THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Personalized Vaccine for the Immune Prevention of Multiple Myeloma 2018-0345

Study Chair: Elisabet E. Manasanch

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if it is possible to give a personalized vaccine, both with and without lenalidomide, for intermediate and high-risk smoldering multiple myeloma (SMM). The safety of this vaccine is also being studied.

This is an investigational study. The vaccine is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can describe how the vaccine is designed to work.

Lenalidomide is FDA approved and commercially available for the treatment of different types of lymphoma and multiple myeloma. The combination of vaccine and lenalidomide is not FDA approved for the treatment of multiple myeloma.

The study vaccine and/or study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

When the vaccine is ready (after up to 24 weeks), you may receive up to 8 vaccines over the course of about 6 months. The vaccine will be provided at no cost to you during the study. You and/or your insurance provider will be responsible for the cost of lenalidomide and imiquimod cream (a drug used together with the vaccine to help the immune system work).

You may choose not to take part in this study. Instead of taking part in this study, you may choose to be on active surveillance (routine monitoring). You may choose to receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Procedures

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests, to check the status of the disease, to learn more about your immune system, to create the vaccine, and to test for hepatitis B and C. This sample will be stored and used to test for the immune response to the vaccine. If you can become pregnant, this sample will also be used for a pregnancy test. To take part in this study, you must not be pregnant.
- Urine will be collected over a 24-hour period to check the status of the disease. You will be provided with a container and instructions for urine collection.
- You will have a bone marrow aspirate and biopsy to check the status of the disease. To collect a bone marrow aspirate/biopsy, an area of the hip or other site is numbed with anesthetic and a small amount of bone marrow and bone is withdrawn through a large needle.
- If the doctor thinks it is needed, you will have an MRI or PET-CT scan to check the status of the disease.
- You may have a series of x-rays (called a skeletal survey) to check the status of the disease, if you do not have a PET-CT scan performed at screening.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 30 patients will be enrolled in this study, 10 in Stage I and 20 in Stage II. All will take part at MD Anderson.

Making the Vaccine

The blood and bone marrow samples collected at screening will be used to manufacture the vaccine. Up to 24 weeks are needed to make this vaccine. You should know that researchers are not always successful in making the vaccine. They cannot and do not guarantee that you will receive a vaccine. If a vaccine cannot be made, you will be taken off study.

If the first dose of vaccine is given more than 22 weeks after your bone marrow is collected at screening, all tests listed under the "Screening Tests" section will need to be repeated.

Study Drug Administration

Each cycle is 28 days (about 1 month). You will receive either a personalized vaccine alone (Stage I) or a personalized vaccine in combination with lenalidomide (Stage II).

Stage I

The vaccines will be given as a series of either 2-3 or 4-6 injections under the skin on Days 1 and 15 of Cycles 1 and 2, and then on Day 1 of Cycles 3-6.

After the first vaccination, you will be observed for 2 hours for side effects. You will be observed for 15 minutes after all other vaccines. After these time periods for each vaccine, imiquimod cream will be applied in a thin layer over each vaccination site.

Stage II

You will receive vaccinations on Days 1 and 15 during Cycles 1 and 2 and then on Day 1 during Cycles 3-6. You will take lenalidomide by mouth on Days 1-21 every 28 days for 6 cycles.

Both Stages

You will be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks. You will no longer be able to receive the vaccine if the disease gets worse or intolerable side effects occur.

Your participation on this study will be complete 1 year after your last vaccination.

Study Visits

On **Day 1 of all cycles**:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, to check the status of disease, and to look at changes that the vaccine is making to your immune system.
- Blood (about 1 tablespoon) and a 24-hour urine sample will be collected to check the status of the disease. If you can become pregnant, one of these samples will be used for a pregnancy test.

On **Day 15 of Cycles 1 and 2** (+/- 3 days):

- You will have a physical exam.

- Blood (about 3 tablespoons) will be drawn for routine tests, to check the status of disease, and to look at changes that the vaccine is making to your immune system.

End-of-Dosing Visit

At the end of Cycle 6, or if at any time the disease gets worse:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests, to check the status of the disease, and to look at changes that the vaccine is making to your immune system. This sample will be stored and used to test for the immune response to the vaccine.
- A 24-hour urine sample will be collected to check the status of the disease.
- You will have a bone marrow aspirate and biopsy to check the status of the disease.
- You will have a skeletal survey, MRI, or PET-CT scan to check the status of the disease.

Follow-up

Every 3 months for 12 months (+/- 30 days):

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests, to check the status of the disease, and to look at changes that the vaccine is making to your immune system. This sample will be stored and used to test for the immune response to the vaccine.
- A 24-hour urine sample will be collected to check the status of the disease.
- If you can become pregnant, part of the above blood or urine sample will be used for a pregnancy test.
- If the doctor thinks it is needed, you will have a bone marrow aspirate and biopsy to check the status of the disease.
- If the doctor thinks it is needed, you will have a skeletal survey, MRI or PET-CT scan to check the status of the disease.

Other Information

It is important to tell your study doctor or nurse about all prescription and non-prescription drugs, herbal preparations, and nutritional supplements that you are taking or planning to take because the effect of the study drug taken with other drugs is not known.

There are certain types of therapy you cannot receive while on study (such as other investigational drugs). Talk with your study doctor about what you cannot take. You cannot receive live vaccines within 30 days before the first dose and while on study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form.

Many side effects go away shortly after the study drug is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving the study drug. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Imiquimod and lenalidomide may cause low blood cell counts (red blood cells, white blood cells and/or platelets):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening symptoms of infection may include fever, pain, redness, and difficulty breathing.

Personalized Vaccine Side Effects

The side effects are not well known. Based on previous studies, personalized vaccines may cause the following side effects:

• fever	• muscle aches	• mild skin reaction at injection site

Imiquimod Risks

Common (occurring in more than 20% of patients)

Imiquimod may commonly cause side effects at the application site such as discharge, swelling, itching, burning, redness, dryness, crusty, hardness, peeling, blisters, pain, thickening, and/or sores.

The drug may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• headache • fatigue • dizziness • fever	• nausea • diarrhea • loss of appetite	• lymph node swelling • joint pain • flu-like symptoms

Imiquimod may cause you to develop another type of cancer (such as squamous cell carcinoma, a type of skin cancer).

Exact frequency unknown but occurring in between 1 and 10% of patients

• chest pain • anxiety • non-cancerous or pre-cancerous skin lesions • pale skin	• skin rash • high blood sugar (possible diabetes) • upset stomach • pain (general/back)	• cough • sore throat • runny rose • application site tingling/bleeding/stinging

Rare but serious (occurring in fewer than 3% of patients)

• irregular/fast heartbeat • heart failure • enlarged heart • tissue swelling • heart attack • stroke • seizure • fainting • shedding and scaling of the skin (possible fatal loss of bodily fluids) • allergic skin reaction • psoriasis	• inflammation of the thyroid gland (possible tenderness in the neck) • inflammation of the colon (possible abdominal pain and/or diarrhea) • inability to urinate • blood vessel inflammation (possible bleeding and/or bruising) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing)	• liver damage • paralysis • swelling of the scrotum • back pain from vertebral disk changes • fluid in the lung (possible difficulty breathing) • decreased supply of blood to a body part (such as the heart or brain) • worsening of existing multiple sclerosis, psoriasis, and/or colon inflammation

Imiquimod may cause you to develop another type of cancer (such as lymphoma, a type of lymph node cancer).

<u>Lenalidomide Side Effects</u>

Common (occurring in more than 20% of patients)

• swelling (arm/leg) • fatigue • fever • dizziness • skin rash/itching	• inflammation of the stomach and/or intestines • diarrhea/constipation • nausea • low blood cell counts (red, platelets, white)	• muscle cramps/spasms • weakness • pain • difficulty breathing • lung inflammation • cough • infection

Occasional (occurring in 3-20% of patients)

• swelling • high blood pressure • low blood pressure (possible dizziness/ fainting) • chest pain (possibly due to heart trouble) • irregular heartbeat • heart attack • heart failure • blood clots in a vein (possible pain, swelling, and/or redness) • chills/shivering • headache • difficulty sleeping • abnormal sensation (such as pins and needles)	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) • sweating • skin redness • dry skin • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • abnormal taste • dry mouth • dehydration • vomiting • weight loss • loss of appetite • abdominal pain	• difficult and/or painful urination • numbness • nerve damage (possible loss of motor or sensory function) • abnormal liver tests (possible liver damage) • kidney failure • kidney stones • runny nose • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • build-up of fluid around the lungs • flu • nosebleed • sore throat • pain and/or inflammation at the tumor site

Lenalidomide may occasionally cause you to develop another type of cancer (such as leukemia [blood cancer], lymphoma [cancer of the lymph nodes], skin cancer, lung cancer, prostate cancer, or other solid tumors).

Rare but serious (occurring in fewer than 3% of patients)

• tissue swelling • stroke • bleeding around the brain • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • skin rash (possible fever/lymph node swelling/inflammation of internal organs/abnormal blood cell counts) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating)	• low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • inflammation of the bile tract (possible blockage) • abnormal blood test (possible heart problems) • bacteria in the blood • liver damage • reactivation of hepatitis B infection (possible liver damage) and/or herpes zoster • abnormal liver tests (possible yellowing of the skin and/or eyes) • low oxygen level in the blood (possible lightheadedness)	• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipients body) • organ transplant rejection

Lenalidomide may rarely cause problems with collecting your own stem cells which may cause you to be unable to receive certain types of stem cell transplants.

It is not known how often the following side effects may occur:

• fast/slow heartbeat • heart failure or other severe heart problems • shock (possibly caused by heart damage) • decreased supply of blood to a body part (such as the heart) • enlarged heart • bleeding around the brain • abnormal blood clotting • difficulty forming or speaking words • migraine • temporary stroke symptoms • confusion	• inflammation of the colon (possible abdominal pain and/or diarrhea) • digestive system bleeding • inflammation of the stomach and/or intestines • difficulty swallowing • chronic heartburn and indigestion • intestinal blockage • hole in the intestines (possibly leaking contents into the abdomen)	• blockage of the bile tract (possible body yellowing and/or abdominal pain) • difficulty walking • falling • painful joint inflammation • pelvic pain • broken bones (such as leg, pelvis, hip, rib, collapsed spine bones) • build-up of bone-like crystals (calcium phosphate) in different parts of the body (possible pain and/or

• depression • loss of alertness • skin condition with fever and skin lesions • skin bump • immune response that causes an overactive thyroid gland (possible fast heartbeat, sweating, weight loss, nervousness, and/or eye bulging) • low blood sugar • inflammation of the pancreas (possible abdominal pain)	• decreased blood flow to part of the bowel or other body part (possibly causing tissue death) • bleeding or blood in stool • pockets of pus in or near the anus • death of spleen tissue • gallbladder inflammation (possible abdominal pain) • tarry stool • blood in the urine • destruction of red blood cells (possible anemia) • bleeding after procedures • liver failure	decreased organ function) • build-up of bodily waste products in the blood (possible kidney damage) • kidney damage • abnormal kidney tests (possible kidney damage) • abnormal growth in the kidneys • difficulty breathing, possibly due to lung damage or fluid in the lung • wheezing • worsening of disease

Study Drug Combination Side Effects

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Bone marrow biopsies/aspirates may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A PET scan may cause you to feel "closed in" while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort, or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study and 60 days after the last dose of study therapy, if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, you must use 2 methods of reliable, highly-effective birth control during the study. Acceptable combination methods of effective birth control include:
Intrauterine device (IUD) and a barrier method (such as a condom) with spermicide
Hormonal birth control method and a barrier method with spermicide

If lenalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby. Because of this risk, all patients taking lenalidomide must read the following statements that apply to them according to gender and menopausal status.

FOR FEMALES WHO ARE ABLE TO BECOME PREGNANT*
*(Sexually mature female who: 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been naturally postmenopausal for at least 24 consecutive months)
Please read thoroughly and initial each space provided if you understand each statement

_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that my unborn baby may have birth defects and can even die, if I am pregnant or become pregnant while I am taking lenalidomide.

_____: I understand that I must NOT take lenalidomide if I am pregnant, breast-feeding a baby or able to get pregnant and not using 2 reliable methods of birth control.

_____: If I am having sexual relations with a man, my uterus and/or both ovaries have not been removed, I have had at least one menstrual period in the past 24 months and/or my menses stopped due to treatment of my disease, I understand that I am able to become pregnant. I must use one highly effective method of birth control plus one additional effective method of birth control (contraception) at the SAME TIME.

Highly Effective Methods	Additional Effective Methods
Intrauterine device (IUD)	Latex condom
Hormonal (birth control pills, injections, implants)	Diaphragm
Tubal ligation	Cervical Cap
Partner's vasectomy	

_____: These birth control methods must be used during the following time periods related to this study: 1) for at least 28 days before starting lenalidomide therapy; 2) while participating in the study; during interruptions in therapy and 3) for at least 28 days after lenalidomide has been stopped. I must use these methods unless I completely abstain from heterosexual sexual contact. If a hormone (birth control pill, injection, patch, or implant) or IUD method is not medically possible for me, I may use another highly effective method or two barrier methods AT THE SAME TIME.

_____: I know I must have a pregnancy test done by my doctor within 10 – 14 days and 24 hours prior to starting lenalidomide therapy, even if I have not had my menses due to treatment of my disease or had as little as one menstrual period in the past 24 months. If I have regular or no menstrual cycles, I will then have pregnancy tests every week for the first 28 days, then every 28 days while I am taking lenalidomide, again when I have been taken off of lenalidomide therapy and then 28 days after I have stopped taking lenalidomide. If I have irregular menstrual cycles, I will have pregnancy tests every week for the first 28 days, then every 14 days while I am taking lenalidomide, again when I have been taken off of lenalidomide therapy, and then 14 days and 28 days after I have stopped taking lenalidomide.

_____: I know I must immediately stop taking lenalidomide and inform my doctor, if I become pregnant while taking the drug, if I miss my menstrual period or have unusual menstrual bleeding, if I stop using 2 reliable forms of birth control, or if I think for any reason that I may be pregnant. I must talk to my doctor before changing any birth control methods.

_____: I am not now pregnant, nor will I try to become pregnant for at least 28 days after I have completely finished taking lenalidomide.
_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children.
_____: I agree any unused drug supply will be returned to the research site at each visit.
_____: I know that I cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.
Study patients who become pregnant will be monitored throughout the pregnancy and will continue to be monitored for 30 days after delivery (premature delivery, aborted fetus, full-term pregnancy, or no longer pregnant).

FOR ALL MALES
Please read thoroughly and initial each space provided if you understand each statement:
_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.
_____: I have been told by my doctor that I must NEVER have unprotected sexual contact with a female who can become pregnant. Because it is not known whether lenalidomide is present in semen, my doctor has explained that I must completely abstain from sexual contact with females who are pregnant or able to become pregnant, or I must use a latex condom every time I engage in any sexual contact with females who are pregnant or may become pregnant. I must do this while I am taking lenalidomide and for 28 days after I stop taking lenalidomide, even if I have had a successful vasectomy.
_____: I know I must inform my doctor if I have unprotected sexual contact with a female who is pregnant or can become pregnant or if I think, for ANY REASON, that my sexual partner may be pregnant. Female partners of male patients taking lenalidomide should be advised to call their own physician immediately if they get pregnant.
_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are able to have children.
_____: I agree any unused drug supply will be returned to the research site at each visit.
_____: I know that I cannot donate blood, sperm, or semen while taking lenalidomide and for 28 days after stopping lenalidomide.

FOR FEMALES WHO ARE NOT ABLE TO BECOME PREGNANT
Please read thoroughly and initial each space provided if you understand each statement.
_____: I understand that birth defects may occur with the use of lenalidomide. I have been warned by my doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.

_____: I certify that I am not now pregnant, nor am I of child bearing potential as I have been in a natural menopause for at least 24 months (been through the change in life without even 1 menstrual period for the past 24 months); or I had my uterus removed (hysterectomy) or had both my ovaries removed (bilateral oophorectomy).
_____: I understand that lenalidomide will be prescribed only for me. I must not share it with ANYONE, even someone that has similar symptoms to mine. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children.
_____: I agree any unused drug supply will be returned to the research site at each visit.
_____: I know that I cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.

ALL PATIENTS
You will be counseled at least every 28 days about not sharing lenalidomide (and other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the “Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies” with each new supply of lenalidomide as a reminder of these safety issues. You must receive counseling and complete phone surveys as required by the Revlimid REMS program.

Pregnant females or females that are able to become pregnant should not handle or administer lenalidomide unless they are wearing gloves.
Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Adelson Medical Research Foundation for this injury. You may also contact the Chair of MD Anderson’s IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary

manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Elisabet E. Manasanch, at 713-792-9420) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. It may be dangerous to suddenly stop study treatment, and the study doctor can discuss ways to safely withdraw. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   The study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Adelson Medical Research Foundation, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

   Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

8. MD Anderson may benefit from your participation and/or what is learned in this

study.

9. This study is sponsored and/or supported by: Adelson Medical Research Foundation.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

Genetic Research

Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or

response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Conflict of Interest

Dr. Elisabet Manasanch (Study Chair) has received compensation from Adaptive Biotechnologies as a Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Adelson Medical Research Foundation, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Adaptive Biotechnologies, Avera Institute for Human Genetics and Bio-synthesis Inc.
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's

contracts require sponsors/supporters to protect this information and limit how they may use it.

Bone marrow biopsy and aspirate will be sent to the Department of Pathology at MD Anderson Cancer Center.

Bone marrow samples and associated de-identified clinical lab data will be sent to Adaptive Biotechnologies (Seattle, WA) for deep sequencing of the VDJ sequence.

DNA and RNA sequencing will be performed to identify neoantigens under the direction of Dr. Neelapu. Bone marrow aspirates will be done at baseline for this purpose and sent to Dr. Neelapu's laboratory. Dr. Neelapu will perform CD138+ cell sorting. Dr. Lizee will perform DNA and RNA extraction. Extracted DNA/RNA and associated de-identified clinical lab data will be sent to the Avera Institute for Human Genetics (University of South Dakota, Sioux Falls, South Dakota) for DNA and RNA sequencing. Peripheral blood will be collected at baseline for germ line DNA analysis.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____

SIGNATURE OF PARTICIPANT DATE

_____

PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

_____ _____

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____

PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____

PERSON OBTAINING CONSENT DATE

_____

PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)