University of Pittsburgh
Department of Medicine
Division of Rheumatology and Clinical Immunology

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: DIMETHYL FUMARATE, TECFIDERA, IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

PRINCIPAL INVESTIGATOR:
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Source of support:
National Institutes of Health
Biogen Idec Corporation will be providing study drug only

Background

This consent form describes a research study to test whether a drug known as Tecfidera is safe to use in systemic sclerosis (also known as scleroderma) patients. Tecfidera is manufactured by Biogen Idec Corporation and is currently FDA approved for multiple sclerosis, an inflammatory disease of the brain. Its use remains experimental in the treatment of systemic sclerosis.

You have been asked to participate because you have pulmonary arterial hypertension associated with systemic sclerosis. We would like to find out if Tecfidera is safe and helps pulmonary arterial hypertension in people who have systemic sclerosis.

Please read the information carefully. If you have questions please ask the investigator or study staff to explain and answer them until you feel completely informed.

Your doctor may be an investigator of this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study

offered by your doctor.

Systemic sclerosis is a disease that affects major organs like the skin, lungs, kidneys, and gastrointestinal tract. It can also affect your joints, muscles, heart, and blood vessels. Systemic sclerosis causes development of excessive connective tissue in the organs. Systemic sclerosis also injures blood vessels, leading to pulmonary arterial hypertension.

Tecfidera is an investigational drug that reduces the activity of chemicals in your body that are triggered by inflammation. This process is called oxidative stress. Oxidative stress is increased with pulmonary arterial hypertension associated with systemic sclerosis. However, at this time we do not know whether Tecfidera will have any effect on pulmonary arterial hypertension associated with systemic sclerosis.

Biomarkers are proteins in your samples that we can look at from one point in time to the next to see if there is any change in your disease. Biomarkers are being investigated as part of the study. We will measure these from blood samples that you will provide at study visits.

You are being asked to participate in this study because you have been diagnosed with systemic sclerosis and your cardiac catheterization results meet the criteria for pulmonary hypertension. The Principal Investigator of this study is Robert Lafyatis, MD.

Purpose

This is a Phase 1b, double-blinded, placebo-controlled pilot study of Tecfidera in pulmonary arterial hypertension (PAH) associated with systemic sclerosis (SSc-PAH): The effect of DMF on clinical disease and biomarkers of oxidative stress. The study is designed to see if Tecfidera is safe and whether it is associated with any improvement in 6-minute walk test in people with pulmonary arterial hypertension associated with systemic sclerosis. It is also designed to see if the drug causes any changes in biomarkers in patients with pulmonary arterial hypertension associated with systemic sclerosis that reflect the level of disease activity and oxidative stress.

What Happens In This Research Study

You will be one of approximately 34 subjects recruited from approximately 5 centers in the United States. Subjects recruited from the University of Pittsburgh will have all of the research procedures performed for this study at the University of Pittsburgh Medical Center (UPMC) in the Arthritis and Autoimmune Center.

After the Screening Visit, subjects agreeing to participate in this study will be randomly selected to receive either Tecfidera or a placebo. There is a 50% chance that you will be randomly assigned (by chance, like with the flip of a coin) to receive Tecfidera and a 50% chance that you will receive placebo. One half of subjects will receive Tecfidera and one half of subjects the placebo. Tecfidera or placebo will be given to you as a pill to be taken twice a day. Tecfidera or placebo comes in pill form and will be provided to you by the study. The first week of the study you will receive 120mg Tecfidera tablets or similar appearing placebo tablets to be taken one tablet per night for the first 7 days. After the first week you will receive one 120mg tablet in the morning and one tablet at night for the next 2 weeks. At the start of week 4, you will be asked to increase dosing to one tablet in the morning and two at night. The final dosing increase will occur at the start of week 8, with two tablets in the morning and two at night. A minimum daily dosing of one tablet in the morning and one tablet at night must be tolerated by the start of week 8. Tecfidera or placebo should be taken with high-fat, high-protein food to reduce the incidence of side effects.

Screening Visit: You will be asked to sign consent before any screening procedures can be performed. Demographic information will be taken. New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification. A complete history and physical examination, including vital signs, a skin score and digital ulcer assessment will be performed. You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes. Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), Brain Natriuretic Peptide (BNP), urinalysis, a pregnancy test (for women of child-bearing potential) to confirm that you are not pregnant, and HIV and HCV/HBV serology. This is for safety evaluation. Blood will be drawn for storage and future analyses. About 4 tablespoons of blood will be drawn at this visit.

After the screening visit test results are known, you will be advised of your eligibility to participate. You may be deemed ineligible for the study for reasons including, but not limited to a positive pregnancy test, positive for Hepatitis B or C, or positive for HIV. If you agree to participate in this study your blood is tested for Human Immunodeficiency Virus (HIV), the virus which causes AIDS. If your test results are positive, you cannot participate in the study. Your HIV test result is given to you in person, not over the phone. Your medical records are kept confidential to the extent permitted by law. If you have any questions regarding the HIV testing or the information provided above, you are encouraged to discuss them with your study doctor. Positive HIV tests are to be reported to the Allegheny County Health Department

Study Visit 1 (Day 0): After all screening evaluations have been completed (within 4 weeks of laboratory tests), you will be scheduled for the first study visit in the UPMC Arthritis and Autoimmune Center. On this visit, inclusion and exclusion criteria will be reviewed.

- Questionnaires will be given including Scleroderma Health Assessment Questionnaire (SHAQ), Raynauds VAS, Systemic Sclerosis Skin Questionnaire,
- Interim history (including safety reporting and medication review) will be taken
- Physical examination including vital signs, a skin score and digital ulcer assessment will be performed.
- New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification.
- You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes.
- Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), B-Type Natriuretic Peptide (BNP), and urinalysis. Research blood will be drawn for storage and future analyses. Women of child-bearing potential (WOCBP) will have a urine pregnancy test performed prior to study treatment. About 4 tablespoons of blood will be drawn.
- Skin biopsies are taken using a tiny circular blade (punch biopsy) on the skin of your forearm. One 3-millimeter (mm) punch biopsy will be collected, removing a small cylinder of skin. For all biopsies, the skin is injected with a local anesthetic (lidocaine) to numb the area to minimize pain and discomfort. Each skin punch site will be closed with steri-strips and a pressure dressing. The wounds usually heal in 7-10 days and during that time you may feel some mild discomfort. If needed, an over the counter pain reliever may be recommended by your study doctor. The

skin biopsy procedure should take approximately 30 minutes to perform. It is very important for you to tell the doctor if you have ever had a reaction to local anesthetics in the past.

- You will then be given study medication, Tecfidera or placebo tablets.

Day 7 Telephone Call: The study coordinator will call you on the telephone to assess any side effects and to confirm that you will increase to the higher study medication dose of two tablets daily (one in the morning and one at night).

Day 28 Telephone Call: The study coordinator will call you on the telephone to assess any side effects. You will be scheduled for an evaluation in the UPMC Arthritis and Autoimmune Center before being given any more study treatment if the study-physician believes any reported side effects are unexpected or serious.

Study Visit 2 (week 8): You will return to the UPMC Arthritis and Autoimmune Center.

- Questionnaires will be given including Scleroderma Health Assessment Questionnaire (SHAQ), Raynauds VAS, Systemic Sclerosis Skin Questionnaire,
- Interim history (including safety reporting and medication review) will be taken
- Physical examination including vital signs, a skin score and digital ulcer assessment will be performed.
- New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification.
- You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes.
- Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), B-Type Natriuretic Peptide (BNP), and urinalysis. Women of child-bearing potential (WOCBP) will have a urine pregnancy test performed prior to study treatment. About 4 tablespoons of blood will be drawn.

Study Visit 3 (week 16): You will return to the UPMC Arthritis and Autoimmune Center.

- Questionnaires will be given including Scleroderma Health Assessment Questionnaire (SHAQ), Raynauds VAS, Systemic Sclerosis Skin Questionnaire,
- Interim history (including safety reporting and medication review) will be taken
- Physical examination including vital signs, a skin score and digital ulcer assessment will be performed.
- New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification.
- You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes.

- Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), B-Type Natriuretic Peptide (BNP), and urinalysis. Research blood will be drawn for storage and future analyses. Women of child-bearing potential (WOCBP) will have a urine pregnancy test performed prior to study treatment. About 4 tablespoons of blood will be drawn.

Study Visit 4 (week 24): You will return to the UPMC Arthritis and Autoimmune Center.

- Questionnaires will be given including Scleroderma Health Assessment Questionnaire (SHAQ), Raynauds VAS, Systemic Sclerosis Skin Questionnaire,
- Interim history (including safety reporting and medication review) will be taken
- Physical examination including vital signs, a skin score and digital ulcer assessment will be performed.
- New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification.
- You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes.
- Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), B-Type Natriuretic Peptide (BNP), and urinalysis. Research blood will be drawn for storage and future analyses. Women of child-bearing potential (WOCBP) will have a urine pregnancy test performed prior to study treatment. About 4 tablespoons of blood will be drawn.
- Skin biopsies are taken using a tiny circular blade (punch biopsy) on the skin of your forearm. One 3-millimeter (mm) punch biopsy will be collected, removing a small cylinder of skin. For all biopsies the skin is injected with a local anesthetic (lidocaine) to numb the area to minimize pain and discomfort. Each skin punch site will be closed with steri-strips and a pressure dressing. The wounds usually heal in 7-10 days and during that time you may feel some mild discomfort. If needed, an over the counter pain reliever may be recommended by your study doctor. The skin biopsy procedure should take approximately 30 minutes to perform. It is very important for you to tell the doctor if you have ever had a reaction to local anesthetics in the past.

Study Visit 5 (week 36): You will return to the UPMC Arthritis and Autoimmune Center.
Questionnaires will be given including Scleroderma Health Assessment Questionnaire (SHAQ), Raynauds VAS, Systemic Sclerosis Skin Questionnaire,

- Interim history (including safety reporting and medication review) will be taken
- Physical examination including vital signs, a skin score and digital ulcer assessment will be performed.
- New York Heart Association (NYHA) Functional Classification: A table that doctors classify patients' heart failure according to the severity of their symptoms the (NYHA) Functional Classification.
- You will be asked to perform a Six Minute Walk test (6MWT) a test to measure the distance you can walk in 6 minutes.

- Safety laboratory testing will include a complete blood count with differential (CBC), comprehensive metabolic panel (CMP), B-Type Natriuretic Peptide (BNP), and urinalysis. Research blood will be drawn for storage and future analyses. Women of child-bearing potential (WOCBP) will have a urine pregnancy test performed prior to study treatment. About 4 tablespoons of blood will be drawn.

The study coordinator will collect the leftover medicine vials at your study visits 2 and 3 when new study medication is dispensed. Details about how the study treatment will be monitored will be explained in detail by the study coordinator.

Risks and Discomforts

Tecfidera:

Tecfidera can cause allergic reactions after the first dose or at any time during treatment. Symptoms of an allergic reaction while taking Tecfidera are: rash, flushing, itching and trouble breathing. When you come to the UPMC Arthritis and Autoimmune Center for your first dose of study treatment, you will be observed for 30 minutes afterward to make sure you do not develop these symptoms, sometimes requiring treatment.

Tecfidera can cause nausea, vomiting, diarrhea, abdominal pain, and dyspepsia in about 1 in 10 people. These symptoms usually decrease over time. Serious gastrointestinal events have been seen in about 1 in 100 people taking Tecfidera. You should seek immediate medical care if you develop any serious gastrointestinal problems.

Tecfidera frequently causes flushing (in about 4 in 10 patients treated with Tecfidera). This generally starts soon after you first start taking Tecfidera and usually improves or resolves over time.

Tecfidera may affect your white blood cell counts, causing a decrease in one type of your white blood cells called lymphocytes (in about 6 in 100 patients). Your white blood cell counts will be monitored during the trial. If your lymphocyte count becomes very low you will be stopped from taking Tecfidera.

In one case a patient who had been taking Tecfidera for 4 years and had very low lymphocyte counts died from an infection in the brain called progressive multifocal leukoencephalopathy.

We do not know the effect of Tecfidera on pregnant women, so if you are a woman of child bearing potential, you will be asked to carefully use birth control during the trial and you will have a pregnancy test on each study visit.

Other Pulmonary Hypertension Therapy: While the study drug is Tecfidera, you will continue taking any other PAH medications at the doses on which you entered the study. These medications may include prostacyclins (epoprostenol, Flolan®), endothelin receptor antagonists (bosentan, Tracleer®), and/or phosphodiesterase inhibitors (sildenafil, Revatio®, Viagra®). There are no known drug interactions with Tecfidera and other PAH medications and none are anticipated. While the physician should have reviewed the side effects of these drugs with you prior to starting them, it is important to emphasize a few points here.

Epoprostenol (prostacyclin) may result in significant hypotension (low blood pressure), and combining it with other drugs that could lower the blood pressure (diuretics, anti-hypertensives) may enhance

this effect. It should never be stopped abruptly as this could result in rebound hypertension (high blood pressure). There is the potential for epoprostanol to increase bleeding in individuals on anti-platelet drugs or anticoagulants (blood thinners). Other side effects reported with this drug include nausea, vomiting, headache, hypotension, and flushing.

Endothelin receptor antagonists have the potential to cause liver injury. They may also result in anemia. It is recommended that liver function tests be checked monthly and blood counts (hemoglobin) be checked every 3 months, which can be done with a simple blood test.

Bosentan or ambrisentan can also cause damage to a fetus, and use of a hormonal contraceptive to prevent pregnancy with these drugs may be ineffective. There are also potential drug interactions with drugs including ketoconazole, rifampicin, statins to treat high cholesterol, and blood thinners.

The phosphodiesterase inhibitors (sildenafil) may have side effects including nose bleed, headache, stomach upset, flushing, insomnia, and muscle aches. There have been rare reports of visual and hearing disturbances or loss at higher doses. If you notice any sudden decrease or loss in hearing or vision it is important that you seek immediate medical treatment. There is a serious drug interaction with a class of drugs called nitrates. Taking both sildenafil and nitrates at the same time should be avoided due to the risk of serious hypotension (low blood pressure). If you are prescribed a new medication for any reason, including an antibiotic for an infection, it is critical that you first contact the physician treating the SSc-PAH to discuss any potential drug effects before starting the new medicine.

Six Minute Walk Test:

During this study you will be asked to perform a six minute walk test. There is a chance of falling during your walk test; a trained member of the research team will also closely supervise the subject when the test is performed

Blood Draw:

During this study you will have samples of your blood taken. Blood samples are obtained by inserting a needle into a vein and can cause discomfort and may result in bruising, clotting, or, rarely, infection. Both discomfort and bruising should disappear in a few days. Common side effects of blood draw (occurring in less than 25% or less than 25 out of 100 people) include: temporary discomfort from the needle stick, bruising, inflammation, bleeding, and lightheadedness. Rare side effects (occurring in less than 1%, or 1 out of 100 people) include: fainting, infection at the site of the blood draw, and spasm with loss of blood flow. Blood will be drawn by trained persons and sterile technique will be used to minimize the risk of infection.

HIV Serology

During this study you will have samples of your blood taken to confirm your HIV status. Blood samples are obtained by inserting a needle into a vein and can cause discomfort and may result in bruising, clotting, or, rarely, infection. Both discomfort and bruising should disappear in a few days. Common side effects of blood draw (occurring in less than 25% or less than 25 out of 100 people) include: temporary discomfort from the needle stick, bruising, inflammation, bleeding, and lightheadedness. Rare side effects (occurring in less than 1%, or 1 out of 100 people) include:

fainting, infection at the site of the blood draw, and spasm with loss of blood flow. Blood will be drawn by trained persons and sterile technique will be used to minimize the risk of infection.

Learning that you tested positive for HIV can be overwhelming and stressful. You may become depressed and anxious. In the event that you test positive, you will be referred to receive HIV counseling services.

Risk of Confidentiality Breach:
There is a risk that your confidentiality may be breached. The investigator and the study staff will take measures to minimize this risk. Your data will be given a unique study number. The investigator will keep a logbook that matches the study number to you. This logbook and your data will be kept in a secure, locked area where access is limited to the investigator and the study staff.

With your consent, the blood you provide for storage will be kept in a freezer that is located in an area where access is limited to the investigator and the study staff. These samples may be analyzed in future studies that may be related to systemic sclerosis. You will not be consented for future use of these samples or data collected for the study. In an effort to minimize breach of your confidential information, these samples will be given a unique study number and will not contain any direct identifiers like your name. The investigator will keep a log that matches the study number to you. This log will be kept in a secure, locked area where access is limited to the investigator and the study staff.

Physical Examination:

During the study the PI will be performing a physical exam at each visit including a skin score and digital ulcer assessment. There are no physical risks in the examination.

Questionnaires:

During the study you will be asked to complete questionnaires. There could be a risk of breaching confidentiality. Subjects may experience embarrassment or increased depression from questions that are asked.

Skin Biopsy:

The most serious possible risk involved with having a skin biopsy would be an allergic reaction to the local anesthetic, lidocaine. Allergic reactions to lidocaine are rare (less than 1% of cases or less than 1 out of 100 people). A severe allergic reaction can be life-threatening. A less severe allergic reaction may cause a rash, hives, or swelling at the injection site. Please inform the researchers if you know that you are allergic to any medication, especially local anesthetics such as lidocaine.

Side effects of a local injection of lidocaine into the skin are also rare (less than 1% of people or 1 of every 100). It is possible that a small amount of the medication may seep into the blood causing mild side effects in some people. Side effects of lidocaine are related to the amount of the medication in the blood. With high levels of lidocaine in the blood, a person may experience nervousness, seizures, sleepiness, irregular or slow heartbeat, high or low blood pressure, blurred vision, ringing in the ears, nausea or vomiting.

The risk of infection from the skin biopsy is also rare. The signs of infection are increased redness,

swelling, pain, or drainage at the biopsy site. Rarely, a patient will experience a small amount of bleeding and may require a pressure dressing.

It is common (1-25 % of people, or 1 to 25 of 100 people) for patients to experience some discomfort at the site of the biopsy, after the local anesthetic wears off. It is also common for the biopsy to leave a small scar. Scarring is minimized by taking three or four smaller side-by-side samples instead of a single larger sample of skin.

Randomization:

There are no risks involved with randomization. The study drug/placebo is not taking the place of the subject's SOC treatments.

Pregnancy:

If you become pregnant while you are participating in this study, it could be dangerous for the baby. Women who are able to become pregnant will be monitored with frequent pregnancy tests throughout the study. You must use birth control if you are a woman having sex with men while you are participating in this study and for three months afterward. You must agree to use two acceptable methods of birth control throughout the study." (i.e. hormonal methods, barrier and mechanical methods, bilateral tubal occlusion, vasectomised partner, true abstinence). You should not participate in this study if you are a woman who has sex with men and cannot use one of these birth control methods.

The effects of Tecfidera on male fertility are unknown.

As with any experimental procedure, there may be adverse events or side effects that are currently unknown and certain of these unknown risks could be permanent, severe or life-threatening and these particular treatments or procedure may involve risks to you (or to the embryo or fetus, if you are or become pregnant), which are currently unforeseeable. Study staff will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study.

Benefits

It is not known whether participation in this study will have any beneficial effect on your disease. The symptoms of your disease may improve, stay the same, or worsen during the course of the study. The information collected during this study will help the doctors and researchers to learn more about the study drug that may benefit you and other people with SSc. However, there is no guarantee that this will happen.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: You do not have to participate in this study to receive treatment for your systemic sclerosis. Other treatments are available for managing the involvement of organ systems such as the lungs, kidneys, and gastrointestinal (gut) symptoms. Your doctor can prescribe medication that is appropriate for you. Your study doctor will discuss with you the risks and benefits of alternative treatments.

Subject Costs and Payments
Some of the tests and procedures in this study are standard of care procedures and would be done anyway for someone with your illness. These tests and procedures will be billed to you or your insurance company. The PAH treatment you are taking are standard of care medications and will continue to be billed to your insurance company. The study will cover the cost of the study drug. You will not be billed for tests and procedures that are performed only because of your participation in this research. This will include all study medical evaluations and administration of the study medication.

At each visit you will be paid $50 on a debit card as payment for your participation. In addition, if you live more than 50 miles away, you will be offered reimbursement for mileage based on IRS regulations. There will be no financial charge for the medication.

Subject's Rights
By consenting to participate in this study you do not waive any of your legal rights. Giving consent means that you have heard or read the information about this study and that you agree to participate. You will be given a copy of this form to keep. If at any time you withdraw from this study, you will not suffer any penalty or lose any benefits to which you are entitled. The investigator or a member of the research team will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury while participating in this research, contact Dr. Robert Lafyatis at 412-637-6700 (24-hour contact).

Compensation for Research Related Injury
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider will be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. There is no provision for free medical care or monetary compensation from the mechanistic study sponsor, the National Institutes of Health.

Right to Refuse or Withdraw
Taking part in this study is voluntary. You have the right to refuse to take part in this study. If you decide to be in the study and then change your mind, you can withdraw from the research. Your participation is completely up to you. Your decision will not affect your ability to get health care at this institution or payment for your health care. It will not affect your enrollment in any health plan or benefits you can get. If you choose to take part, you have the right to stop at any time. If you decide to withdraw from study participation after you have received the study drug, you should participate in additional monitoring follow-up procedures that are being conducted to measure the safety of the study drug If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them as soon as possible. The investigator may decide to discontinue your participation without your permission because he/she may decide that staying in the study will be bad for you There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate (i.e. pregnancy).

- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

STORAGE OF SAMPLES

There is no benefit to you from the storage and sharing of samples and the information learned from the research using them. Your stored blood samples used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

Protection of Subject Health Information

You have certain rights related to your health information. These include the right to know who will get your health information and why they will get it. Although every reasonable effort has been taken to de-identify your research information, confidentiality cannot be guaranteed and it is possible that re-identification of research data/samples may occur. If you choose to be in this research study, we will get information about you as explained below.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally-funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of child abuse and neglect, or harm to self or others

Health Information About You That Might Be Used or Given Out During This Research:

- Information from your hospital or office health records at UPMC or elsewhere. This information is reasonably related to the conduct and oversight of the research study. If health information is needed from your doctors or hospitals outside of UPMC, you will be asked to give permission for these records to be sent to the researcher. The information will be coded and

will not contain your name or other traditional identifying information like social security number or birthday. It would be very hard for anyone to tell to whom the data belongs.
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.
- Your HIV status
- Medication list, date of birth, most recent history, most recent discharge summary, DNA, medical specimens, x-rays, imaging records, EKGs, echocardiograms, pulmonary function tests, cardiac catheterization, CT scans, and lab results.

Why Your Health Information Might Be Used or Given Out To Others

The reasons we might use or share your health information are:

- To do the research described here
- To make sure we do the research according to certain standard set by ethics, law, and quality groups
- To create the unique code, we assign to your health information to prevent it from being linked to you by persons to whom we disclose it.
- To conduct future research involving scleroderma and other rheumatic disorders.
- To develop new medical, diagnostic or genetic tests, new drugs or other commercial products.

People And Groups That May Use Or Give Out Your Health Information People Or Groups Within UPMC:

- Researchers involved in this research study
- The University of Pittsburgh Institutional Review Board that oversees this research

People or Groups Outside UPMC

- People or groups that we hire to do certain work for us, such as data storage companies, or laboratories.
- Federal and state agencies if they are required by law or involved in research oversight. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health.
- Organizations that make sure hospital standards are met
- The sponsor(s) of the research study, and people or groups it hires to help them do the research - Other researchers, including commercial partners such as drug and health companies.
- A group that oversees the research information and safety of this study
- Government agencies in other countries
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must. We ask anyone who gets it from us to protect your privacy. However, once the information leaves the University of Pittsburgh, we cannot promise that it will be kept private. In most cases any health data that is being given out to others is identified by a unique study number and not with your name. So, although in some cases it is possible to link your name to the study data, this is not usually done.

Time Period for Using or Giving Out Your Health Information

This consent does not expire. Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information. University of Pittsburgh research record retention policy states that all research records must be maintained for a period of at least 7 years following final reporting or publication of a project.

Privacy Rights

- You have the right not to sign this form that allows us to use and give out your health information for research. If you don't sign this form, you can't be in the research. This is because we need to use the health information to do the research.
- You have the right to withdraw your permission to use or share your health information in this research study. You have the right to revoke your authorization to participate in the study at any time by providing a written and dated notice of this decision to the principal investigator listed on the first page of this form.
- If you withdraw your permission, you will not be able to take back information that has already been used or shared with others. This includes information used or shared to do this or other research studies or to be sure the research is safe and of high quality.
- If you withdraw your permission, you cannot continue to be in the study.
- You have the right to see and get a copy of your health information that is used or shared for research. However, you may only get this after the research is finished. To ask for this information, please contact the principal investigator listed on the first page of this form.

If Research Results Are Published or Used To Teach Others

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other direct identifying information will not be used for these purposes without your specific permission.

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.

Specimen Banking Storage:

In this study you will have blood drawn for routine labs. In this study you will also have blood samples collected to help tell how the study drug affects your disease. If you give permission below, part of your blood samples, and data collected may also be used for other studies pertaining to systemic sclerosis and other rheumatic disorders. You will not be consented again for future use regarding the samples and the data; all future studies will be reviewed by an ethics committee. You will also have blood drawn for routine labs. You have the right to withdraw consent at any time by writing to the investigators on the study, and we will destroy any unused samples and only keep information already analyzed.

You may refuse to have your blood samples stored. If at any time you wish to withdraw your consent to store specimens, please inform the investigator or study staff. Your samples will then be destroyed.

I consent to the storage of my samples and data for use in future research studies

Yes _____ No _____ (please initial beside your choice)

****

Voluntary Consent:

The above information has been explained to me and all of my current questions have been answered. I understand that I may always request that my questions, concerns or complaints be addressed by Dr. Robert Lafyatis. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation.

By signing this form, I consent to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____	_____
Patient/Subject Signature	Date
_____	_____
Participant's name (Printed)	Time

Certification of Informed Consent:

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date / Time