THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase II Trial to Assess the Efficacy and Toxicity of SGI-110 with DLI for the Treatment of AML or MDS Relapsing After Allogeneic Stem Cell Transplantation
2015-0117

Study Chair: Betul Oran

_____ _____
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.

STUDY SUMMARY

The goal of this clinical research study is to learn if giving donor lymphocyte cells and SGI-110 will help control acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) (including Chronic Myelomonocytic Leukemia [CMML]) in patients who have had an allogeneic stem cell transplant (using someone else's stem cells) and have relapsed (the disease has gotten worse). Researchers also want to find out if giving SGI-110 after allogenic stem cell transplant in high risk AML and MDS patients would help to improve how long they may remain in remission (free of disease) after transplant.

Researchers also want to learn if SGI-110, when given as maintenance therapy for high-risk AML and MDS patients, will reduce the risk of relapse after an allogenic stem cell transplantation.

The safety of this treatment will also be studied.

This is an investigational study. SGI-110 is not FDA approved or commercially available. SGI-110 is made with decitabine, which is FDA approved and commercially available to treat MDS. SGI-110 is currently being used for research purposes only. The use of donor lymphocytes to treat MDS and AML is FDA approved.

Receiving SGI-110 in combination with lymphocytes may help to control the disease. Future patients may benefit from what is learned in this study. 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 (which may be life-threatening or fatal).

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

You may receive up to 12 cycles of SGI-110. You may be taken off study early if the disease gets worse, if intolerable side effects occur, if you develop uncontrolled or severe GVHD, or if your doctor thinks it is in your best interest.

SGI-110 will be provided to you at no cost while you are on the study. You and/or your insurance provider will be responsible for the costs of the donor lymphocyte infusion.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive chemotherapy and an allogeneic stem cell transplant 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

Up to 90 participants will take part in this study. All will be enrolled at MD Anderson.

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 help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine testing and to check for hepatitis B. If you can become pregnant, this routine blood draw will also include a pregnancy test. Urine may also be collected for this pregnancy test. To take part in this study, you cannot be pregnant.
- You will have a bone marrow aspiration to check the status of the disease. To collect a bone marrow aspiration/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 you have had some of these tests or procedures recently, they may not have to be repeated.

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.

Study Treatment Administration

If you are found to be eligible to take part in this study, you will receive SGI-110 as an injection under the skin 1 time a day on Days 1-5 of each 28-day cycle. Day 1 is the first day you will receive the study drug. You may receive up to 12 cycles of SGI-110.

The study doctor will tell you how long each of your cycles may be and when your next cycle will start.

If the doctor thinks it is needed, your dose of SGI-110 may be changed or stopped during the study.

Donor Lymphocyte Infusions

On Day 6 of Cycles 2, 4, and 6, you will receive a donor lymphocyte infusion by vein over about 10-30 minutes. If you have high-risk AML or MDS and you are receiving SGI-110 as maintenance, you will not receive donor lymphocyte infusions.

Graft-versus-host disease (GVHD) may occur after the T-cell infusion. GVHD occurs when donor cells attack the cells of the person receiving the stem cell transplant. If GVHD occurs, you will be given standard drugs that may help control GVHD. You may ask the study staff for information about how the drugs are given and their risks. You cannot continue to receive the study drug until the GVHD is controlled. The study doctor will discuss this with you.

Study Visits

Within **3 days before the start of each cycle, on Day 3 of each cycle, and then one time during Weeks 2 and 3 of each cycle** (if the doctor thinks it is needed), blood (about 2 tablespoons) will be drawn for routine tests and to check your kidney and liver function. Part of this blood sample will be used for a pregnancy test if you can become pregnant. Urine may also be collected for this pregnancy test.

You may be able to have these blood draws performed at a local lab or clinic closer to your home. The results of these tests will be sent to the study doctor at MD Anderson for review. Talk with the study doctor about this possibility.

On **Day 28 of Cycles 1, 2, 4, and 6 or on Day 100 and then at 6 months and 1 year after the stem cell transplant** (if you have high-risk AML or MDS):

- Blood (about 2 tablespoons) will be drawn for chimerism studies, which looks to see how much the blood cells mixed between the donor and recipient. This test shows how well the lymphocyte infusion has "taken."
- If the doctor thinks it is needed, you may have a bone marrow aspiration and biopsy performed to check the status of the disease. To collect a bone marrow aspiration/biopsy, an area of the hip is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.

These tests/procedures may be performed more often, if you doctor thinks it is needed.

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 drug/procedures.

SGI-110 and decitabine 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 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.
- 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.

Guadecitabine (SGI-110) Side Effects

Common (occurring in more than 20% of patients)

• tiredness	• nausea • low blood cell counts (red, white, platelet)	• injection site pain, bruising, irritation, lump, bleeding, redness, discomfort, infection, inflammation, itching, and/or swelling

Occurring in 5-19% of patients

• diarrhea • vomiting • constipation	• loss of appetite • swelling and irritation of mouth and lips	• bruising • nosebleeds • difficulty breathing

Serious side effects occurring in fewer than 5% of patients

• chest pain • fast irregular heartbeat • heart failure • fever • difficulty swallowing • small intestinal blockage	• swelling and irritation of mucus membranes (such as in the nose or digestive system) • high blood levels of uric acid (possible painful joints and/or kidney failure) • build-up of fluid around the lungs	• infection (such as pneumonia) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • severe life-threatening allergic reaction

<u>Decitabine Side Effects</u>
Decitabine is an active part of SGI-110. Decitabine may cause the following side effects:

Common (occurring in more than 20% of patients)

• swelling (including arm/leg) • pale skin • fever • fatigue • headache • difficulty sleeping • dizziness • high blood sugar (possible diabetes)	• 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) • nausea	• constipation • diarrhea • vomiting • loss of appetite • low blood cell counts (red, white, platelets) • shivering • cough • difficulty breathing • infection

Occasional (occurring in 5-20% of patients)

• swelling (face) • abnormal heart sound • low blood pressure (possible dizziness/fainting) • high blood pressure • fast heartbeat	• mouth blisters/sores (possible difficulty swallowing) • weight loss • abdominal pain • abdominal swelling • heartburn	• weakness/tenderness • muscle spasms • joint pain • walking/balance problems (possible falling)

• chest pain • heart failure • pain • chills • confusion • anxiety/depression • numbness • skin rash/redness • itching • night sweats • hair loss (partial or total) • dry skin • hives • lymph node swelling • toothache	• tongue/mouth pain • lip blisters/sores • difficulty swallowing • upset stomach • fluid in the abdomen • dehydration • hemorrhoids • difficult, painful, and/or frequent urination • bacteria in the blood • high blood platelet count (possible increased clotting) • abnormal liver tests (possible liver damage or yellowing of the skin and/or eyes)	• blurry vision • abnormal kidney test (possible kidney damage) • high blood levels of uric acid (possible painful joints and/or kidney failure) • sore throat • low oxygen level in the blood (possible lightheadedness) • fluid in or around the lungs (possible difficulty breathing) • runny or stuffy nose • nosebleed • injection site swelling

Rare but serious (occurring in fewer than 5% of patients)

• irregular heartbeat • enlarged heart • heart attack • heart and lung failure • bleeding around the brain • mental status change • skin condition with fever and skin lesions • blood in the urine	• kidney failure • lung inflammation • blood clots in the lung (possible failure to breathe) • stopped breathing • coughing up blood • enlarged spleen • gallbladder inflammation (possible abdominal pain)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Other Risks

The **donor lymphocyte infusion** may cause GVHD. GVHD may cause rash, liver failure, jaundice (yellowing of the skin), blisters, abdominal cramping, and/or diarrhea. A chronic (long-term) 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.

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 aspiration/biopsy. An allergic reaction to the anesthetic may occur. A scar may form at the aspiration/biopsy site.

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 for 30 days after the last SGI-110 injection, if you are sexually active.

Birth Control Specifications: Talk with the study doctor about which methods of birth control you should use on study and for 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 may 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 Astex Pharmaceuticals 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. Betul Oran, at 713-792-8750) 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. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Astex Pharmaceuticals, 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.

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: Astex Pharmaceuticals.

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

Data

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

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by Astex Pharmaceuticals may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research 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 research samples are used for future research. If future 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 research 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.

Genetic Research
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.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

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
- Astex Pharmaceuticals, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Center for International Blood and Marrow Transplantation Research (CIBMTR)
- 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.

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 _____

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 _____

RELATIONSHIP TO PARTICIPANT _____

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2015-0117.**

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.

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 _____

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 DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)