^{131}I-Metaiodobenzylguanidine (^{131}I-MIBG) Therapy for Refractory Neuroblastoma and Pheochromocytoma

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SUBJECT CONSENT FORM

This study is an expanded access protocol of an experimental new drug for cancer. We are asking if you want to participate in this study because there is not a standard treatment for your cancer at this point. This study only includes patients who choose to take part. Your participation in this study is entirely voluntary. Please read the consent form carefully. You will be given a copy of it to keep if you decide to participate in this study. You may discuss your decision with your friends and family if you would like.

This study is being carried out by Dr. Aarti Kamat at the University of Minnesota Masonic Children's Hospital. Dr. Kamat is an Assistant Professor within the Division of Pediatric Hematology/Oncology at the University of Minnesota.

This is an expanded access protocol for patients who have refractory neuroblastoma or metastatic pheochromocytoma. Studies at other centers have shown that treatment with ^{131}I-MIBG may be beneficial to patients with these tumors. This study is being conducted under an Investigational New Drug (IND) application with the Food and Drug Administration (FDA). This is required because this treatment is not approved by the FDA.

I-MIBG is a radioactive material that is used in MIBG scans. You have had MIBG scans to look at your tumor. In this study we will use radioactive ^{131}I-MIBG at higher doses to try to treat your tumor.

WHY IS THIS STUDY BEING DONE?

We are conducting this study to provide patients with refractory neuroblastoma or metastatic pheochromocytomas access to treatment with ^{131}I-MIBG.

The goals of this study are to:

- Assess disease response to ^{131}I-MIBG therapy for patients with relapsed/refractory neuroblastoma or metastatic pheochromocytomas, to
- Gain more information about the toxicities of ^{131}I-MIBG therapy, and to
- Assess improvement of symptoms, including pain and fatigue, for patients with relapsed/refractory neuroblastoma or metastatic pheochromocytomas who are receiving ^{131}I-MIBG therapy.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We may treat about 10-18 patients at this hospital each year.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study:
You will need to have the following exams, tests or procedures to find out if you can be in the study. 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.

- A medical history
- Review of prior therapy
- Review of medications
- Physical exam
- Vital signs (including blood pressure, pulse, temperature)
- Blood tests
- Urine tests
- Bone marrow aspirates and/or biopsies (if you have neuroblastoma)
- Pregnancy test (if you are a woman who could have children)
- Echocardiogram (ECHO)
- MIBG scan
- We will also do whatever other CT or MRI scans are needed to check your tumor

You will need a responsible caregiver during the therapy. A responsible caregiver will need to confirm they are willing and able to help care for you while you are in the hospital. This is required in order to minimize the radiation exposure to the nurses.

During the study:
If the exams, tests and procedures show that you can be in the study, and you choose to take part, ^{131}I-MIBG will be given as an intravenous (IV) infusion over 1-2 hours. If you have stored stem cells that can be given, the maximum dose you can receive is 18 mCi/kg. If you do not have stem cells your dose must be less than 12 mCi/kg.

An infusion of your stem cells may be needed to help your blood counts recover after high doses of ^{131}I-MIBG.

You will need to stay in a radiation-protected hospital room. We will measure the amount of radiation given off. You will not be able to leave until the emissions are less than 7 mRem/hour. This usually takes 2 – 5 days.

You will need to have an MIBG scan on about day 4, or the day you are discharged from the hospital.

To help protect your bladder, intravenous (IV) fluids will be given to help maintain urine flow and to flush out the radiation. A urinary catheter will be inserted to help prevent accumulation of radioactivity in the bladder. Urine will be drained into a sterile bag in lead shielding. In the event you are unable to cooperate with this catheter and/or isolation, sedation may be necessary. The risks of sedation are explained later in this

consent form.

To help protect your thyroid gland, potassium iodide will be given by mouth. It will be given 8 hours before the ^{131}I-MIBG infusion, and then every 4 hours for 6 days. After Day 6, a smaller dose will be given one time each day through Day 45.
If your neutrophil count (ANC) is less than 750 it is recommended that you receive G-CSF or Neulasta until your neutrophil count recovers.

We will ask you to complete brief questionnaires to assess your pain and tiredness (or fatigue) on the day you receive ^{131}I-MIBG (day 0) and on the day you are discharged from the hospital. These questionnaires will take 5-10 minutes to complete.

An evaluation of your tumor will happen about 6-8 weeks after your treatment. This will include an MIBG scan as well as any other needed CT or MRI scans.
You may be eligible to receive additional therapy with ^{131}I-MIBG if you meet the following criteria:

- It has been at least 6 weeks from your previous ^{131}I-MIBG treatment.
- Your tumor responded or was stable after the first treatment.
- Your evaluation shows you are healthy enough to receive more treatment. An evaluation will include a physical exam, vital signs, blood tests, and urine tests.
- You must have stored stem cells available in order to receive the higher dose.

HOW LONG WILL I BE IN THE STUDY?
You may receive up to three cycles of treatment as long as your tumor is responding, you are healthy enough to receive it, and your doctor agrees. Your doctor may decide to take you off the study if any of the following occur:

- Your tumor gets worse
- The side effects of the treatment are too harmful for you
- You are not able to follow study-related treatment instructions
- New information becomes available
- The study is not in your best interest
- The study is stopped
- If you become pregnant

After you are finished with this treatment, we would like to follow you every three months for the first year, and then every six months. During this time we will monitor you for potential late side effects of the treatment.

CAN I STOP BEING IN THE STUDY?
Yes. 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 ^{131}I-MIBG treatment can be evaluated by your doctor. Also, your doctor can discuss what follow-up care and testing could be most helpful for you.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. In some cases, side effects can be serious, long lasting, or may never go away. We will tell you if we learn any new information that may affect your health, welfare, or decision to stay in this study.

You should talk to your study team about any side effects that you have.

The major risks for patients participating in this study are:

- **Hematologic (blood) toxicity.** It is expected that your blood counts will get low after the treatment. You may have:
    - a low number of white blood cells (which can make it easier to get infections),
    - a low number of red blood cells (which will make you feel tired and weak),
    - a low number of platelets (which causes you to bruise and bleed more easily)

- **Hypothyroidism.** This is a condition where the thyroid gland does not produce enough thyroid hormone. If this happens you may need to take thyroid hormone pills.

During the infusion, you might have:

- Nausea,
- High blood pressure
- Low blood pressure

Rare risks for patients in this study are:

- Dry mouth
- Salivary pain and swelling
- A new cancer or leukemia
- Damage to the bladder, heart, kidney, or liver
- There have been rare cases of death due to liver and lung toxicity following treatment with ^{131}I-MIBG.

There may also be possible late side effects to this treatment. Late side effects can develop months or years after treatment. Because this treatment is new, we do not know what the risks of developing these late side effects are with this treatment. Your doctor will monitor you closely for development of these possible late effects including second cancers and damage to heart, kidney, liver or lung.

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. 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).

Possible risks to the caregiver(s) of the patient getting MIBG treatment:

Caregivers will be exposed to radiation while you are being treated with MIBG. Caregivers who could possibly become pregnant during this time need to avoid contact with the patient because the radiation exposure may increase the unborn baby's risk of developing cancer or other health problems. If your caregiver is pregnant, then special precautions should be used to avoid contact with you during and for 4 weeks after getting MIBG treatment. Should your caregiver or your caregiver's sexual partner be found to have been pregnant while you were getting ^{131}I-MIBG treatment and did not know it at the time, please contact your doctor immediately.

Risks of Sedation

The risks of sedation include decreased oxygen levels due to decreased respiratory drive, disorientation, decreased blood pressure and drowsiness.

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

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

The potential benefit of this treatment is that it may cause your cancer to stop growing or to shrink for a period of time. It may lessen the symptoms, such as pain, that are caused by the cancer. It is extremely unlikely that this treatment will cure your cancer. Because there is not much information about the effect of ^{131}I-MIBG when used for treatment, we do not know if you will benefit from taking part in this study. Information learned from this study may help future patients with cancer.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Talk to your doctor about your choices before you decide if you will take part in this study. Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Focusing on comfort care and quality of life instead of drugs to treat the tumor

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information

will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Representatives of the Food and Drug Administration (FDA) or other agencies involved in overseeing research
- The Institutional Review Board (IRB) and other committees of this University and hospital who oversee research

USE OF IDENTIFIABLE HEALTH INFORMATION

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your child's information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's website at http://cancer.gov/clinicaltrials/learning/insurance-coverage/. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

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

RESEARCH RELATED INJURY

In the event that this research activity results in an injury, treatment will be available including first aid, emergency treatment, and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research-related injury, let Dr. Aarti Kamat know right away.

There are no plans for the study to pay for medical treatment for injuries. However, signing this form does not mean that you are giving up any legal rights to try to get compensation for injury.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your regular medical care from our institution.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

NEW INFORMATION
We will tell you about new information that may affect your health, welfare, or willingness to remain in this study as soon as it becomes available. If during the course of this research study there are significant new findings discovered that might influence your willingness to continue, the researchers will inform you of the new developments.

WHOM DO I CONTACT IF I HAVE QUESTIONS, CONCERNS OR FEEDBACK ABOUT MY EXPERIENCE?
If you have questions about research appointments, the study, research results, or other concerns, contact the researcher, Dr. Aarti Kamat of the University of Minnesota at 612-626-2778. If you are calling after regular business hours, call 612-273-3000 and request the on-call physician.

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your child's rights as a research participant.
- You want to get information or provide input about this research.

WILL I HAVE A CHANCE TO PROVIDE FEEDBACK AFTER THE STUDY IS OVER?
The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please

contact the study team or the HRPP. See the “Investigator Contact Information” on the first page of this form for study team contact information and “Whom do I contact if I have questions, concerns or feedback about my experience?” of this form for HRPP contact information.

WHERE CAN I GET MORE INFORMATION?

A description of this clinical trial will be available at http://www.ClinicalTrials.gov. The registration number for this study is **NCT # 01850888**. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

If you are in the United States, you may call the National Cancer Institute's Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/.

- For NCI’s clinical trials information, go to: http://cancer.gov/clinicaltrials/.
- For NCI’s general information about cancer, go to: http://cancer.gov/cancerinfo/.

If you want more information about this study, ask your study doctor.

STATEMENT OF CONSENT

I have read the above information. I have had the opportunity to ask questions, and my questions have been answered. **I agree to enroll in this study.**

You will receive a copy of this form. A copy of the study protocol is available upon request.

PATIENT NAME Printed):_____

_____ _____
Signature of Patient Date

_____
Printed Name of Legally Authorized Representative
(If Applicable)

_____ _____
Signature of Legally Authorized Representative Date
(If Applicable)

_____ _____
Printed Name of Person Obtaining Consent Date

_____ _____
Signature of Person Obtaining Consent Time

Your signature indicates that you have discussed the information in this form, asked all your questions and had them answered, and decided that you will participate in this study. In no way does your signature reduce any of your legal rights or release the doctors at this medical center from their legal and professional responsibilities.

Was an interpreter utilized to obtain consent? ☐ YES ☐ NO

Was a translated Short Form used? ☐ YES ☐ NO

_____ _____
Signature of Interpreter (if applicable) Date