

What are your costs to be in this study?

You or your insurance company will be charged for continuing standard medical care, hospitalization, tests and treatments of any side effects of sirolimus, and any referrals to other specialists that are made during the course of this study. You may want to check with your insurance company to determine whether costs associated with this drug are covered. In the event that your insurance does not cover them, you may incur additional costs because of treatment side effects.

All study related tests will be provided free of charge. These tests may include: chest x-ray, sirolimus level, oximetry, lung function tests, blood tests, and urine tests. Study medication (sirolimus or placebo) will be provided free of charge by Wyeth, a drug manufacturer.

What are your rights as a participant in a research study?

Your participation in this research study is completely voluntary. Your decision whether or not to participate in this study will not result in any penalty or loss of benefits to you. If you decide not to participate in the study, or if you decide to leave the study before it is over, standard medical care will still be available to you.

How can you get more information about this study and about LAM?

For more information about the MILES Trial, please visit: www.thelamfoundation.org/LAM_Treatment.htm#summary

For more information about LAM, please contact the LAM Foundation at (513) 777-6889 or visit their web site: www.thelamfoundation.org

Another source of information is the Rare Lung Diseases Consortium. Their web site is: www.rarediseasesnetwork.org

Where can you participate in this study?

Institutions participating in this study include Oregon Health and Sciences University (Portland, OR), National Jewish Medical and Research Center (Denver, CO), Brigham and Women's Hospital (Boston, MA), University of Texas Health Center (Tyler, TX), Cleveland Clinic (Cleveland, OH), Medical University of South Carolina (Charleston, SC), Cincinnati Children's Hospital Medical Center (Cincinnati, OH), University of Florida (Gainesville, FL), National Heart, Lung, and Blood Institute (Bethesda, MD), University of Toronto (Toronto, Canada), and National Kinki-Chou Hospital (Osaka, Japan).

This trial is supported by:

The National Center for Research Resources (NCRR) Rare Lung Diseases Consortium (RLDC), the LAM Foundation, the Tuberosus Sclerosis Alliance, Wyeth Pharmaceuticals, and the Adler Family Foundation.

How can you learn about enrolling in the MILES Trial?

Please contact:

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The MILES Trial

Multicenter International
Lymphangiomyomatosis
Efficacy of **Sirolimus**

What is LAM?

Lymphangioleiomyomatosis (LAM) is a rare lung disease affecting almost exclusively women in which abnormal muscle cells grow in the walls of the airways and blood and lymph vessels. Over time, these cells can block the flow of air and blood to and from the lungs, making it hard for the lungs to supply oxygen to the body. LAM occurs in about 33% of women with tuberous sclerosis, an inherited disease that is associated with epilepsy, delayed development, and kidney tumors, and also in women who do not have tuberous sclerosis.

What is the purpose of this study?

The goal of the MILES Trial is to determine whether a medication called sirolimus improves lung function in patients with LAM. Sirolimus is approved by the United States Food and Drug Administration (FDA) to help prevent rejection in patients who receive kidney transplants. It does this by inhibiting the immune system's attack on the transplanted organ. Laboratory studies in animals have shown that sirolimus also suppresses tumor growth in tuberous sclerosis and LAM models. The use of sirolimus to treat tuberous sclerosis and LAM is experimental and has not been approved by the FDA.

Patients in this study will be randomly assigned to receive either sirolimus or a placebo (a sugar pill). This is a blind study: neither patients nor researchers will know whether patients are receiving the study drug or the placebo while the study is in progress.

After 100 participants have been enrolled in the study for one year, the Data and Safety Monitoring Board will evaluate the data collected. If sirolimus is found to significantly improve lung function, those patients taking the placebo will be offered sirolimus for the second year of the study.

What is involved?

This study will last approximately two years. Patients will take either sirolimus or a placebo every morning. The initial dose, which may be adjusted during the study, is two 1-mg pills.

Patients will make two visits to the research center at the time of enrollment, another visit three weeks after enrollment, and then one visit every three months for the first year of the study. During the second year of the study, patients will make one visit every six months. Each visit will take approximately four to six hours. Study visits may include: a physical exam, the completion of questionnaires, pulmonary function tests, a chest x-ray, a volumetric chest CT scan, blood draws, and urine tests. Patients may also receive follow-up telephone calls from the study coordinator. A detailed schedule will be provided to patients before they enroll in the study.

Patients will be asked to keep records of all medication they take during the study, including the study medication and any prescription or over-the-counter medications.

What are the benefits?

If you agree to take part in this research study, there may not be a direct medical benefit for you. You may benefit from the physical exams, pulmonary function tests, and other study procedures. Potential benefits for you may include stabilization or improvement in your lung function. Other potential benefits may include stabilization or decrease in the size of any angiomyolipoma (kidney tumor), or improvement in other problems caused by having tuberous sclerosis (if you have this disorder in addition to LAM). The information learned from this research study may benefit other patients with lymphangioleiomyomatosis in the future.

What are the risks?

There are potentially serious risks associated with this study. A member of the research staff will discuss the potential risks of the study in detail with you before you enroll.

You may be eligible to participate if:

- You are 18 years of age or older.
- You have been diagnosed with lymphangioleiomyomatosis (LAM).
- Your lung function is abnormal (forced expiratory volume in one second of less than or equal to 70% of predicted).

You should not participate if you:

- Are pregnant, plan to become pregnant within the next two years, or are breastfeeding.
- Have serious heart, liver, blood, or kidney disease.
- Have had surgery requiring stitches or entry into a body cavity in the last two months.
- Have taken an investigational (research) drug within the last 30 days.
- Have had a lung transplant or are actively awaiting a lung transplant.
- Know that you have an allergy to sirolimus.
- Have a large chylous fluid collection in your chest or abdomen that could interfere with lung function testing.

Will you be compensated for your participation?

You will not receive any financial compensation for your participation in the research study.

The LAM Foundation has allocated funds to reimburse study participants for allowed travel expenses. You will receive a description of the Foundation's travel assistance program.