:

1) Tumor tissue was removed to diagnose the cancer and tumor will be removed during surgery after Induction therapy. If any of tissue is left over and no longer needed for your medical care, we would like to use some of it for these research studies.
2) For the blood samples, we would like to collect 10 mL (around 2 teaspoons) before you start treatment and 10 mL when you have surgery after Induction therapy. This blood can be taken at the time of routine blood draws and will not require extra needle sticks.

3) Your samples and some related health information will be sent to study researchers for use in the laboratory studies described above. If you agree, remaining samples and some related health information may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
4) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5) Neither you nor your study doctor will be notified when research will be conducted using your banked samples.
6) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. [*Site note: for non-US participants, please verify existence of such laws before including the following text.]* There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank, COG and NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom *COG* sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?
There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?
If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?
If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY STUDIES:
I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory studies described above.

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:
My samples and related information may be kept in a Biobank for use in future health research.

YES NO

2. Optional PET Imaging Study

[Only for subjects who are being treated at hospitals that have PET scanning available.]

We want to find out more about the usefulness of an imaging test called a PET scan for NRSTS. The use of PET scans to measure how your tumor is responding to therapy is not considered standard for people with NRSTS. You do not have to have PET scans to be on this study.

A PET scan requires injection of a small amount of radioactive glucose and is used to determine the activity of the tumor. This type of scan may not be available at all hospitals. We hope that some subjects on this study will have PET scans so we can find out if PET scans are good at showing any tumor changes during therapy. We are requesting that 2 PET scans be done: one before treatment starts and one before surgery for Local Control. If one or both of these PET scans is performed, this may lead to added costs to you or your insurance company.

PET scans involve fasting for several hours prior to the scan. Then, radioactive glucose is given in a vein, which may require a needle stick. The radioactive glucose travels to the places where there are tumor cells. Next, you have to lie very still on the PET scanner table while the pictures are being taken. Some people feel closed-in during the PET scan, but the scan itself does not hurt. The risks of a PET scan include the discomfort of fasting, exposure to the small amount of radiation, pain from the needle stick, and discomfort/feeling closed-in while lying still for the scan.

To help you understand the amount of radiation, we will compare it to the limits suggested by the government for the many doctors, nurses and scientists who work with radiation every day. These limits are the amount of radiation that should not cause harm to a person at any time during his or her lifetime. The amount of radiation you will get from 2 PET scan will be less than that recommended for health professionals on a yearly basis.

I agree to have PET scans performed for the imaging research study.

Yes_____ **No_____**

This is the end of the section about optional studies.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. this may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

My Signature Agreeing to Take Part in the Main Study

I have been given a copy of all _____ pages of this form. The form includes four (4) attachments.
I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study *and any additional studies where I circled 'yes'.*

Participant_____ Date _____

Parent/Guardian_____ Date _____

Parent/Guardian_____ Date _____

Physician/PNP obtaining consent_____ Date _____

IRB# _____ IRB Approved: _____

Attachment #1

Treatment and Procedures Common to all Patients with Non-Rhabdomyosarcoma Soft Tissue Sarcoma in the Non-Chemotherapy Group

The treatment described below is standard treatment for patients with intermediate or high risk NRSTS with a type of tumor that cannot be removed at the time of diagnosis and which is not expected to respond to chemotherapy and for patients with tumors that may respond to chemotherapy but they are unable or unwilling to receive it.

Treatment is divided into 3 stages, called Induction, Local Control, and Continuation.

Induction Therapy: Induction therapy is the use of radiation therapy to shrink the tumor as much as possible before Local Control.

Local Control: Local Control is surgery to remove the tumor, if possible, and will happen upon recovery from Induction.

Continuation Therapy: Continuation therapy is the use of radiation therapy following surgery to kill any remaining cancer cells so that the tumor is less likely to come back. Radiation therapy may not be needed for every patient after surgery.

These 3 stages of therapy are aimed at the primary tumor. That is the location where the cancer first occurred. If the cancer has spread then it is called metastatic cancer. After the Continuation therapy, you may have more surgery or radiation therapy directed at the location of any metastatic cancer.

Non-Chemotherapy Group Tumors					
Induction Phase			**Local Control**	**Continuation Phase**	
Week 1	Week 4	Week 7	Week 10	Week 13	Week 16
Radiation therapy			Surgery	Radiation therapy if needed	

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 function.

Attachment #2

Risks of Standard Radiation Therapy and Surgery

Radiation Therapy Risks
All subjects on this study will have radiation therapy. You will be asked to sign a separate consent form for this therapy. The treatment will be explained to you and your questions about it will be answered by the radiation oncologist when you sign the consent for this therapy. In general, radiation therapy side effects may include: temporary or permanent hair loss, nausea, vomiting, diarrhea, redness or dryness of the skin, low blood counts, mouth sores and/or injury to tissues or organs that are in the path of the radiation. If the ovaries or testes are in the path of the radiation, you may become unable to have children.

Late effects of radiation therapy may include problems with soft tissue or bone growth, vision problems, changes in endocrine function (low hormone levels), learning disabilities or brain injury, and increased risk for developing another cancer. These late effects depend on where in the body the radiation therapy was given, the age of the subject, and the drugs and surgery given at the same time.

Surgery Risks
All subjects on this study will undergo surgery. You will be asked to sign a separate consent for the surgical procedure. The planned surgery will be explained to you and your questions about it answered by your surgeon when you sign the consent for the surgical procedure. In general, surgery may result in one or more of the following side effects: bleeding, infection, problems with wound healing, pain, scar, blockage of the intestines, loss of nerve or organ function, or blood vessel damage. Depending on the type of anesthesia required, there may be one or more of the following side effects: nausea, vomiting, air passage obstruction, breathing problems, or heart irregularity. In rare instances death may occur during or after surgery.

For more information about risks and side effects, ask your study doctor.

Attachment #3

Information on Possible Interactions with Other Agents for Patients and Their Caregivers and Non-Study Healthcare Team

[Note to investigators: This appendix consists of an "information sheet" to be handed to the patient at the time of enrollment. Use or modify the text as appropriate for the study agent, so that the patient is aware of the risks and can communicate with their regular prescriber(s) and pharmacist. A convenient wallet-sized information card is also included for the patient to clip out and retain at all times.]

The patient _____ is enrolled on a clinical trial using the experimental agent **pazopanib.** *This clinical trial is sponsored by the National Cancer Institute. This form is addressed to the patient, but includes important information for others who care for this patient.*

Pazopanib interacts with many drugs that are processed by your liver. Because of this, it is very important to tell your study doctors about all of your medicine before you start this study. It is also very important to tell them if you stop taking any regular medicine, or if you start taking a new medicine while you take part in this study. When you talk about your medicine with your study doctor, include medicine you buy without a prescription at the drug store (over-the-counter remedy), or herbal supplements such as St. John's wort.

Many health care prescribers can write prescriptions. You must also tell your other prescribers (doctors, physicians' assistants or nurse practitioners) that you are taking part in a clinical trial. **Bring this paper with you and keep the attached information card in your wallet**. These are the things that you and they need to know:

Pazopanib interacts with certain specific enzymes in your liver.

- The enzymes in question are ***CYP450 3A4 and 2D6.*** Pazopanib levels are affected by some of these enzymes and can lower the levels of other medicines you take.
- Pazopanib must be used very carefully with other medicines that need these liver enzymes to be effective or to be cleared from your system.
- Other medicines may also affect the activity of the enzyme.
    - Substances that increase the enzyme's activity ("inducers") could reduce the effectiveness of the drug, while substances that decrease the enzyme's activity ("inhibitors") could result in high levels of the active drug, increasing the chance of harmful side effects. Pazopanib should not be taken with any other drugs that are strong inducers or inhibitors of CYP 3A4. Prohibited medications include azole antifungals, some antiepileptic drugs, some antibiotics and some immunosuppressants. Please check with the study investigator before prescribing or dispensing strong inhibitors/inducers of CYP 3A4. Mild/moderate inhibitors/inducers should be used with caution.
    - Pazopanib is considered an inhibitor of CYP 3A4, 2D6, UGT1A1 and OATP1B1 meaning that it can increase the levels of other drugs that are processed or transported by these enzymes. This can lead to harmful side effects and/or reduce the effectiveness of those medications.
- You and healthcare providers who prescribe drugs for you must be careful about adding or removing any drug in this category.
- Before you start the study, your study doctor will work with your regular prescriber to

switch any prohibited medicines that are considered "strong inducers/inhibitors or substrates of ***CYP 3A4***."

- Your prescribers should look at this web site http://medicine.iupui.edu/clinpharm/ddis/table.aspx
- or consult a medical reference to see if any medicine they want to prescribe is on a list of drugs to avoid.
- Please be very careful! Over-the-counter drugs have a brand name on the label—it's usually big and catches your eye. They also have a generic name—it's usually small and located above or below the brand name, and printed in the ingredient list. Find the generic name and determine, with the pharmacist's help, whether there could be an adverse interaction.
- Be careful:
    - If you take acetaminophen regularly: You should not take more than 3 grams a day if you are an adult or 2.4 grams a day if you are older than 65 years of age. Read labels carefully! Acetaminophen is an ingredient in many medicines for pain, flu, and cold.
    - If you drink grapefruit juice or eat grapefruit, Seville oranges, pummelos, exotic citrus fruits or grapefruit hybrids: Avoid these until the study is over.
    - If you take herbal medicine regularly: You should not take St. John's wort while you are taking pazopanib

Other medicines can be a problem with your study drugs.

- You should check with your doctor or pharmacist whenever you need to use an over-the-counter medicine or herbal supplement.

- Your regular prescriber should check a medical reference or call your study doctor before prescribing any new medicine for you. Your study doctor's name is _____ and he or she can be contacted at _____.

INFORMATION ON POSSIBLE DRUG INTERACTIONS

You are enrolled on a clinical trial using the experimental agent pazopanib**.** This clinical trial is sponsored by the NCI. Pazopanib interacts with drugs that are processed by your liver. Because of this, it is very important to:

- Tell your doctors if you stop taking regular medicine or if you start taking a new medicine.
- Tell all of your prescribers (doctor, physicians' assistant, nurse practitioner, pharmacist) that you are taking part in a clinical trial.
- Check with your doctor or pharmacist whenever you need to use an over-the-counter medicine or herbal supplement.

Pazopanib interacts with a specific liver enzymes called **CYP 3A4 and 2D6**, and must be used very carefully with other medicines that interact with this enzyme.

- Before you start the study, your study doctor will work with your regular prescriber to switch any prohibited medicines that are considered "strong inducers/inhibitors or substrates of **CYP 3A4**."
- Before prescribing new medicines, your regular prescribers should go to http://medicine.iupui.edu/clinpharm/ddis/table.aspx for a list of drugs to avoid, or contact your study doctor.
- Your study doctor's name is _____ and can be contacted at _____.

Attachment #4

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.