MC1125 / 11-001987

A Phase I-II Trial of Combined PKCι and mTOR Inhibition for Patients with Advanced or Recurrent Lung Cancer (NSCLC and SCLC) without Standard Treatment Options

NCT01737502

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MAYO CLINIC

Name and Clinic Number

IRB # **11-001987 00**
Consent form approved **September 28, 2022**;
This consent valid through **September 27, 2023**;

1. General Information About This Research Study

Study Title: MC1125, A Phase I-II trial of combined PKCι and mTOR inhibition for patients with advanced or recurrent lung cancer (NSCLC and SCLC) without standard treatment options

Name of Principal Investigator on this Study: Dr. **Yanyan Lou** and Colleagues

A. Study Eligibility and Purpose

You are being asked to take part in this research study because you have advanced or recurrent lung cancer (non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC)). The primary purpose of your participation in this study is to help answer the following research questions:

- To find out what effects (good or bad) the drugs Auranofin and sirolimus have on you and your lung cancer;
- To find out if Auranofin and sirolimus can stop or slow the growth of your lung cancer;
- To learn more about how Auranofin and sirolimus work against lung cancer by testing blood and tissue samples.

The drugs used in this study are considered investigational for lung cancer. Both study drugs are approved for other diseases.

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide. If you decide to participate, you may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

B. Number of Participants

The plan is to have 47 people take part in this study at Mayo Clinic.

C. Additional Information You Should Know

A grant from the National Cancer Institute is funding the study. This grant will pay Mayo Clinic to cover costs related to running the study.

2. What Will Happen To You While You Are In This Research Study?

If you agree to be in the study, you will be asked to participate in the following:

Before you start any study treatment, you will have certain tests and procedures to determine if you can take part in this study. The researcher will look at your medical history, you will have a physical exam, and you will have standard blood tests and a urine test done. If you are a woman who can become pregnant, you will also have a pregnancy test.

Treatment on this study will follow a 4-week schedule, and each 4-week period is known as a "cycle." You will take auranofin and sirolimus by mouth every day. During your first week of medication you will only take the auranofin and will start the sirolimus on day 8. Every cycle of treatment thereafter you will take both drugs by mouth every day. Before the 8th week, your doctors will do tests to see how your cancer is responding to the study treatment. If it stays the same or is helped you will continue to get study treatment but if your cancer gets worse you will be taken off study treatment. If you are responding and stay on the study, you will have tests to see whether your cancer is growing about every 8 weeks. If you come off study treatment, your cancer doctor will talk to you about other treatment options.

Each week during the first cycle of treatment, you will have a blood test (approximately 1 tablespoon of blood) and urine test completed. These tests are needed to measure your blood cell counts and blood chemistries and the protein in your urine. These tests will be repeated about every four weeks while you continue to participate in the study.

You will continue to receive oral auranofin and sirolimus treatment until your disease gets worse and then the treatment will be stopped.

You will be given a diary to record when you take auranofin and sirolimus study drug. While you are on this study you should avoid food and beverages containing grapefruit. Your study doctor can discuss this with you.

3. How Long Will You Be in This Research Study?

You may remain in this study as long as you wish if you are not experiencing serious side effects and your cancer does not get worse. Your health status will be evaluated regularly and the results will be shared with you.

4. Why You Might Want To Take Part In This Research Study

This study may not make your health better. However, your participation in this research study may help develop a new medication for the treatment of Non-Small Cell Lung cancer that might benefit other cancer patients in the future.

5. What Are the Risks Of This Research Study?

Sirolimus

Likely risks of sirolimus (events occurring greater than 20% of the time)

- High blood pressure (Hypertension)
- Headache
- Pain
- Insomnia
- Acne
- Increased fats in blood stream (Hypertriglyceridemia)
- High blood cholesterol (Hypercholesterolemia)
- Low blood potassium levels (Hypokalemia)
- Low blood phosphorous levels
- Trouble passing stools (Constipation)
- Loose stools (Diarrhea)
- Indigestion or heartburn (Dyspepsia)
- Feeling sick to your stomach (Nausea)
- Throwing up (Vomiting)
- Infection
- Decreased number of blood cells (platelets) that help to clot the blood which could increase risk of bleeding (Thrombocytopenia)

- Decrease in red blood cells, which are the oxygen carrying cells, which could make you feel tired (Anemia)
- Joint pain (Arthralgia)
- Shortness of breath (Dyspnea)
- Weakness
- Tremor
- Reduced kidney function or Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)

Less likely risks of sirolimus (events occurring less than or equal to 20% of the time)

- Poor wound healing
- Pale or reddened irregular, elevated patches of skin and severe itching, hives
- Wide-spreading inflammation and/or rash that goes deep into the skin.
- Collection of fluid in the body overall, and/or in the facial area (edema or swelling of the face, hands or feet)
- Collection of fluid or blood in the lungs
- Catheter infection
- Infection in the bloodstream
- Fungal yeast infection
- Urinary tract infection
- Conjunctivitis (infection around the eye, also called pink eye)
- Recurrence of herpes simplex infection, which may cause sores in the mouth or on the lips, inflammation of the gums and throat, and recurrence of genital herpes
- Inflammation of the tongue
- Mouth pain
- Low calcium in the blood that can result in muscle cramps, abdominal cramps, spasms
- Elevated levels of phosphorus in the blood
- Confusion
- Dizziness
- Inability to sleep, or abnormal wakefulness
- Depression
- Dehydration
- Distention/bloating of the belly
- Weight loss
- Anxiety (nervousness)
- Fast heart rate
- Tingling in fingers and toes
- Chest pain not heart-related
- Decreased number of a type of white blood cell (neutrophil/granulocyte)
- Abnormal control of blood sugar level
- Sleepiness

- Problem of the sinuses
- Dry Skin

Rare but serious risks of sirolimus (events occurring less than 2-3% of the time

- A condition in which fluid and proteins leak out of tiny blood vessels and flow into
- surrounding tissues, resulting in dangerously low blood pressure which may lead to multiple organ failure and shock
- Blood clot in vein or artery (Deep venous and arterial thrombosis)
- Abnormal liver function tests/Liver failure
- Hypersensitivity reaction
- Infection that has spread to the bloodstream and can cause low blood pressure, fever, and/or death (Sepsis)
- Cancer of lymph nodes (Lymphoma)
- Kidney failure (Renal failure)
- Inflammation of the tissue and space around the air sacs of the lungs (Interstitial pneumonitis)
- Bleeding from the lungs or respiratory tract (Pulmonary hemorrhage)
- Exfoliative Dermatitis

Sirolimus may cause active immunizations to be less effective. Thus, the use of live vaccines should be avoided while taking sirolimus.

Auranofin

Likely risks of Auranofin (events occurring greater than 20% of the time)

- Rash
- Loose stools or diarrhea

Less likely risks of Auranofin (events occurring less than or equal to 20% of the time)

- Abdominal pain
- Weight loss due to reduction of appetite (Anorexia)
- Flatulence
- Indigestion or heartburn (Dyspepsia)
- Nausea with or without vomiting
- Unpleasant sensation that causes the need to scratch (Pruritis)
- Inflammation of the stomach (Stomatitis)
- Inflammation or infection of the lining of the eyelids (Conjunctivitis)
- Excess serum proteins in the urine (Proteinuria)

Rare but serious risks of Auranofin (events occurring less than 2-3% of the time)

- Constipation
- Alteration in the sense of taste (Dysgeusia)
- Hives (Urticaria)
- Hair Loss
- Inflammation of the tongue (Glossitis)
- Decrease in number of red blood cells (Anemia)
- Decrease in the number of white blood cells (Leukopenia)
- Decrease of platelets in blood (Thrombocytopenia)
- Higher than normal level of white blood cells (Eosinophilia)
- Presence of red blood cells in the urine (Hematuria)
- Elevated liver enzymes
- Rapid swelling of the tissues just below the surface of the skin (Angioedema)
- Inflammation of the gums (Gingivitis)
- Bone marrow does not produce enough new cells to replenish blood cells (Aplastic anemia)
- Low number of neutrophils (Neutropenia)
- An acute disease characterized by high fever, lesions of the mucous membranes and skin, and a sharp drop in circulating granular white blood cells (Agranulocytosis)
- A type of anemia caused by selective depletion of erythroid cells (Pure red cell aplasia)
- Abnormal depression of all the cellular elements of the blood (Pancytopenia)
- Skin and the whites of the eyes are discolored yellow due to an increased level of bile pigments in the blood (Jaundice)
- Inflammation of the tissue and space around the air sacs of the lungs (Interstitial Pneumonitis)
- Damage to nerves of the peripheral nervous system (Peripheral Neuropathy)
- Gold deposits in the lens or cornea unassociated clinically with eye disorders or visual impairment

As with any medication, allergic reactions are a possibility.

The risks of drawing blood include pain, bruising, and rarely, infection at the site of the needle stick.

Risks of Biopsy: The risks of biopsies include, pain, bruising, bleeding and infection at the biopsy site.

Standard of care risks

Your doctor will discuss the risks of radiographic imaging (CT scans, MRIs, X-rays and standard blood tests) as these tests and procedures are part of your standard clinical care.

Pregnancy and Birth Control:

1) Will women of child-bearing-potential be allowed to participate in this study?

   Yes: Women of child-bearing-potential will be able to participate in this study if they have a negative pregnancy test and agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

2) Will pregnant and/or nursing women be allowed to participate in this study?

   No: There is not enough medical information to know what the risks might be to a breast-fed infant or to an unborn child carried by a woman who takes part in this study. Breast-feeding mothers must stop breast-feeding to take part in this study.

3) Do you need to have a pregnancy test done to be part of the study?

   Yes: As part of this study a pregnancy test is required for all women who are able to become pregnant.

   A blood pregnancy test will be done by taking blood from your arm.

   You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

4) Will men who are able to father a child be allowed to participate in this study?

   Yes: Men who are able to father a child will be able to participate in this study if they agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

5) What types of birth control are acceptable?

   Surgical sterilization
   Approved hormonal contraceptives (such as birth control pills, Depo-Provera)
   Barrier methods (such as a condom or diaphragm) used with a spermicide
   An intrauterine device (IUD)
   Abstinence

Risk summary

Many side effects go away shortly after sirolimus and/or auranofin are stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death.

Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

6. What Other Choices Do You Have If You Don't Take Part In This Research Study?

You do not have to be in this study to receive treatment for your condition. Your other choices may include:

- Another chemotherapy
- Other investigational drugs
- No anti-cancer therapy with full supportive care for your symptoms (sometimes called comfort or palliative care)
- Other care measures to manage your symptoms that may include pain, infection, nausea, vomiting, etc., will be offered to you, as needed, regardless of whether you participate in this trial.

You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.

7. Are There Reasons You Might Leave This Research Study Early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo may stop you from taking part in this study at any time:

- If it is in your best clinical interest,
- If you do not follow the study procedures,
- If the study is stopped.

8. Will You Need To Pay For Any Of The Tests And Procedures?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Research tissue samples (baseline and end of treatment, if applicable)
- Oral Sirolimus and Auranofin (daily)
- Lipid panel at baseline, prior to cycle 2, and every other cycle through cycle 6

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care. These tests and procedures are:

- Physical exams (baseline and every 4 weeks and end of treatment)
- Routine Blood Tests (baseline, weekly during cycle 1, every 4 weeks and end of treatment)
- PET/CT or CT scans (baseline, every 8 weeks and end of treatment)
- Urine tests (baseline and every 4 weeks and end of treatment)
- Serum pregnancy test (baseline)
- Tumor biopsy at the end of treatment if your disease progresses
- Lipid panel as clinically indicated

If you have study related questions regarding billing, insurance or reimbursement, stop by:

Arizona: The concourse level Patient Financial Services office or call this office at (800) 603-0558.

9. Will You Be Paid For Participating In This Research Study?

You will not be paid for taking part in this study.

10. What Happens If You Are Injured Or Ill Because You Were In This Research Study?

If you have side effects from the study treatment, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will bill you or your insurer for these services at the usual charge. Mayo will not offer free medical care or payment for any bad side effects from taking part in this study.

11. What Are Your Rights If You Are In This Research Study?

Taking part in this research study will not change your rights and benefits. Taking part in this research study does not give you any special privileges. If you decide to not participate in this study, or stop in the middle of the study, no benefits are taken away from you. You do not have to be in this research study to receive or continue to receive medical care from Mayo Clinic.

You will be told of important new findings or any changes in the study or procedures that may affect you or your willingness to continue in the study.

12. What About Your Privacy?

Authorization To Use And Disclose Protected Health Information

Your privacy is important to us, and we want to protect it as much as possible. By signing this form, you authorize Mayo Clinic and the investigators to use and disclose any information created or collected in the course of your participation in this research protocol. This information might be in different places, including your original medical record, but we will only disclose information that is related to this research protocol for the purposes listed below.

This information will be given out for the proper monitoring of the study, checking the accuracy of study data, analyzing the study data, and other purposes necessary for the proper conduct and reporting of this study. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you.

This information may be given to other researchers in this study, including those at other institutions, or private, state or federal government parties or regulatory authorities in the USA and other countries responsible for overseeing this research. These may include the Food and Drug Administration, the Office for Human Research Protections, or other offices within the Department of Health and Human Services, and the Mayo Clinic Office for Human Research Protections or other Mayo groups involved in protecting research subjects.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

This information may include information relating to sexually transmitted disease, acquired immunodeficiency syndrome (AIDS), or human immunodeficiency virus (HIV). It may also include information relating to behavioral or mental health services or treatment and treatment for substance abuse

If this information is given out to anyone outside of Mayo, the information may no longer be protected by federal privacy regulations and may be given out by the person or entity that receives the information. However, Mayo will take steps to help other parties understand the need to keep this information confidential.

This authorization lasts forever.

You may stop this authorization at any time by writing to the following address:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

If you stop authorization, Mayo may continue to use your information already collected as part of this study, but will not collect any new information.

If you do not sign this authorization, or later stop authorization, you may not be able to receive study treatment.

13. What Will Happen to Your Samples?

Your tissue sample will be kept at Mayo for use in this study. Researchers at Mayo who are not involved with this study may ask to use your sample for more research. You have a say in how your stored sample is used in future research. You can still take part in the study without giving your sample for future use.

Identification information:
If you agree to allow your sample to be used for further research, the sample may be stored forever. The sample will be stored at Mayo and would be given a code (instead of your name) while it is stored and when it is used in research. This code allows your sample to be used without anyone knowing that it is your sample just by looking at the label.

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you will not be offered a share in any profits.

Risks:
Some future studies may be for testing the genes you inherited from your parents (also known as genetic testing). If a researcher finds that future test results may be useful for your health care, you will be contacted and given the choice to learn the test results. At that time, you will be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or family conflicts from learning unknown information about your parents or blood relatives. Test results will only be put into your medical record if you chose to learn the results. Sometimes results should be released only through a genetic counselor, who can help explain the possible risks and benefits of learning the results.

Exceptions when your samples may be used without your permission:

1) When government rules allow your sample to be used without identifying you, even with a code.
2) When use of the sample is not considered human subject research.

At all other times:
-You can let Mayo use your sample.
-You can say NO to have your sample used by Mayo.

Please read the following statements and mark your choice:

1. I permit my tissue sample to be stored and used in future research of lung cancer at Mayo:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my tissue sample to be stored and used in future research at Mayo to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

Who will use your sample?
If you agree to give your sample, it will be the property of Mayo and may be used for research by the investigators and other staff at Mayo Clinic. Researchers at other institutions may also ask for a part of your sample for future studies.

If you want your sample destroyed at any time, write to:
Yanyan Lou, MD
Mayo Clinic in Florida
4500 San Pablo Road
Jacksonville, FL 32224

If you move please send your new address to:
Mayo Clinic in Arizona
Section of Registration
13400 East Shea Boulevard
Scottsdale, AZ 85259

14. Who Can Answer Your Questions?

You can call …	At …	If you have questions concerns about …
Principal Investigator: Dr. Panayiotis Savvides (Arizona) Yanyan Lou, M.D., PhD (Florida)	**Phone:** (480) 301-8000 **Phone:** (904) 953-2000	**Questions about the study tests and procedures** **Research-related injuries or emergencies** **Any research-related concerns or complaints**
Mayo Clinic IRB **Research Subject Advocate**	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	**Rights of a research subject** **Use of Protected Health Information** **Any research-related concerns or complaints**
Patient Account Services	**Toll Free:** (844) 217-9591	**Billing / Insurance Questions**

15. Summary and Enrollment Signatures

You have been asked to take part in a research study at Mayo Clinic. The information about this study has been provided to you to inform you about this study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I am satisfied that I have been given enough information about the purpose, methods, risks, and possible benefits of the study to decide if I want to join.
- I know that joining the study is voluntary and I agree to join the study.
- I know that I can call the investigator and research staff at any time with any questions or to tell them about side effects.
- I know that I may withdraw from the study at any time.
- A copy of this form will be put in my medical records and I will be given a copy of this completed form.

Please sign and date to show that you have read all of the above guidelines. Please do not sign unless you have read this entire consent form. If you do not want to sign, you don't have to, but if you don't you cannot participate in this research study.

(Date / Time)	(Printed Name of Participant)	(Clinic Number)

(Signature of Participant)

(Date / Time)	(Printed Name of Individual Obtaining Consent)

(Signature of Individual Obtaining Consent)