

MEDICAL RECORD	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY <ul style="list-style-type: none"> • Adult Patient or • Parent, for Minor Patient
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INSTITUTE: National Cancer Institute

STUDY NUMBER: 11-C-0024 PRINCIPAL INVESTIGATOR: Mark Roschewski, M.D..

STUDY TITLE: A Phase II Trial of IPH2101 (anti-KIR) in Smoldering Multiple Myeloma (SMM)

Continuing Review Approved by the IRB on 06/11/12

Amendment Approved by the IRB on 03/10/13 (E)

Date posted to web: 3/14/13

Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

Recent studies have shown that a condition called smoldering multiple myeloma (SMM) is thought to have a high risk of progressing to multiple myeloma (MM), a type of cancer involving the bone marrow. People with SMM have a high level of M-protein in the blood and of plasma cells in the bone marrow. Fifty-one percent of people with SMM develop multiple myeloma within 5 years of their diagnosis. The mechanism by which this change takes place is not currently known. Additionally, studies have shown that certain cells in the immune system, known as NK cells or natural killer cells, have activity against MM. The experimental agent in this study, anti-KIR (also known as IPH2101) is a monoclonal antibody (or mAb) that helps NK cells kill MM cells. There are currently no known effective treatments to prevent SMM from

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developing into MM; and there are no known tests for determining who will SMM will develop MM.

In this study we will test whether giving individuals with a diagnosis of SMM this anti-KIR experimental agent will help improve the abnormal blood test results seen in SMM. In addition, this study will evaluate the side effects of the experimental agent, the effects of anti-KIR on the body (pharmacokinetics), the biological activity (research tests) and its ability to prevent MM.

Why are you being asked to take part in this study?

You are being asked to take part in this study because your blood tests show that you have a diagnosis of smoldering multiple myeloma.

How many people will take part in this study?

From 9 to 21 people with SMM will participate in this study.

Description of Research Study**What will happen if you take part in this research study?****Before you begin the study**

Eligibility criteria have been established to ensure that you are a medically appropriate candidate for this trial. These criteria will also help ensure that the results of this study can be useful for making decisions regarding other patients. No exceptions will be made to these criteria for study participation unless agreed upon by the Sponsor and your physician.

To determine if you are eligible you will have a history taken and a physical examination done by one of the study doctors. Standard laboratory blood tests will be done to make sure it is safe for you to participate. You may not participate if you have received any other investigational agent within the past 3 months, if you have amyloidosis or known heart problems. You may not have any active infections or autoimmune disease. If you have previously had a bone marrow or organ transplant or if you are pregnant or breastfeeding a baby, you will not be able to participate for your safety and the safety of your child.

During the study

Once it is determined that you are eligible and you decide to participate, baseline tests will be done. Before starting the anti-KIR experimental agent, approximately 8 tablespoons of blood will be taken from your vein for research blood tests. We will ask you to provide a urine sample, and a bone marrow aspiration will be done for specific research testing.

You will be given the anti-KIR agent through an intravenous line (IV – small plastic tube or catheter put into a vein in your arm). You will receive the anti-KIR over 1 hour, once every other month; therefore in 1 year you will receive 6 doses of anti-KIR. It is possible that you

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might be offered an additional year of therapy (up to 6 additional doses of anti-KIR). In this case, the same schedule of treatment and follow up will be used.

In order to watch you closely, you will be admitted to the Clinical Center hospital for the first dose of anti-KIR. If you do not have side effects during the first infusion, all subsequent doses can be given to you in the Clinical Center Day Hospital.

The nurses and doctors will watch you closely during and after the anti-KIR, taking your blood pressure, heart rate, and temperature frequently during the infusion and for up to 6 hours after the anti-KIR infusion. A heart tracing (EKG) will be done 2 hours after the end of each infusion. If you have any side effects, your next dose may be delayed. But if it is delayed more than one month, you will not receive any further doses of anti-KIR.

Every month we will ask you to come to the Clinical Center for a physical examination, routine blood tests, and research samples (up to 8 tablespoons of blood and a urine sample).

You are not allowed to receive any other treatment for your SMM while on this study. Certain medicines are also prohibited such as corticosteroids (for treatment of SMM) or cytokines. Please check with your study doctor or nurses before taking any new medications, including medicines that may be prescribed by other doctors.

After you have completed treatment

Two months after your last dose of anti-KIR, you will return to the Clinical Center for a physical examination, routine blood tests, and research samples (up to 8 tablespoons of blood and a urine sample). A second bone marrow aspiration and biopsy will be done during that visit to test the effects on your bone marrow cells.

After your first follow-up visit, you will return to the Clinical Center every 3 to 6 months for two years after the completion of therapy. After the two year visit, you will come annually for a total of five years or until the study has completed. At these follow up visits, you will undergo a physical examination and laboratory testing but not a bone marrow biopsy unless your study doctor thinks it is necessary.

What does this study involve?**Birth Control**

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for four months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

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Effective forms of birth control include:

- Abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

Alternative Approaches or Treatments**What other choices do I have if I do not take part in this study?**

Instead of being in this study, you have these options:

- Because there are no known effective treatments for SMM, you may be observed by your doctor for this condition without being in a study
- Take part in another study

Please talk to your doctor about these and other options.

Risks or Discomforts of Participation**What side effects or risks can I expect from being in this study?****Likely: the most frequently reported side effects that have been reported in other studies using Anti-KIR were:**

- Fever
- Fatigue
- Headache
- Chills
- Rash
- Itching
- Slow heart rate

Less Likely: other side effects that occurred in participants of other studies using Anti-KIR included:

- Changes in blood tests showing anemia, lowered platelet count, increase lipase (fat), increased creatinine (test of kidney function), lowered neutrophil count (may increase risk of infection), high level of potassium, high level of uric acid.
- Swelling of the breasts in men
- Lowered blood pressure
- Difficulty breathing

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- Nausea
- Pain in the stomach
- Flushing

Rare but Serious

- One patient in a study of Anti-KIR had sudden onset kidney failure after one dose.

Potential Benefits of Participation**Are there benefits to taking part in this study?**

The aim of this study is to see if this experimental agent will decrease abnormal blood values seen in people with SMM and decrease the risk of developing MM. This study is also testing the side effects of this experimental agent. We hope that you will get personal medical benefit from taking part in this study, but we cannot be certain. Because there is not much information about the drug's effect on SMM, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Research Subject's Rights**What are the costs of taking part in this study?**

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs even if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Stopping Participation in this Study

Your doctor may decide to stop your participation for the following reasons:

- if he/she believes that it is in your best interest

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- if you develop MM during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if the study is completed

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Innate Pharma or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process <http://ethics.od.nih.gov/procedures/COI-Protocol-Review-Guide.pdf>. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to \$15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

Optional Studies

We would like to keep some of the specimens and data that are collected for future research. These specimens and data will be identified by a number and not your name. The use of your specimens and data will be for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

MEDICAL RECORD**CONTINUATION SHEET for either:**
NIH 2514-1, Consent to Participate in A Clinical Research Study
NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

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If you decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use specimens and/or data. Then any specimens that remain will be destroyed and your data will not be used for future research.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My specimens and data may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials _____

2. My specimens and data may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials _____

3. Someone may contact me in the future to ask permission to use my specimens and/or data in new research not included in this consent.

Yes No Initials _____

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OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Mark Roschewski M.D. Building 10, Room 3B40, Telephone: 301-451-9021. You may also call the Clinical Center Patient Representative at (301) 496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/
Legal Representative Date

Print Name

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.

(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian Date

Print Name

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian Date Print Name

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE
FROM JUNE 11, 2012 THROUGH JUNE 10, 2013.**

Signature of Investigator Date Signature of Witness Date

Print Name

Print Name