CHILDREN'S ONCOLOGY GROUP

NCI Pediatric Early Phase Clinical Trials Network

A program funded by the National Cancer Institute of the National Institutes of Health

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A National Cancer Institute-supported member group

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Cancer Therapy Evaluation Program
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National Cancer Institute
Executive Plaza North Room 730
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Dear Ms. Kruhm,

Enclosed please find Amendment #8 to protocol PED-CITN-03, Phase 1 Trial of Hu5F9-G4 (magrolimab) combined with dinutuximab in children and young adults with relapsed and refractory neuroblastoma or relapsed osteosarcoma.

Amendment #8 is in response to a request for a rapid amendment from Dr. Helen Chen (helen.chen@nih.gov). The amendment provides new and/or modified risk information associated with hu5F9-G4 and revises the Comprehensive Adverse Events and Potential Risks (CAEPR) list. Sections of the protocol and consent were updated to reflect these changes.

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

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

Sincerely,

Emma Archuleta, Protocol Coordinator (for)
Robbie G. Majzner, PED-CITN-03 Study Chair,
Brenda Weigel, M.D., PEP-CTN Chair

SUMMARY OF CHANGES: INFORMED CONSENT

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

#	Section	Page(s)	Change
1.	General	All	Updated version date of consent to match the current version of the protocol.
2.	Risks of Study	14-15	• Updated language to match NCI Consent Form Template (latest version: November 2018).
3.	Risks and Side Effects	16	• Added New Risks: • **Common: Low blood pressure which may cause feeling faint** • **Occasional: Pain in belly, Swelling of the body, Infection, especially when white blood cell count is low, Dizziness, Cough, Shortness of breath, Itching** • **Rare: Blood clot, Severe blood infection** • Increase in Risk Attribution: • Changed from Occasional to common: Tiredness • Changed to Occasional from Also Reported on Hu5F9-G4 Trials But With Insufficient Evidence for Attribution': Shortness of breath • Changed to Rare from Also Reported on Hu5F9-G4 Trials But With Insufficient Evidence for Attribution': Severe blood infection • Decrease in Risk Attribution: • Changed from Occasional to Also Reported on Hu5F9-G4 Trials But With Insufficient Evidence for Attribution (i.e. removed from risk list): Dry skin, Acne

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

PED-CITN-03: Phase 1 Trial of Hu5F9-G4 (magrolimab) Combined with Dinutuximab in Children and Young Adults with Relapsed and Refractory Neuroblastoma or Relapsed Osteosarcoma

Study Title for Participants: Testing the combination of two immunotherapy drugs (magrolimab and dinutuximab) in children, adolescents, and young adults with relapsed/refractory neuroblastoma or relapsed osteosarcoma

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

Overview

You are being asked to take part in this study because you have been diagnosed with osteosarcoma or neuroblastoma that has come back or has not responded to standard treatments.

You are being asked to take part in this study because you have been diagnosed with osteosarcoma or neuroblastoma that has come back (relapsed) or has not responded to standard treatments (refractory).

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

The overall goals of this study are to:

- **See if it is safe to give magrolimab with dinutuximab to children, adolescents, and young adults with relapsed/refractory neuroblastoma or relapsed osteosarcoma**
- **Find the best dose of magrolimab to give with dinutuximab in children, adolescents, and young adults with relapsed/refractory neuroblastoma or relapsed osteosarcoma**

- **See if the combination of magrolimab and dinutuximab is safe to give after surgery to remove tumors from the lungs**

If you decide to take part in this study, you will receive the study drugs (magrolimab and dinutuximab) for about 9 months. The magrolimab will be given to you in the doctor's office or clinic. The treatment on this study takes about 10 months. There are two parts to this study, a dose escalation part (ARM A) and a dose expansion part (ARM B). Your doctor will tell you which part you are in.

In the dose escalation part of this study, different people will get different doses of the study drug magrolimab. The first 3-6 people taking part in ARM A will get the dose of magrolimab found to be safe in adults. If magrolimab does not cause serious side effects, you will then receive magrolimab plus dinutuximab. If magrolimab alone or magrolimab with dinutuximab causes serious side effects, the next group (3 – 6) of people in ARM A will receive a lower dose of magrolimab. Once the safe dose of magrolimab and magrolimab plus dinutuximab is found, people will be treated in the dose expansion part (ARM B).

If you are enrolled early in this study you may receive a lower dose than those who are enrolled later. A lower dose may be less likely to have any effect on your tumor. Whatever dose you start at, your dose will not be increased. If you are enrolled in this study at a high dose level you may be more likely to have side effects. If you have bad side effects, your dose may be decreased. Up to 2 different doses of magrolimab may be studied.

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

Common side effects of magrolimab are anemia, and reaction during or following the infusion which may cause rash, and low blood pressure. Common side effects of dinutuximab are fever, pain, cough, and rash. The full list of risks for magrolimab and dinutuximab are available in the section What side effects or risks can I expect from being in the study?

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

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

You have a choice between another treatment for your disease and this clinical trial.

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

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

You are being asked to take part in this study because you have been diagnosed with osteosarcoma or neuroblastoma that has come back (relapse) or has not responded to standard treatments (refractory).

Osteosarcoma is a type of cancer that occurs in the lungs. Neuroblastoma is a type of cancer that occurs in nerve cells that are outside the brain. NBL shows up as a lump or mass in the belly or around the spinal cord in the neck, chest, abdomen or pelvis. It's considered high risk if your disease relapses or is refractory. The term, risk, refers to the chance of the cancer coming back after treatment.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services.

This study is being carried out by the Children's Oncology Group (COG) Pediatric Early Phase Clinical Trial Network (PEP-CTN). COG is an international research group that consists of more than 200 hospitals that treat children with cancer. The PEP-CTN is the group within COG that consists of 21 hospitals and participation in this study will be limited to only these hospitals.

Please take your time to make your decision. You may want to discuss it with your family and friends. 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 of this disease?

Standard treatment is the treatment that most cancer doctors would recommend you receive even if you decide not to participate in a clinical trial. Although there are commonly used treatments for osteosarcoma and neuroblastoma, disease that does not respond to standard treatments is often difficult to treat. The usual approach for patients who are not in a study is treatment with surgery, radiation, chemotherapy, or immunotherapy. Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer.

Why is this study being done?

This study is being done to test the safety and effects of magrolimab in combination with dinutuximab.

Magrolimab is experimental, meaning it has not been approved by the U.S. Food and Drug Administration (FDA). Magrolimab is a monoclonal antibody (man-made antibody that can recognize and attack specific antigens in the body) that blocks a protein (CD47) in the body that prevents the immune system from killing cancer cells. CD47 acts as a *don't eat me* signal. It has

been given to adults with leukemia, lymphoma and solid tumors but has not been previously given to children.

Dinutuximab is approved by the FDA in combination with three other drugs (GM-CSF, IL-2, and 13-cis-retinoic acid) for treatment of children with high-risk neuroblastoma who have had some response to prior treatment. However, dinutuximab is not currently approved by the FDA to be given alone for the treatment of people with neuroblastoma nor alone or with other drugs for the treatment of people with osteosarcoma. Dinutuximab is a monoclonal antibody that targets a GD2 antigen, which is found on specific tumors. Once dinutuximab binds to the GD2 antigen on the tumor cell it can kill the cell. Dinutuximab will be given to you in the hospital as it must be given over 10 to 20 hours for 4 days.

The combination of magrolimab and dinutuximab has not been previously given to humans and is considered experimental, meaning that it is not approved by the FDA.

The overall goals of this study are to:

- **See if it is safe to give magrolimab with dinutuximab to children, adolescents, and young adults with relapsed/refractory neuroblastoma or relapsed osteosarcoma**
- **Find the best dose of magrolimab to give with dinutuximab in children, adolescents, and young adults with relapsed/refractory neuroblastoma or relapsed osteosarcoma**
- **See if the combination of magrolimab and dinutuximab is safe to give after surgery to remove tumors from the lungs**

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your type of cancer. The usual approach is defined as the care most people get for relapsed/refractory neuroblastoma or relapsed osteosarcoma.

What will happen on this study that is research?

If you decide to take part in this study, you will receive the study drugs (magrolimab and dinutuximab) for about 10 months. The magrolimab will be given to you in the doctor's office or clinic. Every 3 weeks, starting with Cycle 1, you will stay in the hospital for about 4 days to be given the dinutuximab. If you only have tumors in your lung(s) and undergo surgery for tumor removal, you will get the study drugs for about 3-4 months.

You will be asked to allow your blood to be drawn for specific research tests to study how these drugs affect your cancer and how they act in your body.

After you finish your treatment, your doctor and study team will watch you for side effects. They will check you within 10 days and one month after treatment. After that, they will check you at 2, 4, 6, 9 and 12 months, and then yearly for 4 more years. This means you will keep seeing your doctor for 5 years after treatment.

Summary of Study Treatments

There are two parts to this study, a dose escalation part (ARM A) and a dose expansion part (ARM B). Your doctor will tell you which part you are in.

In the dose escalation part of this study, different people will get different doses of the study drug magrolimab. The first 3-6 people taking part in ARM A will get the dose of magrolimab found to be safe in adults. If magrolimab does not cause serious side effects after a priming dose and two weekly doses, you will then receive magrolimab plus dinutuximab. If magrolimab alone or magrolimab with dinutuximab causes serious side effects, the next group (3 – 6) of people in ARM A will receive a lower dose of magrolimab. The study doctor will watch each group carefully. Once the safe dose of magrolimab and magrolimab plus dinutuximab is found, people will be treated in the dose expansion part. If you do not have serious side effects while participating in ARM A, you may continue to receive magrolimab and dinutuximab for up to 12 cycles (36 weeks) if your cancer responds or does not worsen.

In the dose expansion part (ARM B) of this study, the highest dose of magrolimab with manageable side effects will be given in combination with dinutuximab to about 70 people in 4 groups. This will help study doctors better understand the side effects that may happen with this drug.

The four groups in ARM B are:

- Group 1: children, adolescents, and young adults with measurable neuroblastoma/ganglioneuroblastoma
- Group 2: children, adolescents, and young adults with evaluable neuroblastoma that cannot be measured
- Group 3: children, adolescents, and young adults with measurable osteosarcoma
- Group 4: children, adolescents, and young adults with osteosarcoma in the lung(s) that can be taken out with surgery.

All participants will be told which dose level they will be receiving. Group 4 may receive study treatment for up to 15 weeks after having surgery to remove osteosarcoma tumor(s) from the lung.

ARM A Treatment Schedule:

- **Priming dose:** Everyone will receive a priming dose of magrolimab. This small dose of magrolimab will be given by infusion (through a vein in your arm or through a central line which is a tube placed in a large vein in your neck, chest, groin or arm) over 3 hours on day 1. After completion of magrolimab infusion you will be observed for at least 1 hour. You will receive several medicines prior to the priming dose to lower the risk of an infusion reaction.
- **Single Agent Safety Cycle:** Magrolimab will be given on Day 1 of Weeks 2 and 3. Magrolimab will be given by infusion over 2 hours.
- **Cycle 1 and subsequent Cycles:** If you did not have serious side effects during the magrolimab Safety Lead-In, you will be given the study agent combination: magrolimab will be given by infusion over 2 hours weekly for 3 weeks (Day 1, Day 8 and Day 15) and

dinutuximab will be given by infusion daily for 4 days (Days 2 through 5) during Week 1 only. After the infusion you will be observed for at least 1 hour. In Cycle 3 and any subsequent cycles, magrolimab will only be given on Day 1 of Weeks 1 and 3; there will be no treatment on week 2.

ARM B Treatment Schedule:

- **Priming dose:** Everyone will receive a priming dose of magrolimab. This small dose of magrolimab will be given by infusion (through a vein in your arm or through a central line which is a tube placed in a large vein in your neck, chest, groin or arm) over 3 hours on day 1. After completion of magrolimab infusion you will be observed for at least 1 hour. You will receive several medicines prior to the priming dose to lower the risk of an infusion reaction.
- **Cycle 1:** Everyone will receive magrolimab at the dose found to be safe in Arm A by infusion over 2 hours weekly for 3 weeks (Day 1, Day 8 and Day 15) and dinutuximab will be given by infusion daily for 4 days (Days 2 through 5) in Week 1 only. If you have severe side effects, the infusion may be slowed or interrupted, or medications can be given to you.
- **ARM B Groups 1-3:** Cycle 1 can be repeated up to 36 weeks (12 cycles) if their cancer responds or does not worsen. In Cycle 3 and any subsequent cycles, magrolimab will only be given on Day 1 of Weeks 1 and 3; there will be no treatment on week 2. There will be up to 20 people in each of these groups.
- **ARM B Group 4:** Some people in this group may undergo surgery to remove osteosarcoma tumor from one lung. Others in this group may have tumor in both lungs and undergo a 'staged resection' where tumor is removed from one lung followed by a second surgery on the other lung. There will be up to 10 people in this group.

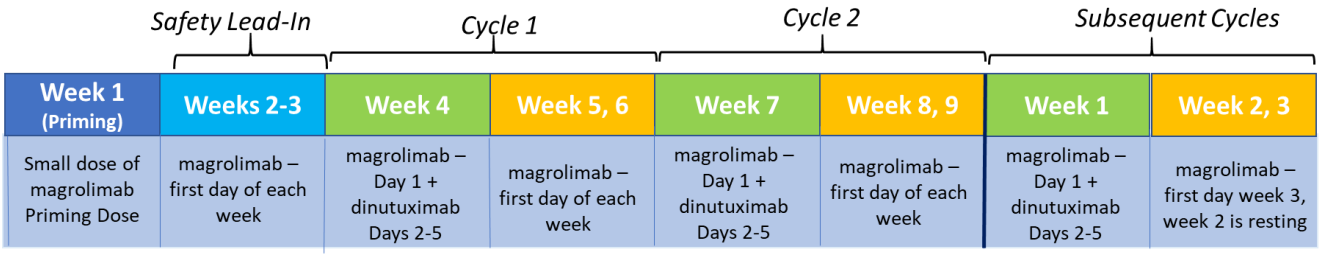
Everyone in this group will receive the priming dose followed by Cycle 1 (at a minimum). If you have already undergone lung surgery, you can repeat Cycle 1 up to 15 weeks (5 cycles) as long as your cancer does not return. After Cycle 2 (Cycle 3 and any subsequent cycles), magrolimab will only be given on Day 1 of Weeks 1 and 3; there will be no treatment on week 2.

If you are undergoing a 'staged resection' you may pause the study agents to undergo your second surgery. Once the surgeon feels it is safe to continue the study agents, you will continue additional cycles (to a maximum of 5) of magrolimab and dinutuximab. You may be given another priming dose if more than 4 weeks has passed since your last dose of magrolimab.

Diagram of Treatment

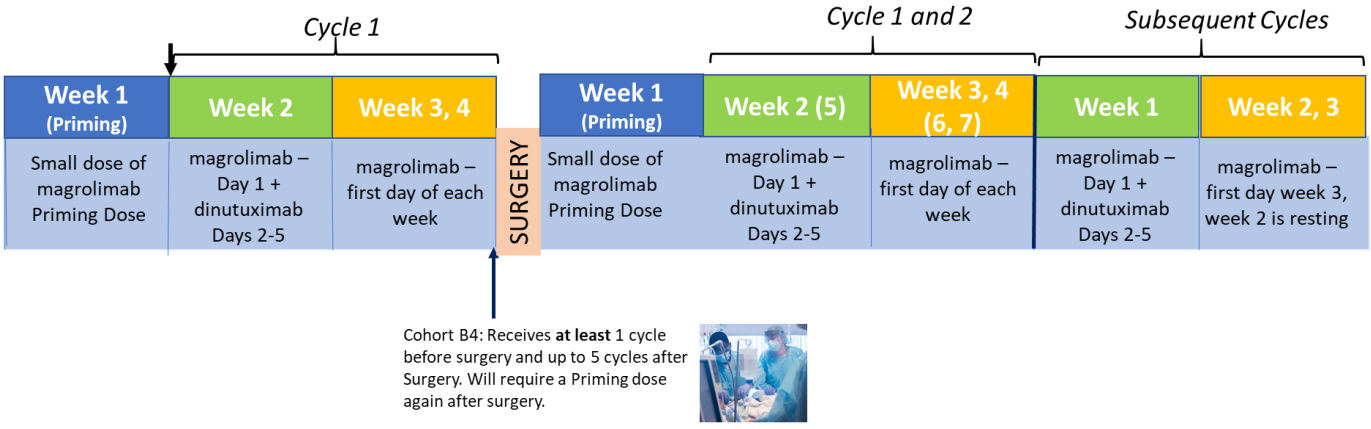
Another way to find out what will happen to you during this study is to read the charts below. Start reading at the left side and read across to the right.

Arm A:



Cycles may be repeated if disease does not worsen, to a maximum of 12 cycles.

Arm B:



Cycles after surgery may be repeated if disease does not worsen, to a maximum of 5 cycles.

Additional Required Research Study Tests

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Laboratory tests on your blood before starting each cycle (Day 1 of each cycle).

- Blood counts will be verified prior to the first two doses of magrolimab and again 3-6 hours after the first two doses of magrolimab. Additional blood counts may be performed if your study doctor feels that they are necessary.
- We will measure your tumor by looking at scans of your body (*e.g.,* CT, MRI, I-MIBG scan, or FDG-PET) at the following timepoints:
    - Before your first infusion of study treatment
    - At the end of Cycles 2, 4, 8 and 12
    - At the end of Cycle 5 (Group 4 only)
    - At each follow-up visit

If you have neuroblastoma, bone marrow will be obtained to measure your disease at the following timepoints: At time of enrollment, at the end of Cycles 2, 4, 8 and 12 and at each follow-up visit. The bone marrow will also be used for research tests to see how your immune system is responding to the study drugs.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in usual care. Listed below are tests and procedures that will be done for research purposes only.

- Blood samples will be collected for required research tests at the following timepoints. The maximum amount of blood in any one day will be 27 mL (5.4 teaspoons).
    - ARM A:
        - At time of enrollment
        - During the Safety Lead-In – Day 1, Day 8, Day 15
        - During Cycle 1 and Cycle 2 – Day 1, Day 5, Day 8, Day 15
        - Additional cycles – Day 1
        - Cycle 4 – Day 1 and Day 5
        - At time of disease evaluation
        - At the end of treatment
    - ARM B:
        - At time of enrollment
        - Before the Priming dose
        - During Cycle 1 and Cycle 2 – Day 1, Day 5, Day 8, Day 15
        - Additional cycles – Day 1
        - Cycle 4 – Day 1 and Day 5
        - At time of disease evaluation
        - At the end of treatment

Additional Optional Research Study Tests

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and neither you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say “no” to any or all of these studies. There is no penalty for saying “no.” You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these 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 in the Specimens for additional optional research tests section.

Optional tumor biopsy study
If you choose to take part in this optional tumor biopsy study, researchers will test a piece of your tumor collected for usual care to learn more about how the immune system affects tumor cells and the effect this study treatment will have on the immune cells in the tumor.

Tissue from a biopsy or surgery that you have done for usual care will be submitted to researchers at the Stanford University.

This biopsy would **not** be used to guide your medical care; it would be done solely for research purposes.

The risks were previously discussed but in summary include: risk of a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person’s response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies:
If you choose to take part in this optional tissue sample submission, if you have a tumor biopsy or surgery for usual care while taking part in the main study, a fresh tissue sample from this procedure may be submitted to researchers at the Stanford University. The tissue will be used to learn more about how the immune system affects tumor cells and the effect this study treatment will have on the immune cells in the tumor. If you have more than one tumor biopsy or surgery for usual care while taking part in the main study, this may be done for each procedure.

If you choose to take part in the optional blood sample submission, blood will be drawn at the same time other bloods are drawn so they do not require any additional needle sticks. Your blood samples will be used to understand how some blood characteristics may affect how

cancer responds to treatment. Your blood will also be tested to see if your body makes antibodies against magrolimab and dinutuximab.

If you choose to take part in the optional bone marrow study, you will have an additional bone marrow aspiration at the end of treatment. The bone marrow aspirate will be submitted to researchers at Stanford University. The sample will be used to learn more about how the immune system affects tumor cells and the effect this study treatment will have on the immune cells in the tumor.

Samples for unknown future studies:
If you choose to take part in this optional study, samples will be stored. Storing samples for future studies is called “biobanking.” The biobank is being run by PEP-CTN and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people’s health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we do not know what research may be done in the future using your blood, bone marrow and/or tissue samples. This means that:

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

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

What is involved in these optional sample collections?

If you agree to take part in the submission of fresh tissue for known studies, here is what will happen next:

1. A sample from the fresh tissue sample that was collected at the time of a tumor biopsy or surgery for usual care while taking part in the main study will be sent to researchers at the Stanford University.
2. Your sample will be used to understand how the immune system works in tumor cells of cancers like yours. It will also be studied to see how the magrolimab and dinutuximab affect the immune cells in your tumor.

If you agree to take part in submission of blood samples for known studies, here is what will happen next:

1. At the time you have blood drawn for usual care while taking part in the main study, an additional ½ teaspoon of blood will be collected from a vein in your arm and sent to researchers at University of Wisconsin or Stanford University.
2. Your sample will be used to understand how some blood characteristics may affect how cancer responds to treatment. Your blood will also be tested to see if your body makes antibodies against magrolimab and dinutuximab.

If you agree to take part in submission of bone marrow aspirate for known studies, here is what will happen next:

1. A sample from the bone marrow aspirate will be sent to researchers at the Stanford University.
2. Your sample will be used to understand how the immune system works in tumor cells of cancers like yours. It will also be studied to see how the magrolimab and dinutuximab affect the immune cells in your tumor.

If you agree to take part in the storage of leftover samples for unknown future studies, here is what will happen next:

1. Any leftover blood, bone marrow and/or tissue samples from the main study will be sent to the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time the biobank will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in these optional studies?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Common side effects of a bone marrow aspiration are a small amount of bleeding at the time of the procedure, bruising, and pain at the examination site. Pain can be treated with regular pain medications. Rarely, an infection can occur or there may be excessive bleeding.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when a tissue sample is submitted to

Stanford University and/or the biobank for these optional studies, your tissue could be used up.

- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

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 to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, Dr. *XXXX* at *XXXX*, who will let Stanford University, University of Wisconsin and/or the biobank know. Then, any sample that remains at Stanford University, University of Wisconsin and/or in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, Dr. *XXXX*, at *XXXX*.

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 chemotherapy can damage normal tissue and produce side effects.

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks of Study
We want to make sure you know about a few key risks right now. We give you more information in the "What side effects or risks can I expect from being in the study?" section.

If you choose to take part in this study, there is a risk that the Hu5F9-G4 (magrolimab) may not be as good as the usual approach at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that doctors know about are:

- Magrolimab: anemia, and reaction during or following the infusion which may cause rash, low blood pressure
- Dinutuximab: fever, pain, cough and rash

There may be some risks that the study doctors do not yet know about.

General Risks
If you choose to take part in this study, there is a risk that the Hu5F9-G4 (magrolimab) may not be as good as the usual approach at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The magrolimab and dinutuximab used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for up to 4 months after your last dose of study drug.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study may use some of this tissue, there is a small risk that it could be used up.

Side Effect Risks
The Hu5F9-G4 (magrolimab) 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 test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs/study approach.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.

4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Hu5F9-G4 (Magrolimab)
(Table Version Date: December 6, 2023)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Hu5F9-G4 (magrolimab), more than 20 and up to 100 may have:
• Anemia, which may require blood transfusion • Tiredness • Reaction during or following a drug infusion which may cause rash • Low blood pressure which may cause feeling faint

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Hu5F9-G4 (magrolimab), from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Pain • Diarrhea, nausea, vomiting • Chills, fever • Swelling of the body • Bruising, bleeding • Loss of appetite • Dizziness, headache • Cough, Shortness of breath • Itching

RARE, AND SERIOUS In 100 people receiving Hu5F9-G4 (magrolimab), 3 or fewer may have:
• Blood clot • Severe blood infection

Treatment with the study drug, Hu5F9-G4 (magrolimab), may make it difficult for doctors to find compatible blood if you were to require a blood transfusion.

Possible Side Effects of Dinutuximab (MoAb 14.18, chimeric (CH14.18))
(Table Version Date: January 10, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Dinutuximab (MoAb 14.18, chimeric (CH14.18)), more than 20 and up to 100 may have:
• **Fever** • **Pain** • **Cough** • **Rash**
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Dinutuximab (MoAb 14.18, chimeric (CH14.18)), from 4 to 20 may have:
• **Anemia, kidney problems which may cause tiredness, bruising, swelling, or may require dialysis** • **Blood clot** • **Abnormal heartbeat** • **Diarrhea, nausea, vomiting** • **Swelling of the body** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat and chills** • **Infection, especially when white blood cell count is low** • **Bruising, bleeding** • **Loss of appetite** • **Numbness, tingling or pain of the arms and legs** • **Difficulty emptying the bladder, which may require catheterization during therapy, and in rare cases catheterization may be required after discharge from the hospital** • **Shortness of breath** • **Itching, hives** • **Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles** • **High blood pressure which may cause headaches, dizziness, blurred vision** • **Low blood pressure which may cause feeling faint**

RARE, AND SERIOUS In 100 people receiving Dinutuximab (MoAb 14.18, chimeric (CH14.18)), 3 or fewer may have:
• **Heart stops beating** • **Vision changes which may include changes in the pupils of the eye** • **Death** • **Swelling of the spinal cord** • **Muscle weakness** • **Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)**

One person participating in this study experienced brain swelling, which may cause headache, blurred vision, and/or confusion. The study doctors think that dinutuximab could have caused this person's brain swelling, but doctors could not be sure because this person's disease in the brain also got worse and they passed away.

Dinutuximab can cause a lot of nerve pain. You will be given narcotics, such as morphine, through the vein before we start the dinutuximab until 2 hours after the dinutuximab finishes. You may need additional narcotics by mouth (oral) to help control the nerve pain. Narcotics carry the risk of addiction.

Additional Drug Risks

Your study doctor will give you a clinical trial wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Both magrolimab and dinutuximab activate a certain immune cell in your body, called macrophages. As noted above, dinutuximab can cause nerve pain. Giving these two drugs together may make that pain worse when they both activate the macrophages or damage your nerves.

The use of opioids, such as morphine to reduce the nerve pain caused by dinutuximab also includes risks. The most common risks include sedation, lightheadedness, dizziness, nausea, vomiting, constipation and sweating. The most serious risk is slowing of breathing. As mentioned previously, all opioids carry the risk of dependence.

Rarely, there are problems getting enough supplies of the study drug(s). If that happens, your doctor will talk with you about your options.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Bone Marrow Aspiration Risks

Common side effects of a bone marrow aspiration are a small amount of bleeding at the time of the procedure, bruising, and pain at the examination site. Pain can be treated with regular pain medications. Rarely, an infection can occur or there may be excessive bleeding. You may sign a separate consent form for the study bone marrow aspiration that describes the risks in more detail.

Imaging Risks

The PET, CT, or PET-CT that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The PET, CT, or PET-CT that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as driving about 500 miles. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

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. 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 while on this study. Also check with your doctor about how long you should not breastfeed after you stop the study treatment(s).

For women: Do not get pregnant or breastfeed a baby while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 4 months after your last dose of study drug.

Are there benefits to taking part in the study?

There is some evidence in animals that giving these two study drugs (magrolimab and dinutuximab) together can attack neuroblastoma and osteosarcoma cancer cells. Treatment with other antibodies combined with magrolimab have resulted in cancer tumor responses in adults. However, we do not know if magrolimab and dinutuximab given together will have this effect when given to people or help them live longer. This study may help the study doctors learn things that may help other people 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 a different research study, if one is available.**
- **You may choose not to be treated for cancer.**
- **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 this study?

The number of people enrolled on this study is expected to be about 82.

How long is the study?

Although it is difficult to predict whom, if any child, may benefit, it is possible that people in this clinical trial may receive treatment on this study for up to 10 months.

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

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

Your doctor or the study doctor may decide to take you off this study:
- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you experience side effects from the treatment that are considered too severe
- if new information becomes available that shows that another treatment would be better for you
- If the tumor gets worse
- Pregnancy

What about privacy?

We will do our best to make sure that the personal information in your medical record will be kept private. 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 a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the Children's Oncology Group will do their best to make sure that any information that goes out to others will not identify who you are. Information about this Certificate of Confidentiality is included in Attachment **1**.

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 and research partners**
- **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. ~"International governmental regulatory agencies" is**

applicable to all studies using drugs since AE reports will be sent to Health Canada.~

- **The Institutional Review Board of this hospital**
- **National Cancer Institute Central Institutional Review Board (CIRB)**
- **The study sponsor and any drug company supporting the study or their designated reviewers.**

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

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

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

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

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.

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- The costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and prevent and treat side effects.
- The costs of getting magrolimab and dinutuximab ready and giving them to you.
- ARM B Group 4 (osteosarcoma in the lung(s)): the surgery or surgeries for removal of tumor in your lung. Only participants in Arm B Group 4 will have mandatory lung tumor removal surgery.
- Your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The research labs using mandatory blood samples collected at the following timepoints:
  - ARM A:
    - At time of enrollment
    - During the Safety Lead-In – Day 1, Day 8, Day 15
    - During Cycle 1 and Cycle 2 – Day 1, Day 5, Day 8, Day 15
    - Additional cycles – Day 1
    - Cycle 4 – Day 1 and Day 5
    - At time of disease evaluation
    - At the end of treatment

  - ARM B:
    - At time of enrollment
    - Before the Priming dose
    - During Cycle 1 and Cycle 2 – Day 1, Day 5, Day 8, Day 15
    - Additional cycles – Day 1
    - Cycle 4 – Day 1 and Day 5
    - At time of disease evaluation
    - At the end of treatment

You or your insurance provider will **not** have to pay for magrolimab and dinutuximab while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work and school.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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.

You will not be paid for taking part in this study. The research may lead to new tests, drugs or other products for sale. If it does, you will not get any payment.

What are my rights as a participant?

Taking part in this study is voluntary. You may choose not to take part 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 have completed 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* Institutional Review Board (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 additional 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 that your specimens can be used for research, some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

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 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.

Samples for optional tumor biopsy study:
Please circle your answer: I choose to take part in the optional tumor biopsy study.

YES NO

Samples for known future studies

Submission of fresh tissue, bone marrow and/or blood for known studies:

- I agree that my fresh tissue sample may be submitted to researchers at the Stanford University as described above.

  YES NO

- I agree that blood samples may be submitted to researchers at the University of Wisconsin as described above.

  YES NO

- I agree that my bone marrow aspirate may be submitted to researchers at Stanford University as described above.

  YES NO

Samples for unknown future studies

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Signature

I have been given a copy of all _____ pages of this form. The form includes 1 attachment .

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/PA obtaining consent_____Date _____

Attachment 1

Certificate of Confidentiality

The Children's Oncology Group is covered by 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.