

**RPCI IRB and UB CYIRB APPROVED**

PER: DH

FROM: 9/20/2014

TO: 9/19/2015

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MR#:

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V.4

Roswell Park Cancer Institute  
Institutional Review Board  
Elm & Carlton Streets  
Buffalo, NY 14263

UB Children & Youth Inst. Review Board  
Women and Children's Hospital  
219 Bryant Street  
Buffalo, NY 14222

**TITLE: A PHASE II TRIAL OF REDUCED INTENSITY ALLOGENEIC STEM CELL TRANSPLANTATION WITH ELUDARABINE, MELPHALAN AND LOW DOSE TOTAL BODY IRRADIATION**

400 cGy TBI

**PRINCIPAL INVESTIGATOR: Hong Liu, MD**

**RPCI PROTOCOL NO.: I 177110**

**CYIRB PROTOCOL NO.: DB 2642**

*Consent Form Given to Patient Taking Part in an Investigational/Clinical Research Study*

*When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.*

It is the principle of medical ethics that the human subjects of a research project be informed of the purpose and benefits of the project, the research methods to be used, the potential risks or hazards of participation, the right to ask for further information at any time during the research procedure. You have the right to know whether medical treatment or compensation is available for physical injuries incurred as a result of participation in the project. Your choice to participate is a voluntary one and you are free to withdraw from the research project at any time. Your signature will indicate that the principal investigator, or his/her agent, has answered all your questions and that you voluntarily consent to participate in this investigation.

You are being asked to participate in a research study. The purpose of this document is to provide you with information to consider in deciding whether you might want to participate in this research study. Your consent should be made based on your understanding of the nature and risks of the treatment, device, or procedure. Please ask questions if there is anything you do not understand. Your participation is voluntary and will have no effect on the quality of your medical care if you choose not to participate.

This is a clinical research study. Clinical research studies include only those patients who choose to take part. Please take your time to make your decision. Discuss it with your family and with people who are important to you.

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We invite you to take part in a clinical research/investigational study for patients with blood disorders and blood/lymph cancers. It has been explained to you that you have a life-threatening condition and that you might otherwise not be candidates for standard blood or marrow transplant (BMT) because of age or poor performance status; or that you have a type of condition for which no adequate conventional treatment is known. For this reason, we are offering you the opportunity to take part in a research study (a clinical trial) of a drug combination being given in a new way.

This study intends to determine the usefulness of this reduced intensity therapy combination in a patient population that is usually not eligible for standard full-intensity allogeneic transplant. This study will evaluate safety and overall outcomes of treatment across a variety of hematological conditions.

It is important that you read and understand several general rules that apply to anyone that takes part in our studies:

It is important that you read and understand several general rules that apply to anyone that takes part in our studies:

1. This study is considered research. It is investigational.
2. Taking part in the study is voluntary.
3. You may withdraw from the study at any time without penalty, loss of any benefits or access to care at to which you are/your child is other entitled at either Roswell Park Cancer Institute (RPCI) or Women & Children's Hospital of Buffalo (WCHOB).
4. If you should decide not to take part in this study, it will not affect your/your child's care now or in the future at either RPCI or WCHOB.
5. You should feel free to get a second opinion. This will not affect your/your child's ability to receive care and treatment at RPCI or WCHOB if you get one.
6. Your/your child's disease may not be helped from taking part in this study, but we may get information that will help others.
7. If we become aware of important new findings that relate to your/your child's participation or continued participation in this study we will discuss them with you.

The type of study, the risks, benefits, discomforts, and other important information about this study are discussed below.

## 1. INTRODUCTION:

You may benefit from a blood or marrow transplant (BMT). However, a traditional high-intensity transplant is not recommended for you because of the high risk of toxicity related to age or other medical issues. For that reason we are offering you participation in a less aggressive

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transplant known as a "reduced intensity allogeneic stem cell transplant". Reduced intensity transplantation (RIT) uses lower doses of chemo-radiation and is now considered an established technique that can provide an alternative to traditional high-intensity BMT.

This particular combination of Fludarabine, Melphalan and low-dose Total Body Irradiation has not been clinically tested together and that there may be side effects and risks resulting from this combination that are unknown at this time. Other reduced intensity transplant techniques, not being offered here, use combinations of Fludarabine with Cytosan or low dose Total Body Irradiation.

## **2. WHAT IS THE PURPOSE OF THIS STUDY?**

You have been invited to participate in a research study being conducted by the doctors at the Roswell Park Cancer Institute and Women & Children's Hospital of Buffalo. The study in which you have been asked to take part will determine what effects (good and bad) this treatment has on you and your type of cancer or condition.

BMT is considered a standard form of therapy for many of the various types of hematologic malignancies or disorders. Your physician will discuss with you the results of treating the specific problem that you have with a BMT. Reduced intensity transplantation (RIT) is a BMT technique that can provide an alternative to traditional high-intensity BMT. There is no guarantee or implied promise that this treatment will be successful.

This research is being done because currently, there is no effective treatment for these types of conditions for patients who may have failed previous treatments. This study uses a new combination and schedule of chemotherapy and radiation therapy to treat the disease.

This study is being done by the doctors at the Roswell Park Cancer Institute and Women & Children's Hospital of Buffalo. The purpose of this study is to attempt to:

- a) slow or stop the growth of your/your child's disease, or prevent it from recurring
- b) understand the usefulness and side effects of the treatment.

## **3. WHO ELSE WILL BE ON THIS STUDY AND HOW LONG WILL IT LAST?**

We expect to enroll 81 patients from Roswell Park Cancer Institute and Women & Children's Hospital of Buffalo over five years.

The treatment phase of this study will be at least 4-6 months. After you have completed treatment on this study you will be asked to return to the clinic for follow-up tests every month for four months, at day 100, and yearly and then as indicated from the date of entry on the study.

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It is possible that because of complications and your medical condition, you may need to be seen more often.

We would like to keep track of your medical condition for the rest of your life to look at the long-term effects of the treatment/procedure you will receive on the study.

#### **4. WHAT WILL HAPPEN IF YOU ARE ON THE STUDY?**

The goal of a transplant is to replace the defective cells responsible for your disease with normal cells from your donor. You will first have tests done to make sure that you are healthy enough to have a BMT. These tests will include: x-rays; heart, lung and kidney function tests; and blood tests.

##### Overview

The treatment on this research study is a modification to the Conditioning Regimen. The conditioning regimen is the chemo-radiation that is given to patients before stem cell transplant in order to weaken your immune system (the white blood cells responsible for fighting infections) in preparation of the introduction of the "stem cells" (mother cells that will eventually develop into white blood cells, red blood cells and platelets) from your donor. The conditioning regimen is given in hospital and most patients remain hospitalized for 4-6 weeks after starting the conditioning. Longer hospitalization may be required if you develop complications.

After you are discharged, you may need to be seen in the doctor's office several times a week. The frequency of your visits will decrease as your/your child's condition improves, but you may need to return every 1-2 weeks during the first six months.

Graft-versus-host disease (attack by the donor cells against your organs) may begin when blood counts start to recover but may be delayed as long as 12 weeks. After the transplant, you will receive medicines to prevent or lower the severity of graft-versus-host disease. These medicines lower the immune system's reactions and will be continued for at least 2-3 months.

This is a difficult treatment that requires the use of powerful medicines. You will remain in the hospital until your blood counts are at a safe level and you have no fever. Average time to improvement in blood counts is 14-21 days and the average time spent in the hospital is 4-6 weeks. Longer hospitalization may be required if you develop complications. The doctors will determine when you can safely go home. After discharge from the hospital, we will continue to follow you very closely. Your response to this treatment will be evaluated periodically for the rest of your life. You and/or your physician will be contacted at regular intervals accordingly.

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#### 400 cGy TBI based Transplant

If you agree to participate, you will receive the chemotherapy drug Fludarabine, 40mg/m<sup>2</sup> by 30 minute Intravenous (IV) infusion for four (4) days. You will receive Melphalan 75mg/m<sup>2</sup> by IV infusion for one (1) day, and Total Body Irradiation (TBI) in two fractions of 200cGy each for one day before you receive your donor's cells. The day you receive your donor's stem cells will be known as "Day 0" or the day of transplant. Fludarabine will be given on Day -5 through Day -2, and Melphalan will be given on day -2. Total Body Irradiation will be delivered in two fractions given at least six hours apart on day -1.

#### Immunosuppressive medication

Donor immune cells may recognize your body as foreign and attack your body. This attack is known as Graft-versus-Host Disease (GVHD). To prevent rejection of your donor's stem cells as well as GVHD, you will receive the drug known as Tacrolimus (FK506) beginning on Day -1 until at least day +60 after which the FK506 will be adjusted. Tacrolimus is an immunosuppressive agent (weakens the immune cells). It is given in an attempt to prevent your new stem cells (donor's stem cells) from recognizing your body as foreign. Celcecept (MMF), another immunosuppressive agent, will be started on day -1 and continued through at least day +30 then it will be discontinued. A third immunosuppressive agent, Methotrexate (MTX), will be given 2.5mg/m<sup>2</sup>/dose IV on days 1, 3, and 6. Immunosuppressive medications may be changed or extended for a longer period if you develop graft versus host disease (this is discussed further in risks).

#### Standard supportive care

After Day 0, you will be given antibiotics to help fight infections; blood transfusions to increase the number of red blood cells in your system; platelet transfusions to assist in helping your blood to clot; and nutritional and general supportive care.

For all transplant patients except for those receiving a cord blood transplant, depending on your response to treatment, you may require up to three additional infusions of lymphocytes from your donor. If necessary, these will be given to you sometime after Day +100 and a separate consent will be taken.

### 5. IF YOU TAKE PART IN THIS STUDY, WHAT TESTS AND PROCEDURES WILL YOU HAVE DONE?

The following tests must be done to make sure that you are eligible for this study. None of the required tests are experimental, they are routine. Depending on when you last had them, you may need to repeat some of these tests:

- Blood tests
- Chest x-ray
- CT/MRI scan of the chest, abdomen, and pelvis

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- Urinalysis
- Heart function- EKG, MUGA and/or ECHO (a heart scan)
- Pulmonary Function Tests (PFT) for lung function evaluation
- Viral tests for Hepatitis, HIV and CMV Test
- Pregnancy test (if you are of childbearing potential)
- Bone marrow aspirate and biopsy

Many of these tests will be repeated during the study. If you participate in this study, some of these tests may be done more frequently than if you were not taking part in this research study.

#### **6. WHY WOULD YOU BE TAKEN OFF THE STUDY EARLY?**

- You may be taken off the study for any of the following reasons:
- Your medical condition changes
- New information becomes known to us that would influence your decision to remain on the study
- If the treatment is no longer helpful to you. Other treatment choices will be discussed with you then.
- The sponsor of the study may decide to stop or change the study
- You do not follow the study schedule or requirements
- You experience unacceptable side effects

#### **7. MUST YOU TAKE PART IN OR STAY ON THE STUDY?**

Taking part in this study is voluntary. You may decide not to enter the study or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, if you decide to stop being in the study, we encourage you to talk with your doctor first about such a choice, so that you are informed about any effects that might have on your health and to discuss stopping study participation. The effects of a BMT sometimes cannot be undone. Therefore, we encourage you to talk with your doctor first about such a choice.

It may be necessary to contact you at a future date regarding new information about the medication or procedures that you have received. For this reason, we ask that you notify your physician's office to update us of any change in your address.

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## 8. WHAT RISKS AND DISCOMFORTS ARE INVOLVED?

Allogeneic BMT is a procedure known to have an extremely high complication rate. All of the treatments used in the preparation for BMT have side effects. There is a risk to life involved with this treatment and may be related directly to the treatment itself, because of your disease, infections, GvHD or some other complication of treatment. You can have a 20% chance of dying from these side effects within the first 100 days after transplant. We will do everything we can to prevent and treat any complications.

While you take part in this study, you may be at risk for the following side effects. You should discuss these with your doctor.

The drug (s)/procedures used in this study may cause all, some, or none of the side effects listed. There may be other side effects of the drugs/procedures that we do not know of yet.

The side effects may be mild, moderate, or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, or may be permanent. It is not possible to tell which side effect will affect you or how mild or severe the side effect might be. We can only tell you what other people have experienced. Please talk with your doctor about these side effects.

It is very important that you notify your doctor right away about any side effects, problems, or unusual experiences you may have while taking this medication/undergoing this procedure. This will decrease the chance that the side effects continue or become worse. Sometimes there are other medications that we can give you to make the side effects better or make you more comfortable. If severe side effects do develop, you and your doctor may decide it is in your best interest to stop taking part in the study.

Side effects are defined as follows:

**Likely Side Effects:** those that occur in approximately 15% - 30% of persons who receive this drug/undergo this procedure.

**Less likely Side Effects:** those that occur in approximately 10% - 14% of persons who receive this drug/undergo this procedure.

**Unlikely Side Effects:** those that occur in approximately 5% to 9% of persons who receive this drug/undergo this procedure

**Rare but Serious Side Effects:** Those that occur in less than 5% of persons who receive this drug/undergo this procedure.

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1. The chemotherapy (fludarabine, melphalan), radiation (TBI) and immunosuppressive medications (methotrexate, tacrolimus and cellcept) used in this program may cause all, some, or none of the side effects listed.

The side effects may be mild, moderate, or severe. In addition, there is always the risk of other side effects occurring that are not yet known. It is very important that you notify your doctor right away about any side effects, problems, or unusual experiences you may have while taking this medication. This will reduce the likelihood that the side effects continue or become severe. If severe side effects do develop, you may be taken off the study in your own best interest.

#### Likely Side Effects:

##### Fludarabine:

- Tiredness, weakness
- Lowered white blood cell count that may lead to infection.
- Lowered platelets which may lead to an increase in bruising or bleeding.
- Lowered red blood cells which may cause anemia, tiredness, or shortness of breath.
- Mucositis- damage to the lining of the mouth and intestinal tract causing sores, painful swallowing, infections and diarrhea.
- Increased risk of infections with or without fever
- Loss of appetite and/or weight loss.
- Diarrhea, nausea, vomiting.
- Dizziness, joint and muscle aches.
- Rash, peeling, itching.

##### Melphalan:

- Tiredness, weakness
- Lowered white blood cell count that may lead to infection.
- Lowered platelets which may lead to an increase in bruising or bleeding.
- Lowered red blood cells which may cause anemia, tiredness, or shortness of breath.
- Mucositis- damage to the lining of the mouth and intestinal tract causing sores, painful swallowing, infections and diarrhea.
- Increased risk of infections with or without fever
- Loss of appetite and/or weight loss.
- Diarrhea, nausea, vomiting.
- Dizziness, joint and muscle aches.
- Rash, peeling, itching.
- Liver or kidney damage.
- Hair will fall out 1-3 weeks after the last dose of chemotherapy, but will grow back when chemotherapy is discontinued. The hair color may change, and is sometimes curlier.
- Possible sterility- loss of ability to bear children.



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### **Radiation (TBI):**

- Nausea and vomiting
- Mouth and throat sores
- Pain
- Diarrhea
- Jaw pain
- Swollen salivary glands
- Dry mouth
- Skin redness
- Hair loss
- Fatigue
- Low blood counts
- Possible sterility- loss of ability to bear children.

### **Methotrexate:**

- Tiredness, weakness
- Lowered white blood cell count that may lead to infection.
- Lowered platelets which may lead to an increase in bruising or bleeding.
- Lowered red blood cells which may cause anemia, tiredness, or shortness of breath.
- Mucositis- damage to the lining of the mouth and intestinal tract causing sores, painful swallowing, infections and diarrhea.
- Increased risk of infections with or without fever
- Loss of appetite and/or weight loss.
- Diarrhea, nausea, vomiting.
- Hair will fall out 1-3 weeks after the last dose of chemotherapy, but will grow back when chemotherapy is discontinued. The hair color may change, and is sometimes curlier.
- Possible sterility- loss of ability to bear children.

### **Tacrolimus:**

- High blood pressure
- Worsening kidney function
- Risk of infection
- Feeling dizzy
- Headache
- Nausea or vomiting
- Diarrhea
- Inability to sleep
- Sunburn

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**Cellcept:**

- High blood pressure
- Risk of infection
- Headache
- Nausea or vomiting
- Anemia, low white blood cell count, and low platelet count
- Diarrhea
- Swelling

**Rare but Serious Side Effects:**

- Damage to vital body organs- such as the heart, lung, brain, kidney or other organ failure. These could require intensive care with artificial life support or even be fatal.
- Late effects may occur many years after transplant- vision change, hearing loss, thyroid function abnormality, loss of bone strength, risk of leukemia or second cancers.

2. **Stem Cell reinfusion** is associated with the following hazards:

- a. Temporary shortness of breath due to the lodging of small particles in the blood vessels of the lungs may occur. This is a less likely side effect.
- b. If the bone marrow or stem cells that are to be used have been cryopreserved (frozen), a chemical called DMSO (dimethylsulfoxide) is used during the freezing process. This chemical is used to protect the cells from damage during freezing. DMSO produces an odor on the breath that lasts 1 to 2 days. In rare instances, severe allergic reaction may occur.
- c. There is also a chance that patients may develop a blood transfusion reaction during the reinfusion of stem cells. In that case, patients may develop the following less likely side effects: chills, back pain, decreased blood pressure, chest pain, and increased rate of breathing. Wheezing, hives and rash, as well as difficulty breathing, and increased heart rate are considered unlikely. Rarely, temporary life support with artificial ventilation is required.
- d. Failure to engraft is a rare complication and it is possible that your own bone marrow might grow back. A second transplant may need to be done.

3. **Graft Versus Host Disease (GVHD)**

This condition results from a reaction of the transplanted donor stem cells against your body organs. This reaction changes from a mild skin disorder to severe involvement of the skin, liver, and/or gut. It may be fatal in some patients. There are two forms: acute (early) and chronic (late). The majority of patients will exhibit some manifestation of GvHD. Severe acute GvHD

may occur in up to 40% of patients. The risk of severe GvHD is increased for older patients and for patients receiving stem cells from partially-matched donors. A chronic form of GvHD is expected to occur in up to 60% of patients. You will be monitored for this complication and given specific treatment to prevent and treat it.

- Acute GVHD may produce skin rashes, liver disease, diarrhea, and an increased risk of infection. All of these can range in severity from mild, likely effects to fatal, unlikely effects.
- To confirm the diagnosis of acute GVHD, you may be required to have a skin biopsy and possibly a liver or gut biopsy.
- The treatment of acute GVHD requires you to take high doses of corticosteroids (steroids). Occasionally, other drugs such as antithymocyte globulin (ATG) are given.
- Acute GVHD can persist and likely become chronic GVHD. Chronic GVHD can also appear in patients without prior acute GVHD.
- Chronic GVHD can affect any organ system. It may produce skin changes, liver disease, diarrhea and an increased risk of infection.
- Chronic GVHD may likely be mild and respond to agents that suppress the immune system, or it could unlikely be very severe enough to cause significant disability. It may also last for over a year.

#### Less likely side effects of GVHD:

- Lung damage (scarring of the lung – which is unlikely).
- Liver damage (unlikely).
- Mouth and throat sores.
- Hives, including severe rash leading to sloughing of skin and mucous membranes.
- Gastrointestinal bleeding.
- Kidney damage (rare).
- Red blood cell destruction by the immune system. Blood may be present in your urine.
- Incoordination or a temporary unsteadiness when walking (rare).
- Hypertension (high blood pressure – which is likely).
- Chest pain (unlikely).
- Heart damage (rare).
- Visual or Hearing loss (rare).

#### Less Likely But Not Serious Side Effects of GVHD:

- Tingling of the fingers and/or toes.
- Weight gain and/or swelling.
- Insomnia.

## **9. REPRODUCTIVE RISKS:**

### **For Females:**

This study may involve risks to you or your unborn child that are not known at this time therefore, you should not become pregnant or father a baby while on this study. Also, you should not nurse your baby while on this study. Females of childbearing potential will be required to take a pregnancy test before being allowed to take part in this study. The pregnancy test must be negative before you enter this study. Taking this medication/treatment now could affect your ability to have children at a later time.

You will be asked to practice an effective method of birth control while you are on this study and for a time after your treatment ends. This includes, but is not limited to, oral birth control pills, an IUD, condoms with spermicide, or abstinence. In females of childbearing age, birth control should continue for six (6) months after the last treatment to ensure the drug/treatment has cleared from the body. Since interactions between the study drug and oral birth control pills cannot be ruled out, a "barrier" method of contraception (condom, diaphragm) must be used as well.

In certain cases, oral birth control pills cannot be used for birth control. Please discuss this with your doctor.

To the best of your knowledge, you are not pregnant and do not plan to become pregnant while taking part in this study. Should you become pregnant during this study, you will immediately tell your study doctor and obstetrician. If you wish you may request a referral for counseling (such as genetic counselor, social worker, or psychologist.)

There is the possibility that this treatment could affect the ability of children and adolescents to have children at a later time. Ask about counseling and more information about preventing pregnancy. Pregnancy tests may be repeated during the study.

### **For Males:**

Male patients must use an effective method of birth control. This can include, but is not limited to, condoms with spermicide, abstinence, or having a vasectomy. When taking part in this study, you should continue use of birth control for three months after receiving the last dose of the drug to be sure the drug has cleared from the body. Males who are receiving treatment should not donate sperm for at least three months after the study is completed. Discuss birth control measures with your doctor.

## **10. WHAT BENEFITS MAY YOU GET FROM THIS STUDY?**

It is not known if this treatment will help you or not. Possible help may include shrinkage or disappearance of your cancer. This would result in a decrease in your symptoms and improvement in your quality of life. It is also possible the investigational treatments may prove to be less useful or even harmful to you. You understand that there is no guarantee that being on the study will help you. Future patients may be helped from the results and information gained from this study.

## **11. WHAT IF YOU DO NOT JOIN THIS STUDY?**

If you do not join this study, you should discuss the options with your doctor. This may include:

1. No treatment, but medications and measures to keep you comfortable. This is sometimes called supportive care only.
2. Usual/standard treatment for your disease or condition may be appropriate. This may include treatment with other drugs, drug combinations, surgery, radiation therapy, or possibly other research programs here or at other centers, which may be testing new drugs for your type of cancer.

There is no clear evidence that other treatments are more effective than this treatment. Feel free to talk with your health care team about your disease and your treatment choices.

## **12. WHAT WILL THIS COST?**

Examinations, scans, laboratory tests, and other medical procedures and treatments that would routinely be needed to monitor and treat your illness are known as "standard of care" services. Charges for these services will be billed to you and/or your insurance carrier in the usual manner. You will be responsible for all co-payments, deductibles, and/or account balances as determined by your individual health insurance contract.

There are many different types of insurance plans and contracts. It is not possible to tell you in advance the exact amount your insurance will pay and what your financial responsibility will be. If you wish, a financial counselor can meet with you to help answer your questions regarding insurance coverage issues before you decide to participate in this study. A Financial Counselor can be reached at 716-845-3161 or the Kaleida Patient Accounts Office at 716-859-7200.

A representative from the Patient Access Department can help you obtain authorizations from your insurance carrier when needed. A representative from the Patient Access Department can be reached at 716-845-1049.

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There are certain insurance plans that will not cover charges for any care related to an experimental or investigational therapy or study. These plans may deny coverage for even the routine, standard of care medical services you will need to receive during the time you are enrolled in the study. If you have an insurance plan that does not cover participation in a clinical research study, or if you currently have no insurance coverage, a financial counselor can meet with you to provide an estimate of the costs that would be associated with participation in this study. A payment schedule can be developed if needed. A RPCI Financial Counselor can be reached at 716-845-3161 or a Kaleida Financial Counselor can be reached at 716-859-8516.

Examinations, scans, laboratory tests and other medical procedures and treatment that are required only for the clinical research study and are not needed for the usual care of a patient with your/your child's disease are known as "research related" services. Research related services will not be charged to you or your insurance.

You and /or your insurance company will be responsible for charges related to the drugs and administration of drugs used in this clinical research study and for charges for medications that may be needed to prevent or control side effects.

If you develop complications or side effects from your/your child's participation in this clinical research study, medical treatment will be provided at the usual charge. A RPCI financial counselor can be reached at 716-845-3161 or a Kaleida Financial Counselor can be reached at 716-859-8516 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

If you have questions about your rights as a research subject or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Cancer Institute Patient Advocate (Support) Office at (716) 845-4474 or the Office of Administration at the Women & Children's Hospital: (716) 878-7551 or 878-7981.

### **13. WILL YOU BE PAID FOR JOINING THIS STUDY?**

You will receive no payment for taking part in this study.

It is possible that this research project will result in developing treatments, devices, new drugs, or procedures. If this happens, you understand that you will not receive any financial payment from the resulting use of information gained and developed through your participation in the research study.

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#### **14. WHO WILL PAY IF I AM INJURED AS RESULT OF TAKING PART IN THIS RESEARCH STUDY:**

Routinely Roswell Park Cancer Institute and Women & Children's Hospital, its agents, or its employees do not compensate for or provide free care for human subjects/participants in the event that any injury results from participation in a research project. In the unlikely event that you become ill or injured as a direct result of participating in this study, you may receive medical care, but it is not the policy of Roswell Park Cancer Institute, Women & Children's Hospital, University at Buffalo Pediatrics or the University at Buffalo, State University of New York to provide this care free even if the injury is a direct result of participation.

#### **15. WHAT IF YOU HAVE QUESTIONS?**

You are free to ask questions at any time about this study and to ask for more information from the doctor identified on this consent. If you have any questions, concerns or complaints about this study, you should contact Hong Lin, MD at RPCI (716) 845-8614 or Barbara Bambach, MD at RPCI (716) 845-2333. In case of an emergency after regular hospital hours, you should telephone: RPCI (716) 845-2300 or WCHOB (716) 878-7000 and ask for the pediatric oncology doctor on call.

If you have questions about your rights as a research subject or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Cancer Institute Patient Advocate (Support) Office at (716) 845-4474 or the Office of Administration at the Women & Children's Hospital: (716) 878-7551 or 878-7981.

You should also feel free to contact the Patient Advocate Office at any time while considering participation, during participation or once your participation is complete. This office is unaffiliated with any specific research study. They can help you obtain additional information regarding your research participation and your rights as a research subject or how to proceed should you feel you have been injured as a result of your participation. They are available to discuss any problems, concerns, questions or input you may have.

#### **16. WHERE CAN I FIND MORE INFORMATION?**

You may call the NCI's Cancer Information Service at  
1-800-4-CANCER (1-800-422-6237)

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. The 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. For accurate cancer information including PDQ, visit <http://cancernet.nci.nih.gov>

## **17. WHAT ABOUT CONFIDENTIALITY AND USE OF PROTECTED HEALTH INFORMATION?**

If you volunteer to take part in this research study, and you sign this document, you give permission to the following providers to use or disclose (release) your/your child's health information that identifies you as part of the research study described in this consent. This means that others may know or be able to find out your/your child's identity. Study information that we may use and/or disclose can identify you in the following ways:

"Protected Health Information" (PHI) can be your/your child's name; address; or patient identification number; medical record number; date of birth; photographs; biometric identifiers; information about your/your child's health, including past medical history, treatment, diagnosis, test results and any other information about your/your child's health or medical condition; or about payment of charges for medical treatment found in your/your child's medical record or other records maintained by Roswell Park Cancer Institute/Women & Children's Hospital of Buffalo.

In addition to researchers, this study may be associated with certain companies and government agencies. They may use your/your child's health information and share it with others. We want you to know who may use this information and how they may use it. We also want to tell you about your rights before you agree to take part in this study.

### **Who may use and give out information about you?**

The study doctor and research staff will have this information and may give it to others during and after the study.

### **Who may see this information?**

The study sponsor may also see this information. The "Sponsor" includes all people or companies working for or with the sponsor or owned by the sponsor. They all have the right to see this information during and after the study.

The following people, agencies and businesses may also get information about you:

- Doctors and healthcare professionals at other sites taking part in the study
- Doctors and healthcare professionals at Roswell Park Cancer Institute/Women & Children's Hospital of Buffalo
- The National Marrow Donor Program and the Center for International Blood and Marrow Transplant Research, organizations involved in research on blood and marrow transplantation and in the coordination of this study
- Members of the Blood and Marrow Transplant Clinical Trials Network
- US Food and Drug Administration (FDA)
- US Department of Health and Human Services (DHHS)



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- National Cancer Institute (NCI)
- National Institute of Health (NIH)
- Government agencies in other countries
- Government agencies that must receive reports about certain diseases and conditions
- Institutional Review Board at RPCI and UB Children and Youth IRB at Women & Children's Hospital of Buffalo and/or their affiliates

**What information may be used and shared?**

Medical information that identified you and relates to your participation will be created if you take part in this study. This may include the following:

- Information from the procedures used to find out whether you are/your child is eligible to take part in this study. This may include physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information that you may release to us, including information about your/your child's health history.
- Information obtained in the course of the study including information about your/your child's response to any treatments you receive, information related to study visits and phone calls, physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information about your participation in this study.

**Why will this information be used and/or shared?**

The information that may identify you will be used and given out to others to carry out the research study. The sponsor will analyze (test) and evaluate the results of the study. The sponsor, its agents, government agencies, and others may visit the research site to follow how the study is being done and may review your information for this purpose.

This information may be given to the FDA. It may also be shared with other governmental agencies in this country and in other countries. This is done for participant protection and so the sponsor can receive marketing approval for any new products that may result from this research. The information may also be used to meet the reporting needs of the governmental agencies.

The results of this research may be published in scientific journals or presented at medical meetings, but your/your child's identity will not be disclosed (shared).

The information may be reviewed by the IRB at RPCI and WCHOB and its affiliates, who perform review of research as needed by law.

PHI may be used and disclosed in the creation and maintenance of a research database or repository. This information may then be used for other research, either de-identified or with further IRB review and approval. This information can be kept indefinitely.

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**What if I decide not to give permission to use and give out my health information?**

If you refuse authorization for us to use and disclose your information as indicated above, you will not be able to be in this research study.

Your decision not to sign this authorization or to withdraw from the study will not involve any penalty or loss of benefits to which you are otherwise entitled and will not affect your access to non-research related health care here.

You may change your mind and revoke (take back) this authorization at any time, except to the extent that RPCI/WCHOB has already acted (used or disclosed PHI) based on this authorization.

**What happens if I want to withdraw my authorization?**

To revoke/withdraw this authorization, you must write to the study doctor and let her know that you are withdrawing your authorization to use and disclose your information. Her mailing address is: Dr. Hong Liu OR Dr. Barbara Bambach, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, New York 14263.

If you should die while enrolled in or after taking part in this study, your PHI may be used or disclosed solely for research purposes without getting any added authorization.

The results of clinical tests or therapy performed as part of the research may be included in your medical record and will not be removed from the record if you withdraw.

If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

**May I review or copy the information obtained from me or created about me?**

To keep the integrity (truthfulness) of this research study, you will not have the right to review or copy your/your child's personal health information related to this research until the study is complete. At the end of this research study and at your written request, you may have access to your/your child's health information. This information is kept in a designated record set, which is a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at RPCI/WCHOB to decide about care and treatment. Access to your/your child's health information in a designated record set is described in the Notice of Privacy Practices provided to you by RPCI/WCHOB.

If it is necessary for your care and/or treatment, your PHI will be provided to you or your referring or primary care doctor.

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**When does this authorization end?**

This authorization has no expiration date. The researchers may continue to rely on this authorization to obtain and use protected health information about you unless you revoke this authorization in writing.

**What happens to my health information after it is given to others?**

If you sign this form, and the information is given to other people, businesses, or government agencies, the information may no longer be protected. There is a risk that your/your child's information will be given to others without your permission.

Your protected health information will go into a database that will be maintained indefinitely. Any future study using this information that falls outside the scope of this current study will be required to follow guidelines designed to govern access to that information and to protect the privacy of that information.

**AUTHORIZATION**

As a participant in this study, you allow the use of protected health information for research purposes. You understand that PHI will be used/disclosed by RPCI/WCHOB as indicated in this document. You understand that you have a right to withdraw your authorization for use of PHI in writing, but that information which has already been used or disclosed before your written withdrawal will continue to be used for research purposes. Finally, you understand PHI that has been disclosed by RPCI/WCHOB through this authorization to the study sponsor, FDA, NCI, NIH, or others may be further disclosed by them, as the PHI will no longer be protected by the federal privacy laws.

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RPCI IRB and UB CYIRB APPROVED

PER DH

FROM: 9/20/2014

TO: 9/19/2015

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**PATIENT'S STATEMENT OF CONSENT/VOLUNTARY CONSENT (Signature Pages):**

I have been given a copy of all 21 pages of this document. The document includes no attachments.

By signing below, you agree that:

- You have been told of the reasons for this study.
- You have had the study explained to you.
- You have had all of your questions answered, including those about areas you did not understand, to your satisfaction.
- You have carefully read this consent document and will receive a signed copy of this form.
- You do not waive any legal rights you have under federal or state laws and regulations.
- You willingly give your consent to voluntarily join in this research study.

☐ Check box if Participant is < 18 yrs of age (Child) and complete Parent/Legal Guardian information below:

Child's Name (PRINT) \_\_\_\_\_

Parent/Legal Guardian (PRINT) \_\_\_\_\_

Relationship to Participant \_\_\_\_\_

Parent/Legal Guardian Signature \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

a. ☐ Check box for Assent of Participant (applicable to children from ages >7 years)

By signing this form, I agree that the study has been explained to me and I have had the opportunity to ask questions and I agree to be in this research study.

(Print) Name of participant \_\_\_\_\_

Signature of participant \_\_\_\_\_

Date \_\_\_\_\_

b. ☐ Check box if Assent of Participant (children from ages >7) is NOT applicable for any reason.

☐ Check Box if Participant is 18 years or above and complete Participant information below:

Participant Name (PRINT) \_\_\_\_\_

Participant Signature \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

Date: 7/22/13

400 cGyTBI

**RPCI IRB and UB CYIRB APPROVED**

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LAR is ☐ Needed ☐ Not Needed \_\_\_\_\_ Initials of Person Obtaining Consent

As the legally authorized representative for (Participant's Name) \_\_\_\_\_, I give permission on his/her behalf to participate in this research study. My decision is based on what I believe he/she would choose for him/herself based on the information I have received about the research. By signing this form, I do not waive any of his/her rights.

LAR Name (PRINT) \_\_\_\_\_

Relationship to Participant \_\_\_\_\_

LAR Signature \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

**Person Obtaining Consent (PI or Designee):**

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained to the above individual(s) and that any questions about this information have been answered. A signed copy of this consent will be given to the Parent/Guardian, Participant or LAR.

Person Obtaining Consent/Permission Name (PRINT) \_\_\_\_\_

Person Obtaining Consent/Permission Signature: \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

**Witness:**

I certify that the individuals named above as "Parent(s)/Legal guardian(s)", "Participant," or Participant (> 18 yrs of age) and "Person obtaining consent/permission/assent" signed this document in my presence.

Witness Name (PRINT): \_\_\_\_\_

Witness Signature \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

**CONSENT HANDLING**

Original to CRA-Regulatory with Race/Ethnicity if applicable

Copy to:

- Patient
- CRS registration
- Medical Records

Date: 7/22/13  
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