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

3500 Terrace Street
BST South Wing, 7th Floor
Pittsburgh, PA 15261
(412) 383-8000

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: Abatacept for the **T**reatment of **My**ositis-associated **I**nterstitial **L**ung **D**isease

(**AT**tack**My**-**ILD**)

PRINCIPAL INVESTIGATOR: Rohit Aggarwal, MD

University of Pittsburgh

Division of Rheumatology & Clinical Immunology

3601 Fifth Avenue, Suite 2B, Pittsburgh, PA 15213

Phone: (412) 647-8708

Date 1/23/2019

ClinicalTrials.gov: NCT03215927

CO INVESTIGATORS:

Chester V. Oddis, M.D., University of Pittsburgh, Division of Rheumatology
Siamak Moghadam-Kia, M.D., University of Pittsburgh, Division of Rheumatology

CLINICAL RESEARCH COORDINATORS:

Kim Goldby-Reffner, RN, BS, CCRC
University of Pittsburgh
Division of Rheumatology and Clinical Immunology
200 Lothrop Street, S 726 BST
Pittsburgh, PA 15261
Phone: (412) 648-4028
goldbyka@pitt.edu

Faith Onelangsy, BS
University of Pittsburgh
Division of Rheumatology and Clinical Immunology
200 Lothrop Street, S 726 BST
Pittsburgh, PA 15261
FLO2@pitt.edu

SOURCE OF SUPPORT: Bristol Myers Squibb

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INTRODUCTION:

This is a proof of concept research study to evaluate the effectiveness and safety of the study drug, abatacept (ABT) in people diagnosed with anti-synthetase-associated interstitial lung disease (Syn-ILD). Anti-synthetase interstitial lung disease is a disorder caused by the abnormal accumulation of cells structures between air sacs of the lungs resulting in thickening and stiffness of the tissues of the lung. Anti-synthetase means the disorder is characterized by the presence of certain antibodies (proteins in your blood). Proof of concept means that there are indications that abatacept may reduce the effects of Syn-ILD, but other research studies are needed to determine if this is true.

You are being asked to participate in this study because you have been diagnosed as having Syn-ILD. This study will enroll a total of 20 subjects across six clinical sites located in the United States. The University of Pittsburgh site plans to enroll up to 4 subjects. If you are enrolled in the study you will receive either study drug or placebo for 24 weeks. Placebo is an inactive substance that contains no medicine. Following the initial treatment phase, you will have the option to participate in the follow up phase and receive active study drug (abatacept) for an additional 24-week period.

Abatacept is a drug used and approved by the Food and Drug Administration (FDA) in January 2005 for the treatment of moderately to severely active adult rheumatoid arthritis and juvenile idiopathic arthritis. In this study, abatacept is considered to be experimental because it is not FDA approved for the treatment of Syn-ILD.

What procedures will be performed for research purposes?

Before any study procedures are done, the study doctor and research staff will explain the study to you and ask you to read the consent form. They will answer any questions you may have about the study and what you are being asked to do. If you decide to participate you will be asked to sign this consent form and a copy will be given to you. You will then be ready to begin the first part of the study (also called the screening visit). You will be asked to give yourself a dose of study drug or placebo subcutaneously (under the skin) once a week for a period of six months. The study doctor will provide instructions on how to administer the study medication. This training should take approximately 15 to 20 minutes of your time. You will be asked to administer the first dose of study drug while at Visit 1 to demonstrate adequate understanding.

Screening Visit

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The study doctor and research staff will want to know if you are taking any medicines and the doses of your medicine. You may be able to continue some of the medicine you take for your Syn-ILD and the study doctor will discuss these with you. Some of the medicines you will be allowed to continue include:

1. If you are taking prednisone you may continue this medicine while you are in the study. The study doctor will discuss this specifically with you and the dose that is allowed for the study. You must be on a stable dose of prednisone for at least 2 weeks prior to the first visit when study/drug or placebo is administered.

2. In addition to prednisone, you are permitted to continue taking **one** of the following immunosuppressive (IS) medications:

Additional IS agent can be either CellCept - (mycophenolate mofetil), or Imuran -(azathioprine). You can take either one of these medications but not both. You must be on a stable dose of Cellcept or Imuran for 4 weeks prior to the first visit when study/drug or placebo is administered. If you are currently taking pifenidone, you will be allowed to continue the medication while in the study.

If you are taking any of the medications mentioned above you may continue the medicine while you are in the study. The study doctor will discuss this specifically with you and the dose that is allowed for the study.

You will not be permitted to take any of the following IS medications during the study :(e.g. IVIG, plasmapharesis, Rituxan (rituximab), methotrexate, Prograf (tacrolimus), Neoral (cyclosporine) or other biologics..

If you are on a stable dose of prednisone your dose will be tapered weekly after beginning study drug at Visit 1. The goal of the investigator is to reduce your dosage of steroid to 5 mg within the first 8 weeks after visit 1.

If you are not currently taking prednisone or other steroid you will not be permitted to start a new course of steroids unless you or your site investigator determine that you are experiencing a flare in your disease. If in the clinical site investigator's opinion there are complications or worsening of disease that necessitate an increase in the prednisone dose (or other forms of steroid) then the smallest reasonable increase is permitted with a maximum dose of steroid not to exceed 20 mg/day. After the increase, the site investigator will resume the prednisone taper noted above.

Please ask the study physician any questions you may have about changing any of your current medications.

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A screening visit is performed to see if you qualify for the study. This visit will last about 2 ½ to 3 hours. If you decide to take part in this research study you will have the following procedures done that are not a part of your standard medical care. Procedures to determine if you are eligible to take part in a research study are called "screening procedures".

For this research study, the screening procedures include:

- Urine Pregnancy (if applicable): Urine pregnancy test for all females of childbearing potential (if you can have a baby). If you are a female and your pregnancy test is positive you will not be allowed to enter the study.
- Blood will be drawn from a vein in your arm to help us to assess your general health and to see if you have ever been exposed to the varicella (chicken pox) virus, hepatitis B or hepatitis C. If either your hepatitis B or hepatitis C test result is positive you will not be able to participate in this study. You will need to have a second test done to make sure the results are the same and the study physician will tell you how to find medical help and counselling. Your health insurer or you will have to pay for the costs of the repeat test, follow up medical care, and/or counselling.
- If either your hepatitis B or hepatitis C test result is positive, it is state law that the results are reported to the State Department of Health. The test results will also be put in your medical record.
- Pulmonary Function Test (PFT): A PFT is a test that measure how well the lungs take in and exhale air and how efficiently they transfer oxygen into the blood. The test will include spirometry, which measures the amount of air you breathe in and out. For this test, you'll sit in front of a machine and be fitted with a mouthpiece. You'll also wear a nose clip to keep you from breathing air out through your nose. The respiratory technologist will explain how to breathe for the test. You may then breathe normally. Your doctor will ask you to breathe in and out as deeply or as quickly as you can for several seconds. They may ask you to breathe in a medication that opens your airways or breathe in certain gases such as oxygen, helium, or carbon dioxide. You'll then breathe into the machine again to see if the medication or gases affected your lung function.
- If a High-Resolution Computed Tomography (HRCT) test has been completed as part of your standard of care for your lung disease, the research coordinator will obtain and record the results of this test for research purposes.
- Brief Evaluation (history/physical): A complete medical and surgical history will be done which will include questions about your current and previous medications and information about your Syn-ILD. The research staff will take your height and weight and take vital signs (oral temperature, blood pressure, heart rate and respiration rate). The study physician will complete a physical examination.

- Screening to see if you are eligible will involve the collection and review of information from your medical record. You will be asked to sign a release of medical information at this visit to obtain your medical records. You will be asked about your vaccination history and whether you have had any boosters for the following: tetanus; diphtheria; influenza; pneumonia; varicella (chicken pox); measles; mumps; rubella; and hepatitis B.

The approximate amount of blood to be drawn at this visit will be 1/2 tablespoon.

If you qualify and want to participate in the study, you will be given instructions on when to come to the study center for Visit 1. A return appointment will be made for you within 1 to 14 days.

If longer than 14 days passes between the screening visit and Visit 1 you will be asked to complete a re-screen process.

All study visits will be conducted at the UPMC Arthritis and Autoimmunity Center located in the Falk Clinic. The research study staff will give you instructions where to report for the study visit appointments.

Visit 1 (Randomization Visit)

At visit 1 you will be randomized (assigned) to receive either the study drug Abatacept or a placebo which contains no active drug. You will have a 50:50 chance of receiving the study drug.

Group A will receive the study drug, abatacept 125 mg by subcutaneous (under the skin) injection every week for 24 weeks.

Group B will receive a placebo by subcutaneous injection every week for 24 weeks.

This study is double-blind, which means that you, the study doctor and the study staff will not know what Group you will assigned to or if you are receiving study drug or placebo. However, this information is available to the study doctor if needed in an emergency.

The following research procedures will be conducted at Visits 1, 3 and 6 unless otherwise noted:

- The study doctor will complete a brief physical exam to assess your overall health.
- Study staff will ask you to perform a timed physical function test to assess how far you can walk in six minutes.
- You will be asked to complete questionnaires that assess your level of activity, daily activities and symptoms that may be caused by your disease. These questionnaires usually take approximately 25-30 minutes to complete.

- The study doctor will manually test of your muscle strength and assess the overall activity related to your disease.
- You will be asked to complete a questionnaire that evaluates your shortness of breath while doing daily activities of living.
- Approximately 2 tablespoons of blood will be drawn from a vein in your arm for general laboratory tests (hematology, chemistry and muscle enzymes) to help us to assess your general health. An additional 2 tablespoons of blood will be obtained for later analysis and storage for research purposes.
- A urine pregnancy (if applicable) will be performed for all females with child bearing potential.
- You will be asked to wear a small physical activity monitor (PAM). The device will measure your physical activity behaviors over the course of the next 7 days. The research staff will provide you with the PAM device at this visit. The activity monitor must be worn for at least 10 hours/day for **a 7 days period each month for 6 months**. The monitor will be worn from the time of awakening to the time of going to sleep (exceptions include daily activities of bathing, swimming, etc.). You will also be asked to complete a Usage log that tracks the time and reason you may have taken the device off during that seven-day period.
- A pulmonary function test will be performed at **visits 2 and 3 only**.
- If a High-Resolution Computed Tomography (HRCT) test has been completed as part of your standard of care, the research coordinator will obtain and record the results of this test for research purposes at **visit 3 only**.
- **At visit 1 only**, you will be instructed on how to do the subcutaneous (under your skin) injection of the study drug. The study personnel will ask you to administer the first dose during this visit to demonstrate adequate understanding. Study drug will be dispensed to you at study visits 1 and 3 to continue weekly at home.

We are requesting your authorization to review your medical records to collect demographic and clinical data related to your disease. This data will be extracted from your medical record and used for research purposes to determine eligibility and to record clinical data to determine if the study drug is effective in managing your Syn-ILD disease. The data to be extracted will include: demographic information (age, race, ethnicity and sex) and clinical information (diagnosis, past medical history of other health conditions, disease specific laboratory results, results from High Resolution Computed Tomography (HRCT) scans performed as part of your usual care and pulmonary functions tests. All data recorded for research purposes will be assigned a random study code and stored indefinitely at the University of Pittsburgh, Division of Rheumatology database.

Unscheduled Visits: You will be seen for an unscheduled visit if any worsening in condition has occurred, that is, new symptoms have occurred during the treatment period, requiring a visit, emergency department evaluation or hospitalization.

The following research procedures will be conducted at an unscheduled visit:

- The study doctor will complete a brief physical exam to assess your overall health.
- You will be asked to complete questionnaires that assess your level of activity, daily activities and symptoms that may be caused by your disease. These questionnaires usually take approximately 25-30 minutes to complete.
- The study doctor will manually test of your muscle strength and assess the overall activity related to your disease.
- You will be asked to complete a questionnaire that evaluates your shortness of breath while doing daily activities of living.

Monthly Follow Up Calls:

Approximately one week after your first visit, the research coordinator will contact you to see if you have experienced any side effects from the injections or had any difficulty with administering the self -injection. Since research visits are conducted every three months, the study team will call you monthly in between visits 1, 2, 3, 4 and 5 to determine if you are experiencing any side effects or worsening in your condition. The follow up phone calls will take approximately five minutes of your time to complete.

Optional Open Label Follow Up Phase

If you have completed the 24-week randomized treatment phase or if your condition has worsened after 8 weeks, you will be given the option to participate in an open label follow up phase during which you would receive 24 weeks of study drug, abatacept in the same fashion you did in the initial randomized phase of the study. The open label phase consists of two study visits that would be conducted at the UPMC Arthritis and Autoimmunity Center located in Falk Clinic.

This phase of the study is optional and you will be provided an opportunity to consent to this optional phase at the end of this document. You have the right at any time during the course of the study to withdraw consent for the open label phase if you choose to do so. Withdrawing

consent to the open label phase will not affect your participation in the initial randomized phase of the study.

If you consented that you are willing to participate, the following study procedures would be performed at Visits 4 and 5:

The same study procedures that were performed at visits 1, 2 and 3 would be performed at these visits with the following exceptions:

- A pulmonary function test will be performed at **visits 5 only**.
- If HRCT was performed as standard of care, the results would be obtained from your medical record for research purposes at **visit 5 only.**
- The PAM device, would **not** be worn during the open label phase of the study.

How will data be transferred from the PAM device?

The PAM device will contain only de-identified data. Data will be extracted from this device on of the following ways: 1) You will be asked to download an application to your smartphone if you have one and the data will be synced a set times via a Bluetooth connection to the PAM website OR 2) if you do not have a smartphone you will be asked to download the application to your computer and plug the device into the computer at the end of each period of use to transfer the data to the website. The study center will create the de-identified accounts on the website when you are enrolled in the study. You will be provided the account login information to sync the device after each period of use during the course of the study.

The PAM device must be returned to the study center at the completion of the study or in the event of early termination.

The study visit schedule, approximate amount of research blood to be drawn at each visit and length of each visit is as follows:

	Study Phase				**Optional Follow Up**	
	Screening	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Time between visits (days)	0	+/- 14	90	90	90	90
Amount of blood (Tbsp.)	2	4	4	4	4	4
Length of visit (hours)	3		2	2	1	2

The total amount of research blood to be drawn for the study phase is approximately 14 tablespoons or 3/4 cup. If you chose to participate in the Open Label Phase an additional 8 tablespoons of blood will be obtained for research purposes.

Future Tests to be performed on Stored Research Specimens:

The collected samples will be stored indefinitely in a secure location at the University of Pittsburgh, Division of Rheumatology for future experimental studies. Blood specimens collected during the course of this trial will be labeled with a study code and contain no personal subject identifiers that could directly identify you.

The Specimen Repository samples will be used for two types of research: immunologic and genetic. The tests performed for this research are being conducted in a research laboratory, not a public certified laboratory. Therefore, you will not be informed of these results and they will not become part of your medical record.

Possible Types of Future Research tests include:

Samples will be used for immunological and genetic testing. Immunology research (study of all aspects of the immune system) tests to be performed on the stored blood are likely to include, but will not be limited to, testing for the presence or amount of immune substances (hormones of the immune system). Research involving immune substances will focus on the study of: 1) connective tissue disease (CTD) treatments, 2) the relationship of immune substances to the onset, features, and/or course of a CTD, and 3) comparison of immunologic substances between individuals with and without a CTD.

Genetic Research - Optional

The use of a blood sample for immunogenetic or genetic research of the CTDs is optional; it will involve only individuals who agree to the possibility of genetic research (see page 17). Tests may include:

a. Immunogenetic testing. This is testing for components of the immune system that are inherited.

b. Genetic analysis. While the exact nature of genetic research studies are not yet fully known, they may involve identifying inherited factors called genes that can: 1) increase

the risk of developing CTDs, 2) modify the severity of the disease, or 3) control components of the immune system (immunogenetic studies). Studies may also compare genetic factors of persons with and without a CTD.

Because the genetic material is stored in a research laboratory, results cannot be given to you. Also, the results of genetic or immunogenetic research will have no effect on your care, and will not become a part of the medical record. Analysis and storage of genetic material is coordinated by the University of Pittsburgh, Division of Rheumatology.

Your blood samples may be shared with other investigators within the University of Pittsburgh and other outside entities including Bristol Myers Squibb who is providing funding for this trial. The samples stored in the study repository do not contain any of your identifiable information.

What are the possible risks, side effects, and discomforts of this research study?

Risks Associated with Study Drugs
The subcutaneous (SC) form of abatacept is being studied for the treatment of a number of disorders including rheumatoid arthritis, psoriatic arthritis, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, systemic lupus erythematosus, and lupus nephritis. The reported adverse side effects are included below for all of the reported studies.

Common Adverse Events

Gastrointestinal: abdominal pain, diarrhea, indigestion and nausea.

Infections: bronchitis, urinary tract infection, upper respiratory tract infection, herpes simplex, ear infections and oral herpes.

Other: Generalized fatigue, injection site reactions, dizziness, headache and cough

Uncommon Adverse Events

Cardiac: bradycardia (slow heart rate), palpitations (rapid heartbeat) and tachycardia (increased heart rate).

Infections: Influenza-like illness, eye infection, pneumonia, herpes zoster (shingles/chicken pox), skin infection, lower respiratory tract infections, tuberculosis (lung infection), common cold, sinus infection and throat infection, stuffy nose, infected skin ulcer, nail fungus, tooth and kidney infection.

Gastrointestinal: stomach inflammation

Hematology: leukopenia (reduction in white blood cells), thrombocytopenia (deficiency of platelets in blood) and increased blood liver enzymes.

Psychiatric symptoms: anxiety, depression and difficulty sleeping.

Pulmonary: wheezing, chronic obstructive pulmonary disease (blockage of airflow) and difficulty breathing.

Musculoskeletal: pain in extremity and arthralgia (joint pain).

Skin conditions: skin rash, skin inflammation, dry skin, excessive sweating, itchy and/or redness of the skin and acne.

Other: dizziness, reduced visual acuity, mouth ulcers, increased weight, tingling and/or numbness, basal cell carcinoma (skin cancer), abnormal or heavy menstruation, hair loss, increased tendency to bruise, flushing, hot flush and low blood pressure and drug hypersensitivity.

If a serious allergic reaction or other serious hypersensitivity reaction occurs, administration of the study drug will be stopped immediately and no further study infusions will be given. Your doctor and/or nurse(s) will be carefully watching you for these reactions. The study site will have appropriate treatment(s) available for immediate use in the event of a severe allergic reaction during the administration of the study medication. You must tell them if you are having any unusual symptoms.

Very Rare Adverse Events

Sepsis (infection of the blood) and diverticulitis (digestive tract infection), sleep disorders, abnormal liver function test and lymphoma (cancer of lymph nodes).

Postmarketing side effects reported with abatacept: vasculitis (inflammation of blood vessels) was reported as an adverse event during post-approval use with abatacept in rheumatoid arthritis patients.

Injection site reactions: mild to moderate injection site reactions can occur and include: hematoma (solid swelling of clotted blood within the tissues), itchiness and redness of the skin.

Hepatitis B infection: In people who carry the virus in their blood. If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become active while you use abatacept. The study investigator will test your blood during the screening process to determine your past and present exposure to the hepatitis B infection.

Vaccinations: Abatacept may also cause some vaccinations to be less effective.

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.

Other Potential Side Effect of Research Procedures:

Physical Activity Monitor Use: There is the possibility of minor skin irritation associated with wearing the PAM device. There may be minor risk of skin irritation from use of the elastic belt if used with the PAM device. Keeping the band clean, dry and loosely fitting will help reduce this risk.

Blood Drawing: You may experience dizziness and/or fainting. You may experience pain, bruising and/or bleeding at the site of the needle insertion for blood drawing. Very rarely an infection may occur at the site. The risks related to the blood draw are minimized by the procedure being done by experienced individuals and the routine use of antiseptics and pressure dressings.

Risk of Breach of Confidentiality: Your study data and blood specimens collected during the course of the trial will be labeled with a study code and contain no personal identifiers that could directly identify you. The samples and study data will be stored in a secure location; however, there is a chance that a breach of confidentiality will occur and your personal or medical health information may be inappropriately distributed. Every effort will be made to ensure that this does not occur and the details of how your personal and health information will be handled during the study are detailed in a later section of this consent form entitled "Who will know about my participation in this research study?"

Data transferred from your PAM device will not contain any identifiable personal information. The data will be stored on a secure network server located in the Department of Medicine, Division of Rheumatology.

There is the possibility that if the results of the research studies involving your biologic samples or genetic material were to become known this information could affect your ability to be insured, your ability to be employed, reputation, and your future plans for children, or your family relationships. The study doctor will discuss this with you and answer any questions you may have.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information

beyond that collected for research purposes may be captured and used by others not associated with this study.

Reproductive Risks: The effect of the study drug on the unborn child is unknown. Pregnant or breast-feeding women cannot take part in this study. To prevent risk to the fetus, it is important that female participants or female partners of male participants take care to avoid becoming pregnant during this study. If you are female and can have a child, (that is you are not surgically sterilized or post-menopausal) you must have a negative pregnancy test at Visit 1, and the following must apply: Avoiding sexual activity is the only certain method to prevent pregnancy. However, females of child-bearing potential must be willing to use an appropriate method of birth control (such as female use of a diaphragm, intrauterine device (IUD), or contraceptive sponge, in addition to male use of a condom) or the female should be using prescribed "birth control" pills, injections, or implants throughout the study. Even with use of these birth control measures, pregnancy could still result. The risks of receiving the study drug while pregnant include potential loss of pregnancy or possible birth defects. Females of childbearing potential will undergo a urine pregnancy test prior to every study visit (screening and visits 1 – 5).

Consequences of additional therapy restrictions: You will be asked to contact the investigator regarding any deterioration in their condition. New symptoms occurring during the treatment period requiring an unscheduled physician visit, emergency department evaluation, hospitalization or change in immunosuppressive therapy will be evaluated by the principal investigator. Determination will then be made by the principal investigator if additional medication is necessary.

Hepatitis B and C blood testing: The hepatitis testing requires the drawing of blood. Being tested for hepatitis may cause anxiety regardless of the test results. A positive test means you have been infected with the hepatitis B or C virus. Receiving positive results may make you very upset. If other people learn about your positive test results, you may have trouble obtaining insurance or employment. There is always the possibility the test result is wrong and therefore a repeat test would be done as previously mentioned in this consent form.

Genetic Samples: It would be rare (less than 1% of cases or in less than 1 out of 100 cases) that if the results of the research studies involving your genetic material were to become generally known this information could affect your ability to be insured, your ability to be employed, your future plans for children, or your family relationships.

6 Minute Walk Test Risks: The common risks associated with this functional test may include changes in your blood pressure and heart rate, as well as shortness of breath, decrease in your oxygen levels and fatigue.

If you have pre-existing heart condition, there is a rare chance that you could experience a arrhythmias (irregular heart rhythm), fainting, heart attack or stroke.

To minimize these risks the study staff will monitor your symptoms throughout the test. If you begin to experience any adverse symptoms, the test will be stopped.

Pulmonary Function Testing (PFT's): PFTs are usually safe for most people. However, because the test may require you to breathe in and out quickly, you may feel dizzy and there is a risk that you might faint. If you feel lightheaded, tell your doctor performing the test. The test may cause you to have an asthma attack if you have asthma. In very rare cases, PFTs may cause a collapsed lung.

What are the potential benefits from taking part in this research study?

A possible benefit of this study may be an improvement in your disease symptoms. However, there may be no direct benefit to participants in this study who may receive placebo. There is no guarantee that you will receive any personal benefit from participating in this research study. It is hoped that the information gained from the study will be beneficial to patients in the future. Because of your participation, there may be advancement in knowledge about anti-synthetase-associated interstitial lung disease (Syn-ILD) and responses to abatacept drug administration.

What treatment or procedures are available if I decide not to take part in this research study?

You do not have to participate in this study to receive treatment for your condition. If you decide not to take part in this study or are withdrawn from the study, you have the option of having your personal doctor manage your disease using available drugs or treatments. The study doctor will discuss these alternative options with you.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

You will be promptly notified if any new information (either good or bad) develops during the conduct of this research study which may cause you to change your mind about continuing to participate. If new information is provided to you, your consent to continue participation in this study will be re-obtained.

Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study?

You or your insurance will not be billed for any research procedures conducted as part of this study. These procedures include: physical examination, study visits, laboratory tests,

pulmonary function tests and other study related costs and will be paid by the study except where noted below. The study drug will be provided and there will be no cost to you for the study drug abatacept. You and/or your insurance will be billed for standard of care costs (not study related) or emergent care that you receive and you will be responsible for costs not covered by your insurance provider. You will be responsible for any applicable co-pays, co-insurances, and deductibles.

Will I be paid if I take part in this research study?

At each visit 1 through 5, you will receive $25.00 as payment for your participation. Participants completing all study visits will receive a total of $125.00.

Who will pay if I am injured as a result of taking part in this research study?

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 may 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. You do not, however, waive any legal rights by signing this form. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below. You will not receive any monetary payment for, or associated with, any injury that you suffer in relation to this research.

Who will know about my participation in this research study?

Any information about you obtained from or for this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in locked file cabinets. Your identity on these records will be indicated by a code number rather than by your name, and the information linking these code numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of research results unless you sign a separate form giving your permission (release). The University of Pittsburgh policy requires that all research records be kept for seven years following the end of a research study.

Your study data (information) and a scanned copy of your signed consent document will be stored in a research database (RDMS – Rheumatic Disease Management System) located at the University of Pittsburgh, Division of Rheumatology. The RDMS database is located on a secure server with limited access via network firewall. Your identity on this research data will be

indicated by a code number as indicated above. The only identifiable information that will be stored in this database is an electronic copy of your consent to participate in this study.

Will this research study involve the use or disclosure of my identifiable medical information?

This research will involve the recording of current and/or future identifiable medical information from your hospital and/or other (e.g., physician office) records. The information that will be recorded will be limited to information concerning the laboratory and pulmonary function testing that you will be scheduled to undergo for screening and follow up procedures, the results of these tests and any adverse events that may have been associated with them. This research will result in identifiable information that will be placed into your medical records held at University of Pittsburgh Division of Rheumatology Offices. The nature of the identifiable information resulting from your participation in this research study that will be recorded in your medical record includes the results of laboratory and pulmonary testing and treatment and any adverse events that may occur as a result of the study drug.

Who will have access to identifiable information related to my participation in this research study?

In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study.

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.

1. Authorized representatives of Bristol Myers Squibb who are the source of funding and study drug and representatives from the University of Pittsburgh acting as the Clinical Coordinating Center for this study will review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analysis of the research data.

Authorized representatives of the U.S. Food and Drug Administration may review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy of the research data. While the U.S. Food and Drug Administration understands the importance of maintaining the confidentiality of your identifiable research and medical information, the University of Pittsburgh and UPMC cannot guarantee the confidentiality of this information after it has been obtained by the U.S. Food and Drug Administration.

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g. diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (e.g. quality assurance).

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?

The investigators may continue to use and disclose, for purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for a minimum of 7 years and for as long (indefinite) as it may take to complete this research study.

May I have access to my medical information that results from my participation in this research study?

In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider unless otherwise specifically stated below.

You agree that, while the study is still in progress, you may not be given access to medical information about you that is related to the study. This may include, for example, information about whether you are receiving study drug that is “blinded” (that is, kept secret during the study to prevent bias). While a request for access to medical information can be denied, the study doctor and staff will not automatically deny a request, but will consider whether it’s medically appropriate under the circumstances to allow access. Your agreement that you may be denied access to your study-related medical information during the study will not be used to deny you access to that information after the study is completed at all locations and study results are analyzed. As previously stated you will not be permitted access to results of the genetic analysis of blood.

Is my participation in this research study voluntary?

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study). Whether you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether you provide your consent for participation in this research study will have no effect on your current or future care at UPMC hospitals or affiliated health care provider or your current or future relationship with a health care insurance provider.

Your physician is involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

May I withdraw, at a future date, my consent for participation in this research study?

You can, at any time withdraw from this research study; you can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

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 I agree to take part in this research study, can I be removed from the study without my consent?

No guarantee is made as to the results of your participation in this study. If certain circumstances were to occur, the physician may stop the study medication and your participation in this study may

be terminated without your permission. These circumstances would be related to either your failure to cooperate fully with the conduct of the study, or the recognition of significant medical risks associated with your continued participation in this study. If your participation in this study is stopped, the reasons will be discussed with you.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Voluntary Consent

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given.

I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. 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 agree to participate in this research study, and authorize Dr. Aggarwal and the members of his research team to access my medical records for the purpose described in this document. A copy of this consent form will be given to me.

PLEASE ANSWER THE QUESTION BELOW BEFORE SIGNING:

Do you agree to the use of a blood sample sample for genetic research? (Please circle response below)

Yes No _____ _____
Subject initials Date

Do you agree to participate in the open label phase of the trial? (Please circle response below)

Yes No _____ _____
Subject initials Date

_____
Printed Name of Participant

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

3500 Terrace Street
BST South Wing, 7th Floor
Pittsburgh, PA 15261
(412) 383-8000

_____ _____
Participant's Signature Date

INVESTIGATOR CERTIFICATION:

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 if placed in medical record)

QUESTIONS ABOUT THE STUDY:

If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

You can contact the study investigator if you have any questions about the study, concerns or complaints. Contact Principal Investigator, Dr. Aggarwal at 412-647-2804 or the Study coordinator at 412-383-8674.