A phase 1b/2a open label study to evaluate anti-tumor efficacy and safety of rhIL-7-hyFc (NT-I7) in combination with anti-PD-L1 (atezolizumab) in patients with anti-PD-1/PD-L1 naïve or relapsed/refractory high-risk skin cancers

NCT03901573

19 January 2023

Notes for Local Investigators*:

- The goal of the informed consent process is to provide potential study participants with clear, accurate, unbiased, and sufficient information so that they can make informed choices about participating in research. The informed consent form is one part of the process. It provides a summary of the study, describes foreseeable risks, discusses the individual's rights as a study participant, and documents their willingness to participate. The informed consent form, however, is only one piece of an ongoing exchange of information between the investigator and potential research participant.
- *[Note to Local Investigator]* or a blank line, "_____", indicates that the local investigator should provide the appropriate information before submitting to the IRB.

*These notes for local investigators are instructional and should not be included in the informed consent form sent to IRBs.

Research Study Informed Consent Form

Study Title for Participants: Testing the Combination of Atezolizumab and NT-I7 as an Experimental Immunotherapy Treatment in Patients with High-Risk Skin Cancers

Official Study Title: A Phase 1b/2a, Open Label Study to Evaluate Anti-Tumor Efficacy and Safety of rhIL-7-hyFc (NT-I7) in Combination with Anti-PD-L1 (Atezolizumab) in Patients with Anti-PD-1/PD-L1 Naïve or Relapsed/Refractory High-Risk Skin Cancers

Protocol #: NIT-106 (ION-02)

Protocol Version Date: Amendment 5_v1.0_18JAN23

Principal Investigator(s)

[Note to Local Investigator: Contact information for principal investigator(s) should be listed here.]

We are inviting you to participate in a research study.

We invite you to join this research study because you have a high-risk skin cancer, such as melanoma, Merkel Cell Carcinoma, or cutaneous Squamous Cell Carcinoma. You may or may not have already been treated with an immunotherapy drug and your cancer is not responding to treatment.

Research is not the same as treatment or medical care. A research study answers scientific questions.

If you agree to join the study, you will be given two experimental immunotherapy drugs, NT-I7 and atezolizumab, for up to two years. During this time, we will do exams, tests, and procedures to follow your condition and to see how the study drugs are affecting your body. Many of these exams, tests, and procedures will be part of your regular cancer care, but some of them may be done more frequently because you are in this study.

The combination of NT-I7 and atezolizumab, referred to as "study treatment" throughout this document, has not been studied in humans. We do not know if the study treatment would help to treat high-risk skin cancers. It is possible that the study treatment could cause side effects.

You do not have to join this study. You could choose to receive standard methods to treat your high-risk skin cancer. You are free to say "yes" or "no" or drop out after joining. If you say "no", you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

We will give you details about the purposes, procedures, risks, and possible benefits related to this study. We will explain other choices that you have. We will also give you any information that you need to make an informed decision about joining the study.

This research study is sponsored by NeoImmuneTech, Inc. of Rockville Maryland and conducted by the Immune Oncology Network (ION). The ION coordinating center is located at the Fred

Hutchinson Cancer Center (FHCC) in Seattle and works with researchers from several cancer centers and universities across the country. NeoImmuneTech is providing financial support to cover the cost of study-specific procedures performed during this study.

The following is a more complete description of this study. Please read this description carefully. Afterwards, you can ask questions that will help you decide whether to join the study. If you agree to join, we will ask you to sign this Informed Consent Form (ICF) and give you a copy of your signed ICF to keep for future reference.

Why are we doing this study?

The purpose of this research study is to test the safety and to find out what effects, good and/or bad, that the study treatment has on you and your high-risk skin cancer. The study treatment consists of two immunotherapy drugs, NT-I7 and atezolizumab. We call these drugs immunotherapies because they work by stimulating the immune system to destroy cancer cells and potentially generate an anti-tumor effect. This study tests different doses of NT-I7 to see which dose is safer and potentially more effective when combined with atezolizumab for treating high-risk skin cancers.

In this study, both NT-I7 and atezolizumab are considered experimental drugs, which means health authorities have not approved either drug for the treatment of high-risk skin cancers. Atezolizumab has been approved by the U.S. Food and Drug Administration (FDA) for treatment of certain types of cancer (including bladder, breast and lung cancers).

What are the study groups?

About 84 patients with high-risk skin cancers will take part in this study.

This study has two steps. Step 1 will happen first and will include up to 24 patients. Step 2 will happen after Step 1 and will include approximately 60 patients.

All study participants will receive the study treatment which will be given in cycles. A cycle lasts 21 days. Atezolizumab will be given to you on Day 1 of each cycle, beginning with Cycle 1, for up to 2 years. NT-I7 will be given to you on Day 1 of every other cycle (Cycle 1, Cycle 3, Cycle 5, etc.), for up to 2 years.

During cycles 1 and 3, you will visit the study site on Days 1 and 8. If you are a Step 1 participant, you may also visit the study site on Day 2 of Cycle 1. This visit is optional. For all remaining cycles you will only visit the study site on Day 1.

On the days you receive the combination of NT-I7 and atezolizumab, you will first be given NT-I7 as an injection into your muscle. Depending on when you join the study, you may get a different dose of NT-I7. This is explained in more detail below. During a given cycle, your study doctor may decide not to give you NT-I7, based on the results of your blood test for that visit. More information about the blood tests performed during this study is provided below.

Atezolizumab will then be given to you through a vein in your arm over 45-75 minutes on the first day of the first cycle. During the following cycle(s), the infusion time may be reduced to 20-40 minutes, if the first infusion went well. Atezolizumab will be given on Day 1 of every cycle, even if your NT-I7 dose is skipped for that cycle. All study participants will receive the same dose of atezolizumab.

Step 1:

Step 1 participants will get NT-I7 at different doses but will get atezolizumab at the same dose.

The first 3 people in Step 1 will be given the lowest dose of NT-I7. If NT-I7 does not cause serious side effects, it will be given to the next 3 people at a higher dose. The doses will continue to increase for up to 4 groups of 3-6 people per group until side effects occur that require the dose to be lowered. The study will then proceed with Step 2.

Step 2:

All Step 2 participants will get both NT-I7 and atezolizumab at the same dose.

Step 2 participants will receive the same dose of atezolizumab as Step 1 participants. The dose of NT-I7 that they receive will be the dose that worked the best and was also safe based on the results from Step 1.

How long will I be in this study?

If you join this study, you would receive study treatment for up to 2 years and return for follow-up visits 1, 2 and 3 months after your last dose of study treatment.

Long-term follow-up means keeping track of someone's medical condition for a long time. After you finish study treatment, your study doctor will continue to watch you for side effects and follow your condition until the study ends, which will occur when the last patient has completed their safety follow visits (3 months after their last dose of study treatment).

If you stop study treatment for any other reason than your disease worsening, you will continue to have imaging scans done every 12 weeks (3 months) for up to 1 year.

If you stop treatment because your cancer has returned or worsened, causing more symptoms, or if you do not respond well to the study treatment, we would either call you or see you in person every 12 weeks (3 months) to see how you are doing, until the study ends. We would also ask your doctor to send a copy of your medical records. This information will help us learn about the long-term effects of the study treatment.

If your cancer grows or spreads while you receive the study treatment, but you do not have other concerning symptoms or have shown other evidences of benefit from the study treatment, your study doctor may talk to you about continuing the study treatment.

The study doctor or study staff or sponsor can remove you from the study at any time, even if you want to stay in the study. This could happen if, for example:

- The study doctor or study staff believes it is best for you to stop being in the study.
- You do not follow directions about the study.
- The sponsor stops the study for any reason.

If you leave the study, the study doctor and study staff will still be able to use your information that they have already collected.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual medical care for your cancer. However, there are some extra exams, tests, and procedures that will only be done for

this study or may be done more frequently for this study.

Before you begin the study:

We will do the following things to find out if you can participate in the study. This is called screening. These exams, tests, and procedures may be part of regular cancer care and done even if you do not join the study. If you have had some of them done recently, we may not need to do them again.

- We will take some blood to do laboratory tests.
    - Some of your blood will be used to test for hepatitis B. The study doctor or study staff will tell you if the test results are positive. If required by state law, the study doctor or study staff may report a positive test result to the local health department. The results of these tests must be negative in order for you to be in the study.
- We will measure your tumor by looking at imaging scans of your body (e.g. CT scan or PET/CT scans, MRI, or x-ray).
- We will take a biopsy of one of your tumors for testing. A small piece of cancer tissue will be removed using a needle, a circular blade called a punch, or a small scalpel. The biopsy will be used to see if your tumor changes over time. This sample is a required part of the study.
    - If you have a previous tumor biopsy available, we may be able to use it for this study.
    - You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.
- If you are a woman capable of having children, we will give you a pregnancy test to make sure you are not pregnant.

During the study:

If the screening process shows that you can be in the study, and you choose to participate, then we will do the following things that may be part of regular cancer care, but may happen more often because you are in this study:

- We will do a physical exam every 3 weeks.
- We will measure your tumor by looking at imaging scans of your body (e.g. CT scan or PET/CT scans, MRI, or x-ray) every 9 weeks for the first two scans, then every 12 weeks after that.
- We will take blood at most visits for safety tests to help us monitor any good or bad effects that the study drugs might have on your body.
- We will take blood at most visits for research tests to help us understand how your body, especially your immune system, is responding to the study drugs. Your study doctor will get some of the results of this testing.
- We will also take blood to learn how your body absorbs, distributes, and gets rid of the drugs. We will collect this blood (between ½ teaspoon to about 2 teaspoons) at:
    - Cycle 1, Day 1
    - Cycle 1, Day 2 (Step 1 participants only and optional)
    - Cycle 1, Day 8
    - Cycle 3, Day 1

- Cycle 5, Day 1
- End of Treatment visit

- We will take a biopsy of one of your tumors for testing at Cycle 2. The study biopsy will be done only if your study doctor considers it can be obtained safely.

After study treatment is stopped:

- You will have an End of Treatment Visit about 30 days after your last dose of study treatment. We will repeat all the procedures that you had done during the study.
- You will have a Safety Follow-Up Visit about 2 months (60 days) after your last dose of study treatment, and another one about 1 month later. You will have the same procedures done at this visit as a regular cancer care visit. If you are a woman capable of having children, you will also have a pregnancy test 3 month after your last dose of study treatment.

What are the side effects or risks?

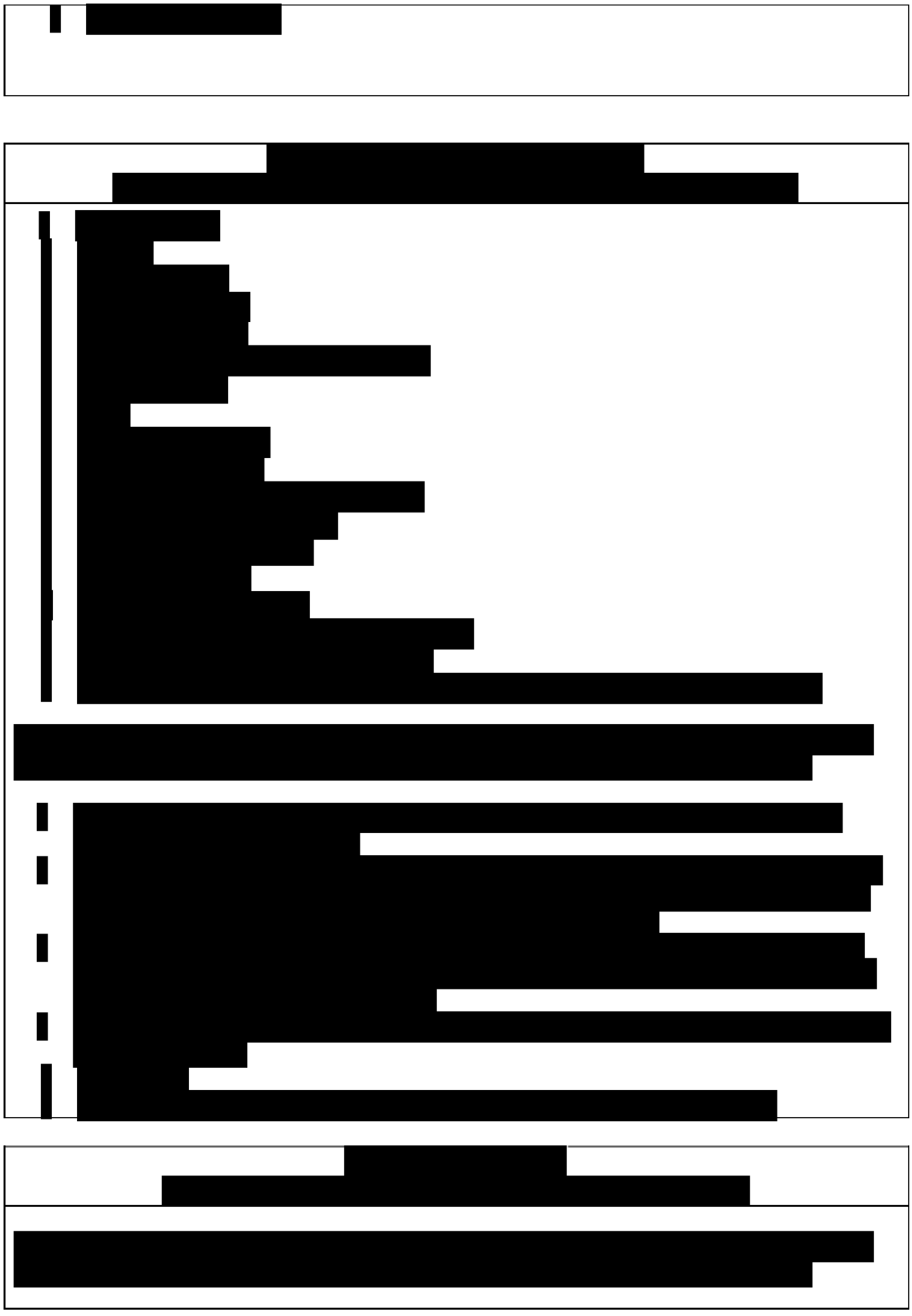
In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. The study drugs could cause side effects we do not know about yet. We will carefully watch everyone in the study for side effects.

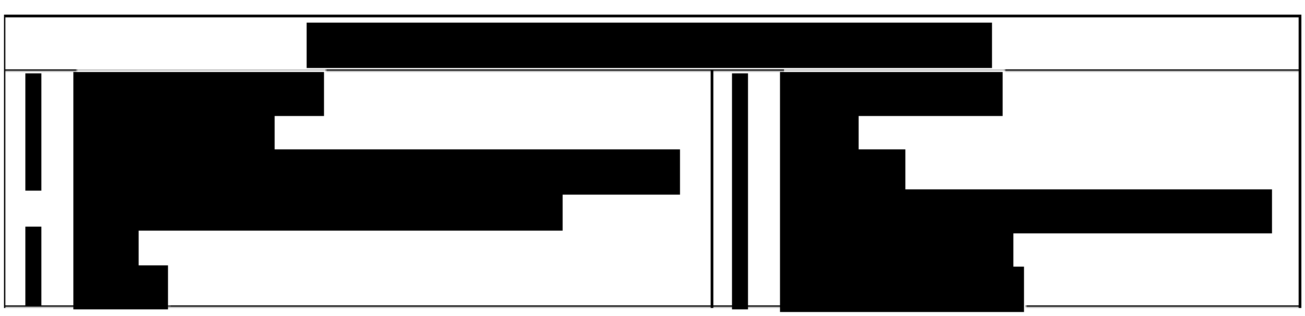
If you join this study, we would tell you if we discover new side effects that could affect you.

Side effects may be mild or very serious. We may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drugs. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

Please talk to us (your study doctor and medical staff) about any side effects you have while you are in the study.
Risks and side effects related to the study drugs are shown below. These are the side effects of the *individual* drugs. Other side effects could occur when we use these drugs *together*.

[redacted]





NT-I7 in combination with or following other anti-cancer treatments could cause an exacerbation of any side effect currently known to be caused by the other treatment, or the combination may result in side effects never previously associated with either treatment.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks:

[redacted]

Genetic testing risks:

The genetic tests used in this study will test your tumor and blood for genetic changes to explain the differences between tumor cells and normal cells and why certain tumor cells respond to treatment. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

The genetic testing is for research only. Results will not be returned to you or put in your regular medical records.

Biopsy risks:

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

Non-physical risks:

If you join this study, you also may have the following discomforts:

- May lose time at work or home and spend more time in the hospital or doctor's office
- Be asked sensitive or private questions about things you normally do not discuss
- May not be able to take part in future studies

What are the benefits?

Taking part in this study may or may not make your health better. We do not know if the study treatment will be more useful against cancer than the standard treatment. What we learn from this study may help other patients in the future.

You have other choices besides this study

If you decide not to take part in this study, you have other choices. For example:

- You may choose to receive the standard treatment for your cancer, including surgery, chemotherapy, radiation therapy, or targeted therapies (such as BRAF or MEK inhibitors for BRAF-mutant melanoma).
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for your cancer.
- You may choose to receive comfort care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to us about your choices before you decide if you want to be in this study.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, there are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor and all collaborating partners, including contract research organizations, who are supporting the study.
- The Institutional Review Board (IRB). An IRB is a group of people who review the research with the goal of protecting the people who take part in the study.
- Office for Human Research Protections (OHRP), Food and Drug Administration (FDA), and other government agencies involved in keeping people in research safe.
- The Immune Oncology Network (ION) and other people who work at the Fred Hutchinson Cancer Center.

Your privacy is very important to us and the researchers will make every effort to protect it. However, we cannot guarantee total privacy. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

We have to report the following information:

[Note to Local Investigators: Include any public health or legal reporting requirements. Bulleted examples should include all appropriate cases (reportable communicable disease, risk of harm to self or others, etc.).]

- *[Item 1]*

[Note to Local Investigators: It is recommended that HIPAA regulations be addressed by the local institution. The regulations may or may not be included in the informed consent form depending on local institutional policy.]

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect your

genetic information.

GINA restricts access to your genetic information so that it cannot be used for health insurance coverage decisions. GINA won't allow health insurance companies or group health plans to:

- Ask for your genetic information you have provided in research studies; or
- Use your genetic information when making decisions regarding your eligibility or premiums.

GINA *does not* help or protect you against genetic discrimination by companies that sell life, disability, or long-term care insurance.

What are the costs of taking part in this study?

The study drugs atezolizumab and NT-I7 will be supplied at no charge while you take part in this study. It is possible that the study drugs may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of your normal cancer care while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

(Note to Local Investigators: Insert a description of any compensation for participation or reimbursement for expenses.)

What happens if I am injured or hurt because I took part in this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact *[name(s)]* at _____ *[telephone number].* NeoImmuneTech, the study sponsor, will offer to pay for medical treatment for study-related injury, but only to the extent that such expenses are not attributable to (i) Fred Hutch Cancer Research Center, participating ION Member Institutions, or other accredited medical care providers' negligence or willful misconduct or (ii) the natural progression of an underlying or pre-existing condition or events, unless exacerbated by participating in the study. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

What are my rights in this study?

- You do not have to join this study. You are free to say "yes" or "no".
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change

your mind about being in this study. If we learn these kinds of information, we would tell you.

- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.

Who can answer my questions about this study?

If you have questions or concerns about this study, you could talk to your study doctor or medical staff anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	[000-000-0000] (Dr. *[full name of PI]*) [000-000-0000] (*[name and title of research staff contact]*)
If you get sick or hurt in this study	[000-000-0000] (Dr. *[surname of PI]*)
Your rights as a research participant	[000-000-0000] (*[IRB Contact Name*, *Title*, *Institution]*) *[Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*
Your bills and health insurance coverage	[000-000-0000]

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications, including over-the-counter medications and supplements, you are taking
    - all new medications that you plan to take while on the study
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study or within 5 months after the last dose of study treatment. **For men:** Do not father a baby or donate sperm while taking part in this study or within 5 months after the last dose of study treatment. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months after the last dose of study treatment.

Where can I get more information?

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.

Participant's Statement & Signature

The study described above has been explained to me. I agree to participate in the main study. I have had a chance to ask questions. I have been told that if I have future questions about the research I can ask one of the contacts listed above. By signing this form, I do not give up any rights that I have as a research participant.

If you have read this consent form or had it explained to you and you understand it, please sign your name below.

Participant's name (print)	**Participant's signature**	**Date** (dd-MMM-yyyy)

For participants unable to read or write, substitute the signature block below:

Participant's name (printed by study staff below)	**Participant's mark** (right thumb unless otherwise indicated)	**Date** (dd-MMM-yyyy)
Witness's name (print; if a study staff member, then must be a different staff member than the person who conducted the consent discussion)	**Witness's signature**	**Date** (dd-MMM-yyyy)

Researcher's Statement & Signature

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Study staff conducting consent discussion (print)	**Signature of study staff conducting consent discussion**	**Date** (dd-MMM-yyyy)