THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

TITLE: Bispecific NK engager AFM13 Combined With NK Cells for Patients With Recurrent or Refractory CD30 Positive Hodgkin or Non-Hodgkin Lymphomas

PROTOCOL NO.: 2018-1092
IRB Protocol #20210964

SPONSOR: Affimed, Inc.

INVESTIGATOR: Yago Luis Nieto, MD PhD
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STUDY-RELATED PHONE NUMBER(S): 713-745-3219
713-792-2121 (24 hours)

Study Chair: Yago Luis Nieto, MD PhD

_____ _____
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.

If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.

This is an informed consent and authorization form for a research study. It includes a summary

STUDY SUMMARY

The goal of this clinical research study is to learn if AFM13-NK cells (a combination of cord blood natural killer cells combined with the antibody AFM13), followed by 3 infusions of AFM13 alone, can help control certain types of lymphoma. The safety of this combination will also be studied.

This is an investigational study. AFM13 and NK cells have each been used in past research. The use of AFM13-NK cells followed by AFM13 infusions is not FDA approved or commercially available. At this time, it is being used in research only. The study doctor can explain how these treatments are designed to work.

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, potential costs, hospitalization, and/or prolonged stays out of town. Choosing to receive this first-in-humans treatment combination may mean you are not able to receive other treatments in the future. Please discuss this with the study doctor.

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

The total length of study treatment is less than 4 months (depending on how the disease responds to treatment), plus the follow-up, up to one year described below.

You will receive NK cells and AFM13 at no cost while you are on the study. You and/or your insurance provider will be responsible for all other costs of the study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive a stem cell transplant or other chemotherapy outside of this study. You may choose to receive other investigational therapy, if available. 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 Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will be performed within 30 days before your first dose of study drugs, to help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, including tests of your liver function, blood sugar level, and ability to clot. Part of this sample will be used to test for HIV (the AIDS virus) and hepatitis B and C. State law requires

positive test results for certain communicable diseases, including HIV and hepatitis, to be reported to a local health agency.
- You will have an echocardiogram (ECHO) or MUGA scan to check your heart function.
- You will have breathing function tests to measure the amount of air that your lungs can breathe in and out.
- You will have imaging scans, including a chest x-ray, a CT scan of the brain (if needed), and a whole-body PET/CT scan (if needed), to check the status of the disease.
- You will have a bone marrow aspiration/biopsy performed. 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 is withdrawn through a large needle.
- Urine will be collected for routine tests. If you can become pregnant, part of this urine sample will be collected for a pregnancy test. To take part in this study, you cannot be pregnant.

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.

You may be given the option to sign a separate consent form for MD Anderson laboratory protocol, Protocol LAB00-099. The study staff will discuss this with you.

Up to 46 participants will take part in this study. All will be enrolled at MD Anderson.

NK Cell Dose Levels

If you are found to be eligible to take part in this study, you will be assigned to a dose level of AFM13-NK cells based on when you joined this study. Up to 3 dose levels of AFM13-NK cells will be tested until the highest tolerable dose level is found. Each new group will receive a higher dose than the group before it, if no intolerable side effects were seen. This will continue until the highest tolerable dose of AFM13-NK cells is found.

When the highest tolerable dose is found, more participants may be enrolled and will receive only the highest tolerated dose of AFM13-NK cell combination for all Day 0 infusions.

Study Drug Administration

The study treatment cycle is 28 days.

Before the treatment cycle begins, you will have pre-treatment days (called “negative days”) in which you will receive other drugs to prepare your body for the infusion.

You will be admitted to the hospital either on **Day -6** or **Day -1**, and on that day you will be given fluids by vein to hydrate you. The doctor will let you know when you need to be hospitalized.

On **Days -5, -4, and -3**, you will receive fludarabine by vein over 1 hour and cyclophosphamide by vein over about 30-60 minutes as part of your standard therapy. These may be given either as an in-patient or an out-patient.

On **Days -2 and -1**, you will receive no treatment.

On **Day 0**, you will receive AFM13-NK cells by vein over about 30 minutes.

On **Days 7, 14, and 21**, you will receive 3 more doses of AFM13 alone by vein over about 4 hours.

If you join the study after the highest tolerable dose level has been found, you will receive preloaded NK cells (NK cells with AFM-13) by vein over about 30 minutes and AFM-13 by vein over about 4 hours on **Days 7, 14, and 21**.

During each infusion, you will be monitored for side effects about every 15 minutes for 1 hour, and then every 30 minutes until the end of the infusion and one hour after the end of the infusion, as needed.

If your doctor thinks it is needed, you may receive additional treatment (such as filgrastim-sndz (Zarxio) as an injection) to help treat certain kinds of side effects.

If the disease does not get worse after completing the first AFM13-NK Cell treatment cycle, you will receive a second treatment cycle. If the disease responds to treatment after completing the second cycle, you may be able to receive additional treatment cycles based on the status of your health and if NK cells are available. The study doctor will discuss this with you.

If you receive a second treatment cycle, you will receive the same dose as you received in Cycle 1, and the tests and procedures described below will be repeated during that treatment cycle as well.

Study Tests

Around **Days 0, +2, +7, +14, and +21, and then around Week 4, Week 8, Day +100, Day +180, 9 months, and 1 year of treatment**, blood (about 8 tablespoons) will be drawn for routine tests.

At baseline (before you receive chemotherapy), on **Day 0, Day 2, around Days +7, +8, +14, +15, +21, +22 and then at Week 4, and Day +100**, blood (about 4 tablespoons) will be drawn for research tests to study how long NK cells stay in your body and how well they function. Two (2) samples will be drawn on Day 0, and 1 sample will be drawn at baseline and on Days +7, +14, and +21, and then around Week 4 and Day +100.

Depending on when you enter the study, blood (about 1 tablespoon) will be drawn around **Days 0, +14, and +21** to check for AFM13 antidrug antibodies.

Depending on when you enter the study, blood (about 1 tablespoon) will be drawn around **Days 0 and +21 before your infusion of AFM13-NK and on the morning on Days +1 and +22** to check the status of the CD30 tumor marker.

If possible, the blood needed for this study will be collected during standard of care blood draws so that no additional needle sticks will be needed.

Blood samples for routine tests and research tests to study NK cells will be repeated as described above if you receive additional cycles of treatment.

Blood samples to check for AFM13 antidrug antibodies and to check the status of the CD30 tumor marker will be repeated as described above if you receive a second cycle of treatment. If you receive additional cycles after that, blood will be drawn for these tests only on Day 0.

Around **Day +7 of treatment**, you will have a physical exam. You will also have a bone marrow aspiration/biopsy to check the status of the disease and for research tests to check for AFM13-NK cells.

Around **Day +28 (4 weeks) of treatment**:

- Blood (about 4 tablespoons) will be drawn for routine tests.
- You will have imaging scans to check the status of the disease.
- You will have a bone marrow aspiration/biopsy to check the status of the disease and for research tests to check for AFM13-NK cells.

If you have to have a second cycle of treatment, the timing of some of the above tests will change. Please discuss this with the study doctor.

Around **9 months and 1 year** after the infusion, you will have a chest x-ray to check the status of the disease, if your doctor thinks it is needed.

Around **Days 100 and 180** and then **at 9 months and 1 year** after the infusion, if your doctor thinks it is needed:

- Blood (up to 4 tablespoons each time) will be drawn for routine tests. Some of these blood draws may also be used for research tests, tests to learn how the body has accepted the transplanted cells, and tests to check the status of the disease.
- You will have a physical exam.
- You will have imaging scans to check the status of the disease.
- You will have a bone marrow aspiration/biopsy to check the status of the disease. If this is done at the Day 180 visit, some of this bone marrow will be used for research tests to check for AFM13-NK cells.

You may be taken off study early if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

The study staff will also stay in contact with your local doctor to find out if the disease comes back and to check how you are doing.

If new lesions appear and the doctor thinks they may be a sign of the disease coming back or getting worse, you will have a tumor biopsy. The tissue sample will be processed and stored at MD Anderson's Institutional Tissue Bank for research studies. Part of the tissue may be sent to Dr. Rezvani's lab at MD Anderson to check the status of the disease and to check for NK cells.

Pharmacokinetic (PK) Testing

Depending on when you enter the study, blood will be drawn 12 times (up to about ½ teaspoon each time) for PK testing at the below time points. PK testing measures the amount of study drug in the body at different time points.

- On **Day 0**, blood will be drawn before and after your infusion of AFM13-NK cells.
- On **Days 0, +7, +14, and +21**, blood will be drawn before and after your infusion of AFM13.
- On **Days +1, +2, +9, and +22**, blood will be drawn in the morning.

PK blood testing will be repeated as described above if you receive a second cycle of treatment. If you receive additional cycles after that, either blood will be drawn only before the dose on Day 0, or PK blood testing will be done using an existing blood sample that has already been drawn on Day 0 if the sample is large enough. The study doctor will discuss this with you.

Additional Research

You may be asked to sign a separate consent for Protocol LAB00-099 and take part in additional research sample collections. The study staff can discuss this with you. You do not have to agree to additional research studies in order to take part in this study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. 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 treatment is stopped, but in some cases, side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs or transplant. In addition to these risks, taking part in this research may hurt you in unknown ways. These may be minor or so severe as to cause death.

Cyclophosphamide, filgrastim-sndz, and fludarabine may each cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- 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/or difficulty breathing.

NK-cells Side Effects

Treatment with NK cells may cause GvHD. GvHD may cause rash, liver failure, jaundice (yellowing of the skin), blisters, abdominal cramping, and/or diarrhea. A chronic form of GvHD can occur, which involves the lungs, eyes, mouth, muscles, joints, skin, liver, and/or gastrointestinal tract. If you develop chronic GvHD, it can cause cough, shortness of breath, dry eyes, dry mouth, sore muscles, stiff joints, liver dysfunction, and/or diarrhea. Immunosuppressive therapy with steroids is used to treat GvHD if it occurs. GvHD can result in death.

Treatment with NK cells may also cause Cytokine Release Syndrome (CRS). This involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills) and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, confusion, difficulty speaking, and/or decreased brain function (possible paralysis and/or coma).

AFM13 Side Effects

This is an early study of AFM13 in a combination regimen with NK cells in humans, so the side effects of AFM13 in this setting are not well known. Based on studies of AFM13 in animals and early human studies of AFM13 given either alone or in combination with another drug called pembrolizumab, AFM13 may cause the following side effects:

• fever • chills • headache	• nausea • vomiting • abnormal liver tests	• swelling and skin irritation at the infusion site

• low blood pressure • skin rash • itching • hives	(possible liver damage)	• infusion reaction

AFM13 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.

AFM13 may cause an allergic reaction called an infusion reaction. This may result in tissue swelling, low oxygen level in the blood, tightening of the airways, build-up in the lung tissues, and/or a lung problem with difficulty breathing. It also may cause heart attack, shock caused by heart damage, and/or irregular heartbeat.

AFM13 may cause cytokine release syndrome. This involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills), and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, confusion, difficulty speaking, and/or decreased brain function (possible paralysis and/or coma).

Cyclophosphamide Side Effects

Common (occurring in more than 20% of patients):

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • inability to regulate water/salt balance which can cause frequent urination and dehydration	• headache • abdominal pain • loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle • low blood counts (red, platelet, white)	• fever with dangerously low white blood cell count (febrile neutropenia) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, acute leukemia [a type of blood cancer], lymphoma [a type of lymph node cancer], thyroid cancer, and/or sarcoma [a type of cancer that can start in the soft tissue, bone, or other tissue].

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

• irregular heartbeat • build-up of fluid around the heart (possible heart failure) • build-up of blood in the sac around the heart (possible impaired heart function) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding) • heart damage/failure, death of heart tissue, or other severe heart problems • heart attack, which can be serious and life-threatening • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall) • very severe blistering	• wound healing problems • low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding) • inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function • blood in the urine • blurry vision	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing) • problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multi-organ failure • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

skin disease (loss of large portion of skin)		

Filgrastim-sndz Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue	• nausea • enlarged spleen	• low platelet counts • bone pain

Occasional (occurring in 3-20% of patients)

• chest pain • high blood pressure • swelling (arm/leg) • dizziness • headache • difficulty sleeping • skin rash • hair loss (partial/total) • abnormal blood test • vomiting • loss of appetite	• high levels of uric acid (possible painful joints and/or kidney failure) • low red blood cell counts • abnormal liver tests (possible liver damage) • pain (muscle/joint/limb) • weakness • muscle spasm • numbness • lung inflammation	• cough • difficulty breathing • nosebleed • allergic reaction • reaction to blood transfusion • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

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

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

• low blood pressure (possible dizziness/fainting) • irregular heartbeat • heart attack • fast heartbeat • blood vessel inflammation (possible bleeding and/or bruising) • swelling (face) • bleeding in the brain	• skin condition with fever and skin lesions • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • diarrhea • blood in the urine • enlarged liver • sickle cell crisis in patients with sickle cell	• loss of bone strength (possible broken bones) • decreased kidney function (possible kidney failure) • coughing up blood • bleeding in the lungs and/or airways • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or

• painful skin bumps • worsening of an existing skin disease (psoriasis)	disease • ruptured spleen	organ failure) • immune reaction

Fludarabine Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue • pain • loss of appetite	• nausea • vomiting • low blood cell count (red, white, platelets)	• weakness • difficulty breathing • cough • infection

Occasional (occurring in 3-20% of patients)

• chest pain (possibly due to heart trouble) • heart failure • heart attack • fast and/or irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • vein inflammation • swelling • chills • stroke • headache • difficulty sleeping	• skin rash and/or itching • sweating • hair loss (partial or total) • high blood sugar (possible diabetes) • mouth blisters/sores (possible difficulty swallowing) • diarrhea/constipation • digestive system bleeding • gallstones • blood in the urine • difficult and/or painful urination	• inability to urinate • abnormal liver tests (possible liver damage) • abnormal sensation (such as pins and needles) • vision problems • hearing loss • sore/swollen throat • lung damage/inflammation (possible difficulty breathing) • coughing up blood

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

• build-up of fluid in the tissue around the heart • weakness in wall of artery (possible serious bleeding complications) • multiple blood clots (possible organ dysfunction and/or failure) • bleeding in the brain • abnormal brain function	• painful blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • dehydration • abnormal pancreas tests	• nerve damage affecting the eye and/or causing wrist weakness • paralysis • blindness • inflammation of an eye nerve • kidney failure • high blood levels of uric acid (possible painful joints and/or kidney

(affecting balance and coordination) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • mental status change • coma • seizure • 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)	• bladder inflammation with bleeding (possible pain and/or urge to urinate) • bone marrow failure due to abnormal tissue growth • destruction of red blood cells and platelets due to abnormal antibodies • anemia due to destruction of red blood cells • condition causing increased bleeding and/or bruising • liver failure • nerve damage (possible numbness, pain, and/or loss of motor function)	failure) • bleeding in the lungs and/or airways • failure to breathe • low oxygen level in the blood (possible lightheadedness) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Fludarabine may rarely cause you to develop another type of cancer (such as skin cancer and/or acute myeloid leukemia [a type of blood cancer].

Frequency Unknown

• testes/sperm damage	• graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body)

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.

Certain pre-medications are required before each infusion of study drug. Dexamethasone may cause upset stomach, vomiting, headache, difficulty sleeping, and anxiety. H1/H2 antagonists may cause drowsiness, dry mouth, nausea, and irritability. Ibuprofen or other NSAIDs may cause upset stomach, stomach ulcers, and nausea. Acetaminophen may cause rash, itching, allergic reaction.

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.

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

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.

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.

Chest x-rays send x-rays through the body. 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.

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

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. The study drug may pose unknown risk to an unborn or breastfeeding baby. You must

use birth control from at least 14 days before starting the study until at least 60 days after your last dose of study treatment, if you are sexually active.

Birth Control Specifications: Ask your doctor about acceptable forms of birth control and how long to use them.

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.

BENEFITS

You may or may not benefit from your participation in this research.

The information learned during this research study may be of benefit to other patients in the future.

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. There are no plans to reimburse you for expenses or for you to be compensated financially by MD Anderson or Affimed GmbH for this injury. You may also contact the study doctor 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 billed 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

1. If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the study doctor (Dr. Yago Nieto, at 713-745-3219 or 713-792-2121 (24 hours). If you have questions about your rights as a research subject or if you have questions, concerns, or complaints about the research, you may contact WCG IRB at researchquestions@wcgirb.com or (855) 818-2289.

2. 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 to which you are otherwise entitled. 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. If you withdraw from this study, you can still choose to be treated at MD Anderson.

3. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Affimed GmbH, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or WCG IRB.

4. 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.

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

6. This study is supported by: Affimed GmbH

7. 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, ask the study doctor.

8. The MD Anderson Conflict of Interest (COI) policy states that MD Anderson employees may not serve as the study chair or co-chair on a research study if they have received funds that are greater than the amount allowed by the policy or own stock in the sponsoring or supporting companies.

The COI policy and the IRB require that you be told about financial relationships that the study investigators may have with the study sponsor(s).

The MD Anderson Institutional Conflict of Interest policy requires that you be told about financial relationships that MD Anderson Institutional Decision Makers may have with the study sponsor(s) and significant financial relationships that MD Anderson may have with the study sponsor(s).

At this time, no financial relationships with the study sponsor(s) have been disclosed by any of the study investigators or Institutional Decision Makers.

There is a significant financial relationship between MD Anderson and Affimed GmbH. This relationship has been identified as a financial conflict of interest.

The results of this study may result in a financial benefit for MD Anderson.

MD Anderson has taken steps to manage this financial conflict of interest.
This financial conflict of interest may affect your willingness to take part in this study. If you have any questions or concerns related to MD Anderson's significant financial relationship with Affimed GmbH, please call the MD Anderson Institutional Compliance Office at 713-745-6636. That office will provide you the contact information for a non-MD Anderson ethicist who can assist with your questions and concerns. In the event, a non-MD Anderson ethicist is not available, an MD Anderson ethicist will contact you to assist with your questions and concerns.

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 WCG IRB 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 the rights of study participants.

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

Genetic Research

Samples collected from you as part of this study may 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.

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
- Affimed GmbH, who is a supporter of this study, and/or any future sponsors/supporters of the study
- spm2, a clinical research organization
- Center for International Blood and Marrow Transplantation Research (CIBMTR) and any future sponsors or licensees of the study technology
- 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.

Blood samples for research tests will be sent to Dr. Katy Rezvani's laboratory at MD Anderson.

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, it may be necessary 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 AND ASSENT INSTRUCTIONS

Patients that do not have the capacity to legally consent for themselves cannot be enrolled in this study The IRB determined the LAR section below cannot be used.

*Children ages **15-17** may be enrolled once MTD is determined. All children are required to assent, unless the investigator determines that the capability of the child is so limited that the child cannot reasonably be consulted. If so limited, check "The participant's intellectual age is less than seven" under the "ASSENT OF MINOR" section. If assent is obtained have the person obtaining assent document assent below.*

CONSENT/AUTHORIZATION

(Adult Participants Only)

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

SIGNATURE OF LAR _____ DATE _____

PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2018-1092.

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

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

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

PARENT/GUARDIAN PERMISSION

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____

SIGNATURE OF PARENT/GUARDIAN DATE

_____

PRINTED NAME OF PARENT/GUARDIAN

_____ _____

SIGNATURE OF PARENT/GUARDIAN DATE

Signature of Other Parent (Optional, unless required by the IRB.)

_____

PRINTED NAME OF PARENT/GUARDIAN

X The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____ Other parent is deceased, unknown, incompetent, or not reasonably available.

____ Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

____ The IRB has determined that the signature of both parents is NOT required.

WITNESS TO PARENTAL/GUARDIAN PERMISSION

I was present during the explanation of the research to be performed under Protocol 2018-1092. The child participant was also present. In my opinion, the parent(s)/guardian provided permission for the child to participate in the research.

_____ _____

SIGNATURE OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____

PRINTED NAME OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION

ASSENT OF MINOR

(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other: _____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____
SIGNATURE OF MINOR (Age 13-17) DATE

_____
PRINTED NAME OF MINOR

WITNESS TO ASSENT

I was present during the explanation of the research to be performed under Protocol 2018-1092. The child participant was also present. In my opinion, the child assented to participate in the research. (Note: If obtaining assent, a witness signature is required.)

_____ _____
SIGNATURE OF WITNESS TO THE ASSENT (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____
PRINTED NAME OF WITNESS TO THE ASSENT

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 below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) DATE

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION