Informed Consent Form

Protocol Title: Individualized Treatment for Relapsed/Refractory Multiple Myeloma Based on High Throughput Chemosensitivity and Genomics Data

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University of Washington
Fred Hutchinson Cancer Center

Consent to take part in a research study:

Individualized Treatment for Relapsed/Refractory Multiple Myeloma Based on High Throughput Chemosensitivity and Genomics Data

Principal Investigator: Danai Dima, MD. University of Washington; Fred Hutchinson Cancer Center. 206-606-6721

Emergency number (24 hours): 206-598-6190 page operator

Ask paging operator to page Dr. Dima or the hematology fellow on-call

If you are serving as a legally authorized representative, or a guardian, the terms "participant", "you", and "your" refer to the person for whom you are providing consent or parental permission.

We invite you to join this research study.

We invite you to join this research study because you have relapsed or refractory multiple myeloma. Up to 40 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?

Although all the patients on this study have the diagnosis of multiple myeloma, we know that every single patient's multiple myeloma is unique, and has its own features that determine how well it will respond to treatment. For many years, we have been giving all patients with multiple myeloma the same drug combinations for treatment. But now, for all cancers, we are beginning to recognize that it may be better to base treatment decisions on individual features of the cancer. This is also true for multiple myeloma.

This study will evaluate our ability to perform personalized drug testing and to choose a drug or drug combination therapy depending on the results. We will test multiple myeloma cells obtained from each patient's blood in a laboratory test. The test is called a high throughput screen (HTS) because it tests many different drugs that kill multiple myeloma cells in individual chambers at the same time. The current test we are doing checks how well each of 49 drugs or drug combinations kills multiple myeloma cells. We will also look at the genetic information contained with your multiple myeloma cells through two additional laboratory tests. We hope that matching a drug or drug combination to a patient using these techniques will improve our ability to help patients by choosing drugs that work well for their disease. The HTS is an investigational device and has not been approved by the US Food and Drug Administration.

If a compatible drug or drug combination is selected by your doctor for treatment, you will be given more information about that drug or combination. This additional information will describe how the drug or drugs work and the possible side effects.

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

We will take approximately 5 teaspoons of bone marrow aspirate and/or a core biopsy and test it in the laboratory against 49 drugs or drug combinations to see if your multiple myeloma cells are killed by any of the drugs or drug combinations in the test panel.
A bone marrow aspiration means that a needle will go through the skin and puncture the bone in order to remove a small amount of fluid and cells from inside the bone, called bone marrow. A bone marrow core biopsy removes a small amount of solid bone marrow tissue in addition to the liquid portion of the bone marrow. It is not necessary to immediately puncture the bone again in order to obtain marrow suitable for use in the research test. However, if it is later determined that this initial marrow sample does not contain enough cells for the test, we may have to perform another bone marrow aspiration with your consent. In addition, we will use the same blood for other laboratory tests which provide information on whether certain genes within your multiple myeloma cells are normal or abnormal. If you have a high amount of plasma cells circulating in your bloodstream, we may also take about 5 to 6 teaspoons of blood to ensure there are enough cells for the laboratory test.

If your multiple myeloma is present in a location other than the bone marrow, some of the fluid or a biopsy from that lesion (for example, a biopsy of cells from bone or soft tissue, sample of body fluid, blood) will be collected for this study as well. The bone marrow sample will be obtained at the same time you are having a bone marrow done for clinical purposes.

If we are unable to obtain enough cells to test, then you will not be able to participate in the rest of the study.

How long would you stay in this study?

The part of the study where your bone marrow and/or blood is tested will last approximately 2 weeks. Your results will be provided to you and your treating physician, and any treatment decisions will be made between you and your treating physician.

Your course(s) of treatment and overall condition as described in your medical record will be followed until up to 2 years after your treatment was started.

The study doctor or your doctor 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.
- You are having unacceptable side effects.

- Your disease is getting worse.

If you are thinking about dropping out of this study, please tell the study doctor. The doctor can tell you about the effects of stopping treatment. You and the doctor can talk about what follow-up care and testing would help you the most.

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.

We would like to do long-term follow-up.

Long-term follow-up means keeping track of your medical condition. We would do this by talking with your doctor or calling you on the telephone every three months for the first two years from the start of your treatment.

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. There may be side effects we do not know about yet. We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, ask the doctor or nurse.

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

Bone marrow aspirations and biopsies may result in discomfort during placement of the needle and during the aspiration or biopsy itself. Discomforts often associated with bone marrow aspiration or biopsy include local pain, bruising and minor bleeding. As with any invasive procedure, there is a very small risk of local infection. We will use strict sterile procedures and expert care during the aspiration of the bone marrow to minimize potential complications.

For most people, needle punctures for blood draws do not cause any serious problems. However, drawing blood from your arm may cause pain. You might get a bruise. Some people feel lightheaded after a blood draw. Very rarely, you could get an infection where the needle entered the vein. If you have a central venous catheter, we will use this to draw the blood, which may lessen the discomfort but the small risk of infection remains.

If your multiple myeloma is present in a location other than your bone marrow (lung, bone, soft tissue, etc.), there is a possibility that we may use tissue or fluid leftover from tests done to care for you in order to perform the drug, mutation, and gene expression tests. This will not result in additional needle sticks or discomfort; this will only require material that has already been collected from you as part of your regular care.

The HTS is an investigational device. It is not yet known if it will select the best drug(s) for treating your cancer. The information we gather from this trial may help to answer this question.

Additional Information

We hope to be able to identify a drug or drug combination that will work for your disease as a result of this testing. If a treatment is identified that your physician thinks would be beneficial to you, your physician will have a discussion with you about the drug or drug combination, how the drug(s) work, and what side effects may be possible. In general, many chemotherapy drugs have the side effects of hair loss, nausea, vomiting, mouth sores, lowering of blood counts, and risk of infection or bleeding. Individual drugs may have specific side effects on certain organs. Some of these drug options may only be available in a clinical trial.

What are the benefits?

We do not know if this study will benefit participants. We hope the information we learn from this study will help to better match multiple myeloma patients with drug treatment for their disease. You may benefit if the drug has an anti-cancer effect by lowering the amount of myeloma in your plasma and/or reducing its effects on your normal blood counts, but we do not know if this will happen.

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”.

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.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect therights and welfare of research participants.
- Fred Hutchinson Cancer Center
- University of Washington
- U.S. Office for Human Research Protections,
- U.S. Food and Drug Administration

We will do our best to keep personal information confidential, but we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to 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 you authorize others 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 prevent 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. Should a product and/or patent result from this study, you will not receive any remuneration or compensation.

Would you have extra costs if you join this study?

There are no charges for the drug screening test and the genetic tests that take place in the laboratory. Study procedures and the blood tests used to screen your blood cells against select drugs will be paid out of study funds. If we need to do an additional bone marrow aspiration or blood draw to obtain more cells, this will also be covered by study funds and not billed to you or your insurance company. However, you and/or your insurance company will be responsible for the normal costs of treating your multiple myeloma. This includes, but is not limited to, the cost of the initial diagnostic bone marrow aspiration, follow-up and treatment response bone marrow aspirations, and the cost of whichever drug or drug combination your doctor recommends based on the results of the drug screening test.

Some insurers will not pay for research. Check with your insurer before you join 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 **Dr. Dima at (206) 606-6721.** They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

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.

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.

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.
- Prevent pregnancy.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you could 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) 606-6721 (Dr. Danai Dima, MD) (206) 606-8311 (Kim Quach, Research Manager)
If you get sick or hurt in this study	(206) 606-6721 (Dr. Dima)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	(206) 606-1113 (Patient Financial Services, FHCC)

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

Signatures

If you have read this form (or had it read to you), asked any questions, and agree to participate, please sign:

Participant / Printed Name, Signature, and Date

Legally Authorized Representative: If you have read this form (or had it read to you), asked any questions, and consent on behalf of the participant, please sign:

Legally authorized representative / Printed Name, Signature, and Date

Relation to the participant

If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

Witness or Interpreter / Printed Name, Signature, and 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, and Date