Study Protocol Title:	A Phase 1 Study of Lenalidomide in Combination with Vorinostat in Pediatric Patients with High Grade or Progressive Central Nervous System Tumors
NCT Number:	03050450
Date:	10/05/2018

1. OBJECTIVES

1.1 Primary Objectives

1.1.1 To conduct a phase I study to evaluate the safety and tolerability of this combination of chemotherapy agents.

1.1.2 To determine the response of children with recurrent or refractory central nervous system tumors with this combination of chemotherapy agents.

1.2 Secondary Objectives

1.2.1 To compare the response and toxicity with historical controls in prior published studies of patients with the same disease.

1.2.2 To estimate the 2- and 5-year survival with children treated with this regimen.

1.2.3 To provide safety and efficacy data to recommend further larger studies.

2. PATIENT SELECTION

2.1 Inclusion Criteria

2.1.1 Patients must have histologically confirmed (exception: diffuse intrinsic pontine glioma or optic pathway tumor) central nervous system malignancy for which standard curative measures do not exist or are no longer effective (i.e. patient must have received prior standard therapy in order to be considered eligible).

2.1.2 Patients must have measurable disease (see section 10.1.2 for definition of measurable disease).

2.1.3 Prior therapy restrictions:

- Patient may not have received vorinostat and lenalidomide in combination.
- At least 3 weeks since prior chemotherapy.
- At least 6 weeks from last nitrosurea.
- At least 6 weeks from autologous transplant.
- At least 3 months from bone marrow donor transplant.
- At least 3 weeks from focal radiation.
- At least 6 weeks from craniospinal radiation.
- Must have not received growth factors within 1 week of study entry.
- Must be on a stable or decreasing dose of steroids for 1 week prior.
- Must not be receiving any chemo, biologic, or radiation therapy.
- Must not be receiving enzyme inducing anticonvulsants or valproic acid.

- Must not be receiving pro-thrombotic agents

2.1.4 ≥1 Age (in years) <21

2.1.5 Karnofsky or Lansky performance status ≥50%

2.1.6 Life expectancy of greater than 8 weeks

2.1.7 Patients must have normal organ and marrow function as defined below:

Absolute neutrophil count	≥1,000/mcL
Platelets	≥100,000/mcL
Pulse oximetry	>93%
Total bilirubin	≤ 1.5 x upper limit of normal (ULN)
AST(SGOT)/ALT(SGPT)	≤2.5 × institutional upper limit of normal
Creatinine	within normal institutional limits **OR**
Creatinine clearance	≥60 mL/min/1.73 m^2 for patients with creatinine levels above institutional normal.

3.1.7 Pregnancy and breast feeding

The effects of vorinostat and lenalidomide on the developing human fetus are unknown. For this reason and because agents used in this trial are known to be teratogenic, women of child-bearing potential must commit to complete abstinence or use TWO methods of birth control (one highly effective (i.e. IUD, birth control pills, injections, implants, tubal ligation, partner's vasectomy), and one additional method (i.e. male condom, diaphragm, cervical cap) for the duration of study participation and at least 28 days after completion. Females of childbearing potential must agree to ongoing pregnancy testing and counseling every 28 days about pregnancy precautions. If a female has not had a menstrual period in the preceding 24 consecutive months or has had a hysterectomy, the two methods of birth control requirement does not apply. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men treated or enrolled on this protocol must agree to use condoms for the duration of study participation, and 28 days after completion.

3.1.8 Patient or guardian ability to understand and provide written informed consent.

3.1.9 Must be able to swallow lenalidomide capsules.

2.2 Exclusion Criteria

2.2.1 Patient has not recovered from acute toxic effects of all prior therapies.

2.2.2 Patients who are receiving any other investigational agents.

2.2.3 History of allergic reactions attributed to compounds of similar chemical or biologic composition to vorinostat or lenalidomide.

2.2.4 Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, dyspnea at rest, symptomatic congestive heart failure, history of thromboembolism unrelated to central line, patients with known predisposition syndrome for thromboembolism, patients receiving anticoagulation therapy, unstable angina pectoris, cardiac arrhythmia, patients receiving enzyme inducing anticonvulsants, patients receiving valproic acid, patients receiving antiplatelet agents (aspirin, anti-inflammatory drugs), or psychiatric illness/social situations that would limit compliance with study requirements.

2.2.5 Pregnant women are excluded from this study due to the potential for teratogenic effects. Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with these agents, breastfeeding should be discontinued if the mother is being treated and not resumed until 28 days after completing therapy.

2.2.6 HIV-positive patients on combination antiretroviral therapy are ineligible because of the potential for pharmacokinetic interactions with these agents. In addition, these patients are at increased risk of lethal infections when treated with marrow-suppressive therapy.

2.4 Inclusion of Women and Minorities

Both males and females of all races and ethnic groups are eligible for this trial.

3. TREATMENT PLAN

Treatment will be administered primarily on an outpatient basis, although may be given inpatient based on location or status of patient. Reported adverse events and potential risks are described in Section 7. Appropriate dose modifications are described in Section 6. No investigational or commercial agents or therapies other than those described below may be administered with the intent to treat the patient's malignancy.

Each cycle will begin with ANC >1000 and platelet count >100 without transfusion support. At the beginning of each cycle pregnancy testing must be confirmed negative for females of child bearing potential and counseling regarding pregnancy risks must be confirmed for all patients

4. STUDY SCHEMA

This is a phase I study of the combination of vorinostat and lenalidomide.

Cycle		Days			
Medication	**Route**	**1-7**	**8-14**	**15-21**	**22-28**

Lenalidomide	PO/GT/JT	X	X	X	Rest
Vorinostat	PO/GT/JT	X	Rest	X	Rest

Dose Escalation Schedule		
Dose Level	**Dose**	
	Lenalidomide mg/m^2	**Vorinostat mg/m^2**
Level 1	25	180
Level 2	50	180
Level 3	100	180
Level 4	150	180
Level 5	150	230

5. ADVERSE EVENT REPORTING

All Adverse Events of any grade must be reported in routine study data submissions. AEs reported to the IRB in an expedited manner (i.e. adverse events meeting the IRB's definition of an unanticipated problem) must also be reported in routine study data submissions. All relevant follow-up information concerning adverse events should be collected as soon as possible.

6. STUDY CALENDAR

Baseline evaluations are to be conducted within 2 weeks prior to start of protocol therapy. Scans and x-rays must be done ≤4 weeks prior to the start of therapy. In the event that the patient's condition is deteriorating, laboratory evaluations should be repeated within 48 hours prior to initiation of the next cycle of therapy.

Timing of protocol therapy administration and response assessment studies are based on schedules derived from the experimental design or on established standards of care. Minor unavoidable departures (up to 72 hours) from protocol directed therapy and/or disease evaluations for valid clinical, patient and family logistical, or facility, procedure and/or anesthesia scheduling issues are acceptable (except where explicitly prohibited within the protocol).

Procedure	**Pre-Study**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 5**	**Wk 6**	**Wk 7**	**Wk 8**	**Wk 9**	**Wk 10**	**Wk 11**	**Wk 12[c]**	**Off Study[d]**
Informed consent	X													
Lenalidomide		A	A	A		A	A	A		A	A	A		
Vorinostat		B		B		B		B		B		B		
Demographics	X													
Medical history	X													
Concurrent meds	X	X----------											----------X	
Physical exam	X	X		X		X		X		X		X		X
Vital signs	X	X		X		X		X		X		X		X
Height	X	X		X		X		X		X		X		X
Weight	X	X		X		X		X		X		X		X
Performance status	X	X		X		X		X		X		X		X
CBC w/diff, plts	X	X		X		X		X		X		X		X
Serum chemistry[a]	X	X		X		X		X		X		X		X
ECG	X												X	x
MRI brain/spine[e]	X												X	
Adverse event		X----------											----------X	X

evaluation														
B-HCG	X[b]	X[b]	X[b]	X[b]	X[b]				X[b]				X[b]	

A: Dose as assigned; administration schedule
B: Dose as assigned; administration schedule
a: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, SGOT [AST], SGPT [ALT], sodium.
b: Serum or urine pregnancy test (women of childbearing potential). Obtain 10-14 days prior to study enrollment and again within 24 hours prior to Day 1 of each cycle. Obtain weekly during cycle 1. Females with irregular menstruation must have a pregnancy test every 14 days while receiving protocol therapy (including breaks in treatment). Pregnancy test is also required if patient misses her period or has unusual menstrual bleeding. Pregnancy testing must also occur at Day 28 (and at Day 14 if female has irregular menstruation) after lenalidomide discontinuation).
c: Continue pattern of measurements while on study.
d: Off-study evaluation
e: As indicated based on diagnosis and tumor location.

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **ACH CNS 005- A Phase 1 Study of Lenalidomide in Combination with Vorinostat in Pediatric Patients with High Grade or Progressive Central Nervous System Tumors**

Application No.: **IRB00085329**

Sponsor: **Stacie Stapleton, M.D.**

Principal Investigator: **Stacie Stapleton, M.D.**
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St. Petersburg, FL 33701
Phone: 727-767-4176
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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and Johns Hopkins All Children's Hospital.
- 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.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.
- If children and adults can join this study, the word "you" in this consent form will refer to both you and your child.
- The person being asked to be in this research study may not be able to give consent to be in this study. You are therefore being asked to give permission for this person to be in the study as his/her decision maker.

2. Why is this research being done?

This research is being done to determine the safety and effectiveness of using lenalidomide and vorinostat. Independently, both lenalidomide and vorinostat have shown promising activity in pediatric central nervous system tumors. This study is to evaluate the safety of lenalidomide and vorinostat in central nervous system (brain and spine) tumors in children.

Lenalidomide is approved by the Food and Drug Administration (FDA) for the treatment in adults of relapsed mantle cell lymphoma, multiple myeloma and myelodysplastic syndrome (a bone marrow disorder).

Vorinostat is approved by the FDA for the treatment in adults of primary cutaneous T-cell lymphoma.

The use of lenalidomide and vorinostat together in this research study is investigational. The word "investigational" means that lenalidomide and vorinostat are not approved for marketing by the FDA to treat pediatric central nervous system (CNS) disorders.

The purpose of this study is to determine the safety of using these two drugs together.

People with recurrent or relapsed or refractory CNS tumors may join.

How many people will be in this study?

This study will be a multi-institutional study. We anticipate enrolling up to 20 participants on this study. About 12 people will take part at Johns Hopkins All Children's.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to follow a study drug plan. The plan will consist of lenalidomide and vorinostat given by mouth (PO). Lenalidomide capsules must be swallowed whole. Vorinostat may be swallowed whole, or a suspension is available, or may be given via a gastrostomy tube (g-tube) or jejunostomy tube (j-tube) .Lenalidomide will be given on days 1-21 of a 28 day cycle. Vorinostat will be given on

days 1-7 and days 15-21 of the same 28 day cycle.

A diagram of study drugs is below:

Cycle		Days			
Medication	**Route**	**1-7**	**8-14**	**15-21**	**22-28**
Lenalidomide	PO/GT/JT	X	X	X	Rest
Vorinostat	PO/GT/JT	X	Rest	X	Rest

Please note:
Lenalidomide should be taken without food if possible.
Vorinostat should be taken with food if possible.

You will need to have the following exams, tests or procedures to find out if you can be in the study and to check how you are doing during taking the study drugs. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Physical exam every 2 weeks
- Blood tests every 2 weeks
- Electrocardiogram every 3 cycles (every 12 weeks) to evaluate your heart's rhythm
- MRI scans to determine whether your tumor is responding to study drug every 3 cycles (every 12 weeks)
- If you are a female of childbearing potential (capable of getting pregnant), you will need a serum (blood) or urine pregnancy test 10-14 days prior to study enrollment and again within 24 hours prior to Day 1 of each cycle. If you are a female with irregular periods, you will have a pregnancy test every 14 days while on the study. Pregnancy tests may be performed if you are a female who misses her period or has unusual menstrual bleeding. Pregnancy testing will also occur at Day 28 (and at Day 14 if irregular periods) after stopping lenalidomide.
- Counseling about pregnancy prevention will occur prior to every cycle

How long will you be in the study?
You may receive study drugs for up to 2 years if you are responding well and tolerating the medications.

4. What are the risks or discomforts of the study?

Risks and side effects related to lenalidomide include those which are:

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

- Anemia which may require blood transfusion
- Constipation
- Diarrhea
- Tiredness
- Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving lenalidomide, from 4 to 20 may have:

- Nausea, vomiting
- Chills, fever
- Swelling of arms, legs
- Infection, especially when white blood cell count is low
- Weight loss, loss of appetite
- Pain
- Muscle spasms
- Dizziness, headache
- Difficulty sleeping
- Cough, shortness of breath
- Increased sweating
- Itching, rash
- Sores on the skin
- Blood clot which may cause swelling, pain, shortness of breath
- Change in mood (e.g. depression)
- Change in mental status
- Change in neurologic function
- Thoughts of suicide
- Seizures
- Irregular heartbeat

RARE, AND SERIOUS

In 100 people receiving lenalidomide, 3 or fewer may have:

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat and may cause death
- Damage to organs in the body when immune cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin, or muscle weakness
- Kidney damage which may require dialysis or may cause swelling
- Cancer of bone marrow caused by chemotherapy
- Damage to organs which may cause infection, bleeding, changes in thinking, or may require transfusions
- Increased tumor size
- A new cancer resulting from treatment of earlier cancer
- Severe skin rash with blisters and can involve inside of mouth and other parts of the body
- Heart attack
- Liver damage which may cause yellowing of eyes and skin, swelling, and may cause death
- Stroke which may cause paralysis weakness
- Difficulty stimulating enough stem cells in the bloodstream for future transplant

On rare occasions a second cancer arises after patients have undergone cancer therapy, including therapy using chemotherapeutic agents. Recently, in clinical trials of patients with newly diagnosed multiple myeloma (a tumor with cells that are usually found in bone marrow), a higher number of second cancers has been reported in patients treated with high doses of chemotherapy (induction therapy) and/or stem cell transplant followed by prolonged (maintenance) lenalidomide therapy compared to those who received induction therapy and/or transplant without maintenance lenalidomide.

We do not know at this time whether prolonged lenalidomide therapy in this clinical setting actually increases the risk of second primary cancers.

No increase in second primary cancers has been observed in patients receiving lenalidomide therapy who have relapsed multiple myeloma or other types of cancer.

We will be carefully monitoring these events (second primary cancers) in on-going studies of lenalidomide therapy and will inform you if there are any changes.
We want you to be aware of this possibility and to continue to follow standard medical advice for prevention and early detection of other cancers during and after your study drugs.

Please Note: If capsules cannot be swallowed whole, they may be opened and sprinkled on applesauce. Proper handling must be used to avoid exposure to this drug. A handout will be given to you to describe this process.

Participants should not donate blood during the study or for 28 days after stopping lenalidomide.

Risks and side effects related to vorinostat include those which are:

COMMON, SOME MAY BE SERIOUS In 100 people receiving vorinostat, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Tiredness • Bruising, bleeding • Loss of appetite • Changes in taste

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving vorinostat, from 4 to 20 may have:
• Belly pain • Constipation, heartburn • Dry mouth • Fever

- Infection, especially when white blood cell count is low
- Weight loss
- Dehydration
- Muscle spasms or weakness
- Dizziness
- Cough, shortness of breath
- Hair loss

RARE, AND SERIOUS
In 100 people receiving vorinostat, 3 or fewer may have:

- Damage to the skin
- Formation of clot in a blood vessel
- Elevated blood sugar levels

Some drugs or supplements may interact with your study drug plan. Talk to your doctor, pharmacist, or study team before starting any new prescription or over-the-counter drugs, herbals, or supplements and before making a significant change in your diet. Supplements may come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided.

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study. You will be monitored for side effects and supportive care will be given if needed.

5. Are there risks related to pregnancy?

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Findings from a monkey study indicate that lenalidomide caused birth defects in the babies of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. You have been informed that the risk of birth defects is unknown.

Women must not become pregnant while taking lenalidomide. If you or your partner can get pregnant, it is important for you to use 2 forms of birth control or not have sex before starting lenalidomide, while on this study, and for 4 weeks after you stop being treated on this study. Check with your study doctor about what kind of birth control methods to use.

Some birth control methods might not be approved for use in this study. Women should not breastfeed a baby while on this study or for 28 days after study drug is over.

Men should not father a baby while on this study. When taking lenalidomide, the drug is present in semen of healthy men at very low levels for three days after stopping the drug. For patients who may not be able to get rid of the drug, such as people with kidney problems, lenalidomide may be present for more than three days. To be safe, all men should use condoms when engaging in sexual intercourse while taking lenalidomide, when temporarily stopping lenalidomide, and for 28 days after permanently stopping

lenalidomide if their partner is either pregnant or able to have children. Men should not donate sperm or semen while on this study or for 28 days after study drug is over.

The effects of vorinostat and lenalidomide on the developing human fetus are unknown. For this reason and because agents used in this trial are known to be teratogenic, women of child-bearing potential must commit to complete abstinence or use TWO methods of birth control (one highly effective (i.e. IUD, birth control pills, injections, implants, tubal ligation, partner's vasectomy), and one additional method (i.e. male condom, diaphragm, cervical cap) for the duration of study participation and at least 28 days after completion. Females of childbearing potential must agree to ongoing pregnancy testing and counseling every 28 days about pregnancy precautions. If a female has not had a menstrual period in the preceding 24 consecutive months or has had a hysterectomy, the two methods of birth control requirement does not apply. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men treated or enrolled on this protocol must agree to use latex condoms for the duration of study participation, and 28 days after completion.

This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to being in the study?

Benefits include possible improved tumor control and improved clinical symptoms. We do not know that the information from this study will help doctors learn more about treating central nervous system tumors. This information could help future cancer patients.

7. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. Other treatments include regimens that would be individualized based on your prior treatment and diagnosis. You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).

- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

No, you will not be paid if you join this study.

10. Can you leave the study early?

You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the therapy can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful
- You need treatment not allowed in the study
- You fail to follow instructions
- You become pregnant
- The study is cancelled
- There may be other reasons to take you out of the study that we do not know at this time

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form.
They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV

status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

14. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies.
You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 727-767-4275. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. Stacie Stapleton at 727-767-4176. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 727-767-4275.

c. What should you do if you are injured or ill as a result of being in this study?
If you think you are injured or ill because of this study, call Dr. Stacie Stapleton at 727-767-4176 during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call the oncology office at 727-767-4176 during regular office hours and the on-call oncologist at 727-767-4176 after hours and on weekends.

d. What happens to Data that is collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The data you provide is important to this effort.

If you join this study, you should understand that you will not own your data, and should researchers use your data to create a new product or idea, you will not benefit financially.

15. Assent Statement

This research study has been explained to my child in my presence in language my child can understand. He/she has been encouraged to ask questions about the study now and at any time in the future.

16. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

_____

_____

Signature of Participant (Print Name)

Date/Time

_____

_____

Signature of Person Obtaining Consent (Print Name)

Date/Time

_____

_____

Signature of Legally Authorized Representative (LAR) (Print Name)

Date/Time

For ADULTS NOT CAPABLE of GIVING CONSENT (*Persons from the following categories in order of priority may be a Legally Authorized Representative: Health Care Agent; Legal Guardian; Spouse; Adult child; Parent; Adult sibling; Friend or other relative)*

_____

_____

Relationship of LAR to Participant (indicate why the LAR is authorized

Date/Time

to act as a surrogate health care decision-maker under state or applicable local law)

_____

_____

Signature of Parent (Print Name)

Date/Time

_____

_____

Signature of Legally Authorized Representative (LAR) (Print Name)

Date/Time

For CHILD PARTICIPANT

_____

Description of LAR's authority under state or applicable local law to act as surrogate health care

Date/Time decision-maker for **child** research participant (for example, Legal Guardian, court-ordered representative)

_____

Signature of Child Participant (optional unless IRB required) (Print Name)

Date/Time

_____

Signature of Witness to Consent Procedures (Print Name)

Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

_____

Signature of Participant, LAR or Parent/Guardian (Print Name)

Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.