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Fred Hutchinson Cancer Center
University of Washington School of Medicine

**Consent to take part in a research study:**

# Phase 1b study of ST-067 (decoy-resistant IL-18) with Teclistamab in multiple myeloma

RG1123948

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UWMC Paging Operator
Please ask the operator to page the hematology/oncology fellow on call

## Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to evaluate the safety and determine the optimal dose of ST-067 in combination with Teclistamab in multiple myeloma (MM).

People who agree to join the study will be asked to attend up to 40 extra visits over 20 months; however, for people where the study drug works, this may be as few as 6 extra visits. This would be in addition to visits for the Teclistamab which your doctor has prescribed. The study involves physical examinations, blood draws, bone marrow biopsies/aspirates, and study drug infusions.

We do not know if ST-067 in combination with Teclistamab would help treat multiple myeloma, and it could even make your condition/disease worse. ST-067 has not yet been studied in multiple myeloma. ST-067 could cause side effects such as allergic reactions and cytokine release syndrome, as described below in this form.

You do not have to join this study. You can choose to receive standard methods to treat multiple myeloma instead of participating in this study. 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 other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

## We invite you to join this research study.

We invite you to join this research study because you have multiple myeloma. Up to 20 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say "yes" or "no", or to 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.

## Why are we doing this study?

We are doing this study to examine whether ST-067 in combination with Teclistamab is a safe and tolerable treatment for patients with multiple myeloma. We want to know the optimal dose of ST-067.

We are studying ST-067 in combination with Teclistamab. ST-067 is an investigational study drug, which means that it is not approved by the FDA for use in human beings. It can only be used for testing in research studies. ST-067 is a modified variant of human interleukin-18 (IL 18). Your body already makes natural human IL-18 which has limited effect on cancer cells. The study drug IL-18 has been modified to tell your immune system to fight cancer cells. Teclistamab is currently FDA approved to treat heavily pretreated relapsed and refractory multiple myeloma.

From this point on, the term "study drug" refers to ST-067 only, and "study treatment" refers to ST-067 in combination with Teclistamab.

In this study, we want to learn:

- what effects, good or bad, ST-067 has on people with multiple myeloma
- how much ST-067 can be given safely.

People who join at the beginning of the study will receive very low amounts of ST-067. People who join later will receive larger amounts, until effects (good or bad) appear. We will watch carefully for any side effects.

## What research tests, procedures, and treatments are done in this study?

If you join this study, we would do these tests and procedures:

- **Medical history.** You will be asked questions about your medical history. This includes ongoing medical conditions you have and drugs you are taking.
- **Physical examination.** Physical exams will assess your overall health status and include measuring your vital signs. This includes temperature, heart rate, breathing rate, and blood pressure. Your weight and your height will also be recorded. You will also be asked how easily you perform daily activities.
- **Routine laboratory tests.** Blood samples will be taken for routine tests. Blood will be taken at visits which require blood draws, and your blood will be tested for levels of certain components to see if it is safe for you to receive treatment.
    - Research Laboratory tests: A maximum of 9 teaspoons of blood will be taken at certain clinic visits for other research testing. The results will not be reported in your medical record.
- **Pregnancy test.** If you are a female who could become pregnant, you will have a pregnancy test. A blood or urine sample will be taken for this test.
- **Bone marrow aspirate and biopsy.** Bone marrow aspiration and biopsy may be done to see if your cancer has spread to the bone marrow. For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle inserted into a bone in your body. For biopsy, a small piece of bone is removed. These tests are done under local anesthesia.

After you have finished taking the study treatment, you would enter the **follow-up** part of the study. We would follow your medical chart for 20 months.

We will also conduct genetic testing on your tissue. Your tissue contains DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests.

## How long would you stay in this study?

If you join this study, you would stay in this study for about 20 months.

You would first receive ST-067 every week for up to 2 months, with Teclistamab (which your treating doctor will prescribe) beginning in the second month. After that, you will receive ST-067 every 2 weeks for as long as Teclistamab is prescribed by your treating doctor. For patients where the ST-067 is working, we can give the ST-067 on the same days you are here for your Teclistamab. After that, we would follow your medical record for 5 years.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.

- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

**Long-term follow-up** means keeping track of someone's medical condition for a long time. If you join this study, we would follow your medical record every 3 months for 5 years to see how you are doing. 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 ST-067.

You do not have to be in long-term follow-up. You could say "yes" or "no". Either way, you could still join this study. If you drop out of the study, you would be asked if we could check your medical record every 3 months for up to 5 years.

If you choose not to join long-term follow-up, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

## Study Calendar

| **Procedures** | Screening | Cycle 1 | | | | Cycle 2 | | | | Cycles 3 and onward | | | | End of Treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Day* | *-28* | *1* | *8* | *15* | *22* | *1* | *8* | *15* | *22* | *1* | *8* | *15* | *22* | |
| Informed Consent | X | | | | | | | | | | | | | |
| Medical History | X | X | X | X | X | | X | X | X | X | | X | | X |
| Physical Exam | X | X | X | X | X | | X | X | X | X | | X | | X |
| Bone Marrow Biopsy | | | | | | | | | | X | | | | |
| Blood Draws | X | X | X | X | X | X | X | X | X | X | | X | | X |
| Pregnancy Test (if applicable) | X | | | | | | | | | | | | | |
| Teclistamab Administration | | *There is no teclistamab during the first month of the study.* | | | | X | *Teclistamab will be ordered by your doctor, including at least 1 week in the hospital for the initial doses.** | | | | | | | |
| ST-067 Administration | | | X | X | X | | | X | | X | | X | | |
| Hospitalization | | X | | | | Typically 1-2 weeks. † | | | | | | | | |

* Doses of teclistamab will be scheduled at least 48 hours from any dose of ST-067 (the study drug) at first. However, if the myeloma numbers come down at least 50% (a "partial response" or better), ST-067 and teclistamab can be dosed the same day beginning in Cycle 3.

† Teclistamab (which your doctor will order) will require hospitalization for 1-2 weeks to get started even without this study. We will give one dose of ST-067 (the study drug) during this time while you are hospitalized for teclistamab.

## What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. ST-067 could cause side effects we do not know about yet. We 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.

This form lists side effects of *individual* drugs. Other side effects could occur when we use these drugs *together*.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop taking ST-067 and Teclistamab. In some cases, side effects can last a long time or never go away. There also is a risk of death.

**ST-067 Risks**

ST-067 has been given to 53 study participants in other research studies.

All risks of ST-067 are not known at this time. At least 15 patients who have received ST-067 experienced the following side effects: cytokine release syndrome, reaction at the site of injection with or without itching, nausea, fatigue, fever, chills, diarrhea, and vomiting. For most patients these side effects were manageable, and resolved with treatment if it was needed. Two study subjects experienced moderate/severe reactions at the injection site; the first study subject developed an ulcer at the injection site, and the second study subject experienced moderate to severe redness, swelling, pain, and scabbing where ST-067 was given. These patients received treatment for this side effect. Some changes in laboratory tests were observed reflecting minor changes in red and white blood cells, and liver function tests.

Cytokine release syndrome (CRS) is an acute inflammation that occurs when the body is trying to fight various diseases and treatments and it has been observed with therapies that act on the body's immune system. It can vary widely in severity, from a fever, overall feeling of discomfort, feeling very tired, to life-threatening low blood pressure, and low oxygen in your blood requiring support in an intensive care setting. Study subjects treated with ST-067 indicate that CRS may occur following dosing and has the potential to be moderately severe. Before each of your ST-067 doses, your study doctor, who is experienced in dealing with this syndrome, will prescribe medications which are known to minimize or prevent CRS. You will continue these medications after the treatment as your doctor feels necessary.

If your tumor has spread to your lungs, you may be at an increased risk of worsening of your respiratory function after administration of the study drugs. It is possible that you could experience some more intensive adverse events which could affect your breathing. Your doctor will discuss this possibility with you before making a decision on whether to enter the study.

Two study subjects with tumors in their lungs have died due to serious respiratory adverse events. One study subject experienced respiratory distress (difficulty breathing) after her fourth injection of ST-067. She declined active treatment for this complication and died the following day. This subject was known to have extensive tumor involvement in her lungs and required oxygen therapy for poor lung function at the time she was enrolled to the study. There is a small possibility that ST-067 played a role in the onset of respiratory distress.

A second subject with lung cancer and history of blood clots in the lung and shortness of breath experienced severe hypoxia, a condition in which the body's tissues don't have enough oxygen. This occurred after the patient received her fourth injection of ST-067 and her second dose of pembrolizumab. The subject subsequently died of severe hypoxia and the study doctor believed her death to be related to the study drug she received.

One additional study subject with lung tumors and a history of shortness of breath experienced CRS that required treatment with oxygen. She then developed serious pleural effusions, a condition that occurs when fluid builds up in the area between the lungs and the chest wall. This subject was hospitalized, treated with high-dose steroids and diuretics and made a full recovery. However, the study doctor felt that these adverse events were related to ST-067 treatment.

You will receive oral acetaminophen 650 mg every 4 to 6 hours as needed for the first 24 hours post-dose, IV or oral diphenhydramine 30-60 minutes prior to dosing with ST-067. You may also be given intravenous fluids prior to dosing with ST-067.

In short-term use of acetaminophen, possible side effects include liver injury especially if combined with alcohol, and skin reactions. Serious allergic reactions are rare.

In short-term use of antihistamines, such as diphenhydramine, possible side effects include dry mouth, nose, and throat, drowsiness or dizziness, nausea, vomiting, loss of appetite, constipation, and problems with urination. Serious allergic reactions are rare.

If you were to get COVID-19 while taking ST-067, you could have a worse case of COVID-19. It is important that you take all precautions as provided by the CDC to not be exposed to COVID-19 during the study.

**Allergic Reaction Risks**

Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some signs that you may be having an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Sudden change in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat or eyes
- Fast pulse
- Sweating

You should get medical help immediately and contact the study doctor or staff if you have any of these or any other side effects during the study.

### Other possible side effects

Blood Draws
Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or get an infection. Infection rarely happens. There may be redness and irritation at the place where the needle enters your vein.

### Reproductive risks

Taking the study treatment may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you could not join this study if you are pregnant, if you are planning to become pregnant, or if you are breast-feeding.

If you join this study, you would have to use an effective method of birth control from the time this form is signed until at least 5 months after the last dose of the study drug. You should discuss this with the study doctor or a member of the study staff.

If you became pregnant after joining this study, you would have to notify the study doctor immediately. Participation in this study would end, and you would receive counseling and follow-up throughout the pregnancy and for about 6 months after the child is born.

The effects of the study treatment on a pregnancy you could cause are also unknown. If you could get someone pregnant, you must also agree to use one or more forms of effective and acceptable birth control from the time this form is signed until at least 5 months after the last dose of the study treatment. You should discuss this with the study doctor or a member of the study staff.

## What are the benefits?

We do not know if the study treatment would help treat multiple myeloma. We hope the information we learn will help people with multiple myeloma in the future.

Although the study will not benefit you directly, we hope the information we learn will help people with multiple myeloma in the future.

We do not know if this study would help you. The use of the study drug is still investigational, and we are testing it to find the highest safe dose. We hope the information from this study will help us test the study drug further in the future.

## You have other choices besides this study.

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment, including other FDA-approved treatments for multiple myeloma that do not require a clinical trial. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Other choices include: Standard Treatment, Another Research Study, No Treatment, Comfort Care.

Enrollment in this study may exclude you from other research studies.

## Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Simcha IL 18, Inc. (the funder of the study and provider of ST-067) and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and the University of Washington.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be disclosed if required by law. For example, we are required to report certain diseases and infections to public health authorities. We are also required to report suspected abuse or neglect of children and vulnerable adults. Workplace safety rules may require health workers to contact you about lab tests. Or a court may order that study information be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

## How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

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

## Would we pay you if you join this study?

There is no payment for being in this study.

The study will reimburse you for out-of-pocket costs to you at the IRS Business Rate. This would include:

- Transportation costs to the clinic or hospital for study tests and visits, up to $200 per visit.
- Costs of hotel stays necessary while you are undergoing study tests and visits, up to $135 per visit, if you are traveling greater than 50 miles one-way.

IMPORTANT: You will need to give us receipts that clearly show your costs.

## Would you have extra costs if you join this study?

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

You would **not** be billed for:

- The study drug (ST-067)

If ST-067 is approved as a treatment while this study is still going on, you or your insurance company might have to pay for ST-067 in order to complete this study.

## What if you get sick or hurt after you join 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 the study doctor listed on page 1 of this consent form. They will treat you or refer you for treatment. You or your insurance company may be billed for the treatment.

Simcha IL-18, Inc., the company providing the study drug (ST-067), will pay for reasonable medical treatment if the injury was directly caused by a defect in the manufacture or shipment of the study drug. Simcha IL-18, Inc. will not be responsible for payment of medical costs for injuries resulting from study team negligence, misconduct, or misuse of the study drug.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

## What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study. In particular, the research team will use these tests to help better understand how ST-067 and teclistamab work together to help the immune system fight myeloma.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, we do not expect any test results that would affect your care, so we do not plan to return results to you.

## Will my information and/or tissue samples ever be use for future research?

After we do tests on tissue in this study, some tissue may be left over. We invite you to donate this leftover tissue for future research. This may include genetic research. We also would like to use your information for future research.

If you join this study, you would not have to donate tissue or information for future research. You would be free to say “yes” or “no.” Regular medical care would not change if you say “no.”

If you say “no,” your tissue and information (even if made anonymous) will not be used in future research.

If you donate tissue and information, it would be stored in a secure location. If we want to use your tissue for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated tissue and information would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with tissue and information might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the tissue.

If you donate tissue and information for research, you could withdraw the donation at any time by calling Dr. Banerjee at 206-606-1453. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated tissue to you or your doctor, but we might be able to destroy the donated tissue. We could not destroy tissue if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

## Your rights

- 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.
- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping the study treatment. You and the doctor could talk about the follow-up care and testing that would help the most.
- Before you leave the study, the doctor might ask you to continue in the long-term follow-up part of the study.

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.

## Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.

- Tell us about side effects.

## For more information

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

| If you have questions about: | Call: |
|---|---|
| This study (including complaints and requests for information) | 206-606-1453 (Dr. Rahul Banerjee) |
| If you get sick or hurt in this study | 206-606-1453 (Dr. Rahul Banerjee) |
| Your rights as a research participant | 206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center)<br>206-543-0098 (Human Subjects Division, University of Washington) |
| Your bills and health insurance coverage | (206) 606-1377 (Patient Financial Services, Fred Hutchinson Cancer Center) |

# Emergency number (24 hours): (206) 598-6190

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Do you agree to have blood collected at screening, during treatment, and at the end of treatment visit for research testing?

(circle one)

**YES** **NO**

Do you agree to allow the study team to check your medical record after you have completed the end of treatment visit, every 3 months for up to 5 years?

(circle one)

**YES** **NO**

## Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant:

| Printed Name | Signature | Date |
|---|---|---|

If you were a witness for a participant who was not able to read this written consent form, sign below to indicate (1) you were present at the consent discussion in person, (2) you witnessed the verbal presentation of the written consent form, and (3) the participant had the opportunity to ask questions and agreed to take part in the study.

Impartial Witness:

| Printed Name | Signature | Date |
|---|---|---|

## Researcher's statement

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.

Person obtaining consent signature:

| Printed Name | Signature | Date |
|---|---|---|

Protocol: RG1123948
Current consent version date: 09/17/2024
Previous consent version date: 02/19/2024
Copies to: Researcher's file
Subject
Subject's medical record