Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer

NCT04515004

December 8, 2022

VA | U.S. Department of Veterans Affairs	**Agreement to Participate in Human Subject Research** IRB Protocol #: **H220087**
Study Title: Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer	
Principal Investigator: Jenny T. Mao, M.D.	
VA Facility: VA San Diego HealthCare System	

Participant Name**:**	Date**:**

STUDY SUMMARY

You are being asked to participate in a research study. This section summarizes key information about this study to assist you, or your legally authorized representative, in understanding the reasons why you may or may not want to participate in the research. Your participation is voluntary. You may refuse to participate or withdraw at any time. You will not lose any services, benefits or rights you would normally have if you chose not to volunteer. Carefully review this section and the detailed information that follows before you agree to participate.

WHAT IS THE STUDY ABOUT AND WHY ARE WE DOING IT? The purpose of this research is to gather information on the safety and effectiveness of a standardized grape seed extract supplement, leucoselect phytosome, as a pre-surgical experimental therapy in patients with early stage lung cancer. It is being funded by the Department of Veterans Affairs.

WHAT DOES THE STUDY INVOLVE AND HOW LONG WILL IT LAST?

- If you are diagnosed with early stage lung cancer and will not be receiving immune therapy and chemotherapy before your surgery, you will be given the extract to take prior to your lung cancer surgery.
- We will collect your health information and some tissue samples collected from your clinical procedures.
- We will collect new lung tissue and tumor samples for research at the time of your surgery.
- Blood and urine samples will be collected at screening, initial enrollment and follow up visits.
- We will contact you by phone or you will come into the clinic to complete questionnaires about how you are feeling while you are taking the grape seed extract and after your surgery.
- You will be in the study for a total of around 4 years, including clinic visits and follow-up phone calls.
- You will be asked if we may keep all of the data and samples collected from you for future research. This is required for you to be in the study.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY? You are being asked to participate in this study because abnormalities have been found in your lungs that may be cancer and you will be undergoing standard clinical diagnostic procedures. If lung cancer is found, you may be eligible to enroll and receive study drug for about 2-3 weeks before your lung cancer surgery. By doing this study, we hope to learn more about the effects of leucoselect phytosome on you and your body's ability to fight lung cancer. If you agree to take part in this study, there may not be any direct medical benefit to you. There may be possible benefits from treatment of lung cancer including preventing recurrence, but this is unknown. We hope the information learned from this study will benefit other people at risk of lung cancer in the future.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY? Your participation in this study is completely voluntary. In March 2022, the Food and Drug administration (FDA) has approved a new pre-surgical Immunochemotherapy known to benefit certain early stage lung cancer patients. You should talk to your treating provider about this standard care option. If you qualify for and decide to undergo immunochemotherapy, you will not be eligible to participate in the treatment portion of the study.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS? The person in charge of the study is Dr. Jenny T. Mao of the VA San Diego Healthcare System. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact: 858-552-8585 ext. 7347.

Study Title: Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer

Principal Investigator: Jenny T. Mao, M.D.

VA Facility: VA San Diego HealthCare System

RESEARCH DETAILS

WHO IS CONDUCTING THIS RESEARCH AND WHY? Jenny T. Mao, M.D. is asking for your consent to this research. The study is sponsored by the VA Clinical Science Research and Development.

The purpose of the research is to determine what effects, good and bad, Leucoselect phytosome has on you. Studies done with animals have shown that dietary grape seed extract has anticancer effects, including inhbition of lung cancer growth or development. Leucoselect physotosome has been available over the counter for decades, mainly being used to promote heart and blood vessel health. Recently a small phase I clinical study using leucoselect phytosome in heavy active and ex-smokers at high risk of developing lung cancer has shown potential preventive benefits, thereby setting the stage for this early phase IIa study to determine its potential for enhancing the probability of a cure and reducing the chance of a recurrence. About 30 people will be enrolled in this study at the VASDHS.

The use of leucoselect phytosome is investigational, which means that it is not approved by the Food and Drug Administration (FDA).

FOR HOW LONG WILL I BE IN THE STUDY? If you are eligible for the entire study, you will be in the study for up to approximately 4 years. Approximately 10-15 hours of your time will be needed to complete the entire study. After you complete the study drug, there will be follow up over the phone at approximately 3-4 weeks, 6 months and annually for up to 4 years. If you have side effects thought to be related to the study drug, you will be followed by telephone or visits to the clinic until the side effects go away.

Summary of visits and follow up schedule:

Study Day	0	1	7	14-21	18-28	39-52	225	405	770	1135	1500
Visit #	**1(S)**	**2**	**3(P)**	**4**	**5**	**6(P)**	**7(P)**	**8(P)**	**9 (P)**	**10(P)**	**11(P)**
History & Physical exam	x	x	x	x	x	x	x	x	x	x	x
Serum Chemistry	x			x							
CBC, PT, PTT	x			x							
Blood samples	x	x		x							
Serum cotinine	x										
EKG	x										
PFT	x										
Chest CT, PET/CT	x										
Bronchoscopy	x				x						
Urine	x	x		x							
Carbon Monoxide	x										
Pregnancy test*	x										
Surgical samples					x						
Questionnaires	x		x	x	x	x	x	x	x	x	x

P = phone interview. S = screening. *When applicable.

WHAT WILL HAPPEN AND WHAT CAN I EXPECT IF I TAKE PART IN THIS STUDY?

You will go through the screening process described below:

- First, you will sign this consent and HIPAA form.
- You will complete respiratory/general health questionnaires, food frequency self-assessment questionnaires.
- You will be asked about your lung cancer risk factors, medical history, symptoms, and any other medications you may be taking.
- You will have a physical examination, including vital signs (blood pressure, heart rate, breathing rate, body temperature), oxygen level, body height and weight.
- The study investigators will access your medical records from your standard clinical visits, including x-ray imaging data, pulmonary function test (PFT), 12-lead EKG, clinical labs (complete blood chemistry panel, blood cell counts, PT, PTT).
- The investigator will collect and store some of your samples from the clinical diagnostic procedures, such as bronchoscopy or needle aspiration. No new samples will be taken from you at this time.
- Blood samples and urine samples will be collected for research. The total amount of blood taken is about 1-2 tablespoons.
- A pregnancy test will be done if you are a woman who is able to have children.
- We will ask your permission to store your data and a portion of the blood, urine, tissue and cell samples collected, and if you agree, they will be kept for future research.
- You will give a blood sample to test for your level of exposure to tobacco smoke.
- You will have your clinical diagnostic procedures as usual standard of care. If you are found to have stage I or II lung cancer and after reviewing the above tests and questionnaires, you are still eligible to be in the study, you will be enrolled in to receive the study drug:

Leucoselect phytosome 4 capsules (450 mg/cap) a day for about 2-3 weeks until 4-7 days before your lung cancer surgery.

Day 1 You will keep a diary of the amount of study drug you take each day and any side effects you may experience. You will bring both the diary and any unused study drug to every return visit. It is important that you take the study drug as prescribed and keep your diary up-to-date so that you can continue to take part in the study. If you miss a dose, you should take the next dose as scheduled. You should not take a double dose.

- You will take the first dose in the morning in the study office.
- Blood will be collected before you take the study drug and again between 60-90 minutes after you take that morning's dose of medication. You should not eat for at least 10 hours before the blood test.

One week after you begin the study drug, you will be contacted by phone by Dr. Mao or a member of the study team.

- At this time, we will ask you if you have noticed any side effects since starting the study drug.
- If you are not experiencing any side effects or only mild side effects, you will continue to take the study drug at 4 capsules a day for the rest of the study treatment duration – up to a total of 2-3 weeks until your lung cancer surgery.
- If you are having side effects that require further testing or treatment, you will be asked to return for a clinic visit and the necessary care will be arranged for you.

Two to three weeks after you begin the study drug, you will return to study clinic for a follow up visit with Dr. Mao or a member of the study team.

- A first void of the day urine sample will be collected for research studies.
- At this time, you will return any leftover study drug. We will review the study drug diary, discuss other medications you are taking and record any side effects you may be having.
- You will have a physical examination.
- You will take the final dose in the morning in the study office.
- Blood samples (about 1-2 tablespoon), will be collected before you take the study drug and again between 60-90 minutes after for research purposes (such as how much of the study drug is absorbed into the blood, the effects of treatment on the cells and molecules in the blood. Some will be stored for future research.
- A portion of the blood will be used for repeat blood tests to monitor your liver and kidney functions, blood sugar level and complete blood count. You should not eat for at least 10 hours before the blood test.

Three to four weeks after you begin the study drug and in the morning of your lung cancer surgery,

- A first void of the day urine sample will be collected for research studies.
- At this time, we will record any side effects you may be having.
- You will have a physical examination.
- A portion of the bronchoscopy, lung and tumor samples left over from clinical diagnostics will be obtained for research during the operation.

One month after your surgery and finishing your study drug Dr. Mao or designee will contact you by phone.

- You will be asked to complete a set of questionnaires to assess your overall well-being and recovery from surgery.
- Dr. Mao will make recommendations to you if any follow up care is needed. At your request she may discuss with your regular doctor about additional follow up care that may be needed, beyond the scope of the research. Your doctor may then provide for your care.

You Should Not Participate in This Study If You:

- Have had cancer before (unless there is a 5 year period of time when you were free from cancer) except for, non-melanomatous skin cancer, localized prostate cancer, carcinoma in situ (CIS) of the cervix, or superficial bladder cancer, with your last treatment greater than 6 months prior to registration onto this study.
- Have had a solid organ or bone marrow transplant.
- Have severe psychiatric disorders.
- Are currently taking any anticoagulants such as coumadin or heparin, or a history of clotting/bleeding problems.
- Are using supplemental oxygen (continuous or intermittent use) or have severe lung disease.
- Have uncontrolled ongoing illness including an active infection, congestive heart failure, unstable chest pains, irregular heartbeat, recent stroke, chronic kidney or liver disease or uncontrolled high blood pressure.
- Have a history of allergic reactions attributed to grapes or grapes-related products.
- Are currently taking other investigational drugs or supplements.
- Are taking more than 10 mg of prednisone or comparable dose of systemic steroids a day by month.
- Are pregnant. Women of child bearing capacity must be on an acceptable form of birth control for the duration of the study (i.e. condom, oral contraceptives, etc.).
- Are breast feeding.
- Are unwilling to refrain from drinking more than 1 glass of wine a day.

Responsibilities and expectations of the participant:

- Take the study drug as instructed.
- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigator or research staff if you believe you might be pregnant or might have gotten your partner pregnant.
- Keep the study drug in a safe place for your use only and away from children
- Fill out your diaries as instructed.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

WHICH PROCEDURE/S OR TREATMENT/S ARE DONE FOR RESEARCH? Leucoselect phytosome (the grape seed extract supplement) is being given for research purposes. The procedures that are done for research purposes only include, blood collection at screening, study enrollment and follow up; washing of the part of the diseased lung with sterilized saline to collect cells and molecules in the diseased lung before surgical removal. We will collect some of the lung tissue and tumor samples for research at the time of your diagnostic procedure as well as surgery." The questionnaires, follow up phone calls and storage of specimen and data for future use are all part of the research procedures. The medical diagnostic procedure and/or surgery are not part of the research but are standard of care for your condition.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY? Since you are already undergoing clinical procedures for diagnostic reasons (i.e., diagnosis of a lung tumor, pre-operative evaluation of the airways prior to a thoracic surgery procedure), no significant additional risks are expected from obtaining research samples leftover from non-research, clinical procedures than the well-known risks associated with the clinical procedures. However, additional sampling in the lung abnormality or lymph nodes at the time of the initial diagnostic procedure may be required to obtain enough cells and tissue for both clinical diagnosis and research. As a result, there may be a very small increase in risk of bleeding, dropping the lung, and respiratory insufficiency (low oxygen in the blood). Furthermore, at the time of surgery, a part of the lung with lung tumor that will be taken out will be washed with saline to allow collections of cells and molecules in the diseased lung before surgical removal; because that portion of the lung is to be removed anyway, we do not anticipate significant increase in risk from this washing procedure that takes about 3-5 minutes.

While on the study drug, you are at risk for certain side effects. You should discuss these with the study doctor and/or your regular doctor. There may also be other side effects that we cannot predict. Many side effects go away shortly after the drug is stopped, but in some cases side effects can be serious or long-lasting or permanent. Taking the study drug may have benefits, may have no effect, and may have only side effects.

Potential Risks and side effects related to Grape seed extract:

- In general, grape seed extract is well tolerated when taken by mouth.
- Potential side-effects most often include headaches a dry, itchy scalp, dizziness or nausea.

- Grape seed extract may have blood thinning effects. This is speculative base on some internet information.
- Interactions between grape seed extract and medicines or other supplements have not been carefully studied.

Risks and side effects of blood draws include:
The risks of venipuncture (inserting a needle into a vein to obtain blood samples) include: mild stinging when the needle is inserted, fainting, infection, bruising, and formation of a blood clot, pain, and/or bleeding at the site of the needle puncture.

Reproductive risks: The safe use of leucoselect phytosome in pregnant women and nursing mothers has not been established. Consequently, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant that are unknown. Women of childbearing potential enrolling in this study must (i) have been using a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the previous three months, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Women are considered to be of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

Risks of Genetic Testing and other risks: If you agree to have your sample stored for future testing, this may include genetic testing. There are risks of loss of getting insured, being employed, and stigmatization (treated badly due to your genetic testing results). There are risks of stress, emotional distress, inconvenience, and possible loss of privacy and confidentiality.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY? If you agree to take part in this study, there may not be any direct medical benefit to you. There may be possible benefits from treatment of lung cancer including preventing recurrence, but this is unknown. We hope the information learned from this study will benefit other people at risk of lung cancer in the future.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY? You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from participating in the research or new alternatives to participation that might change your mind about participating in this study.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY? Every reasonable safety measure will be used to protect your well-being. If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures. No additional compensation is available. You do not give up any of your legal rights and you do not release the VA from any liability by signing this form. Further information can be obtained by calling the Office of Regional Counsel, Pacific-South Region: 602-212-2091. VA will provide treatment for research related injury in accordance with applicable federal regulations (38 CFR 17.85).

In the event of illness or injury, you may contact Dr. Jenny T. Mao during the day at (858) 552-8585 at extension 7347 or contact the VA Operator, after hours at (858) 552-8585 and ask for her or the pulmonary attending on call. You may also contact the VASDHS Emergency Department at 858-642-3386) for emergencies ONLY.

DO I HAVE TO TAKE PART IN THIS STUDY? Your participation in this study is voluntary. You do not have to take part in this study, but if you do, you can stop at any time. You have the right to choose not to participate in any

study activity or completely withdraw from continued participation at any point in this study without penalty or jeopardy to the medical care you will receive at this institution or loss of benefits to which you are entitled.

For data already collected prior to the participant's withdrawal, the investigator may continue to review the data already collected for the study but cannot collect further information, except from public records, such as survival data. Specimens already used cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION The investigator may withdraw you from participating in this research if circumstances arise which warrant doing so. This may happen if, in the medical opinion of the study doctor, it is not in your best interests to continue participating in this study. If you are withdrawn from the study, you will be asked to (1) stop taking the study drug; (2) to return all remaining study drug to the study coordinator; (3) you will be scheduled to return to the study site for study completion procedures.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY? There will be no costs to you or your insurance for any procedures or testing done only for the research study. Contact Dr. Mao If you receive a bill for services that you think may be related to your study participation.

You or your insurance company will be charged for procedure or test that is medically necessary for the treatment of your illness, including the Diagnostic procedures, surgery and related tests. You will be responsible for all insurance co-payments and deductibles. The study drug Leucoselect phytosome and study related blood test, sample collections, etc. will be provided at no cost.

Medical care and services provided by the VA that are not part of this study (e.g., normal medical testing, procedures, hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

WHAT COMPENSATION WILL I RECEIVE IF I TAKE PART IN THIS STUDY? You will not receive any payment for participating in this study.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS? If you have any questions, complaints, or concerns about the research or other related matters, you may contact Dr. Mao or her associates at 858-552-8585, ext. 7347.

If you have any questions or concerns about your rights as a research subject, the validity of a research study, or research personnel you can contact the Research Compliance Officer at 858-642-3817, VA Research Service at 858-642-3657, VA Regional Counsel at 858-642-1540, or the VASDHS Institutional Review Board at 858-642-6362. This is the Board that is responsible for overseeing the safety of human participants in this study.

POSSIBLE FUTURE RESEARCH USE OF TISSUES COLLECTED IN THIS STUDY Dr. Mao and her associates would like to keep some of the samples along with the data collected during this study for future studies of any major disease or health condition, including genetic testing. These samples will include some of the collected data and specimens will be stored at the databank and tissue repository at the VASDHS, San Diego Medical Center supervised by Dr. Mao (and will be maintained in accordance with the VA record control schedule). All your specimens will be stored until none is left. Your samples will be stored with your unique study number to protect your identity, so that your name, initials, SSN, date of birth or other unique identifiable information (such as medical record number) will not be present on any stored samples. However, Dr. Mao and her associates will

maintain a "link" to your name in order to be able to match your cells with other information you have provided in this study (such as in the questionnaires or your medical records) that will help Dr. Mao and her associates better understand lung cancer and other diseases.

Your cell and tissue samples will be used for research in pulmonary dieases purposes but the specific nature of the research to be performed will vary and may not be fully known at this time. Other researchers from other universities, hospitals, or health organizations may contact Dr. Mao and request samples or information for their studies. However, other researchers must receive approval from the Institutional Review Board committee and Dr. Mao before they receive any samples or study information. No one outside the VASDHS will be able to link your name with any of the cells or other information gained from this study; this is strictly confidential. The research that may be done with your cells/tissues may not specifically benefit you, but it might help others with major medical conditions. Reports about research done with your cells and samples will not be given to you or your doctor. These reports will not be put in your health records, and the research using your samples will not affect your care.

In the future, if approved researchers use your samples and need to know more about your health, Dr. Mao or her associates may give them reports about your health, but they will not give them your name or any other information that will let the researchers know who you are.

If you decide now that your cells/tissues can be kept for future research, you can change your mind at any time by contacting Dr. Mao or her associates at the VASDHS (858-552-8585, ext 7347) and let them know that you no longer want your cells/tissues used for future research. The research team will continue to use any information that they have already collected to ensure the integrity of the research; however, no new information will be collected from you.

Reports about research done with your samples will not be given to you or your doctor because they will not have any direct clinical benefit to you at this time.

Your specimens will be used for research and such use may result in inventions or discoveries that could become the basis for new products or diagnostic or therapeutic drugs. In some instances, these inventions and discoveries may be of potential commercial value. There are no plans for you to receive any money or other benefits derived from any commercial or other products that may be developed from the use of your specimens.

Genetic material (Deoxyribonucleic acid: DNA and Ribonucleic acid: RNA) may be isolated from the samples that you donate. Collected specimens may be used for future studies of any major disease or health condition, including genetic studies.

A new federal law, the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained from this research.
- Health insurance companies and group health plans may not use your genetic information obtained from this research when making decisions regarding your eligibility or premiums.
  Employers with 15 or more employees may not use your genetic information obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 5 or more employees must follow this law as of November 21, 2009.

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. It also does not prohibit discrimination on the basis of already known genetic disease. In California, state law (CalGINA) requires that employers with 5 or more employees may not use your genetic information, obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, these laws do not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of already known genetic disease.

FUTURE USE OF DATA AND RE-CONTACT I agree that data, cells and tissues collected from me may be stored by Dr. Mao or her associates at the VASDHS databank and tissue repository, and may be used and shared with other researchers at VASDHS or at insititutions outside for unspecified future studies of any major disease or health condition, including genetic studies.

YES_____ Initials_____

I give Dr. Mao and her associates permission to contact me in the future to ask me to take part in more research. A "yes" answer does not require your participation, it only gives us permission to contact you.

YES_____ NO_____ Initials_____

I give Dr. Mao and her associates permission to contact my alternative contact person. Before contacting this person, all efforts will be made to contact me using the information I have already provided.

YES_____ NO_____ Initials_____

HOW WILL MY SPECIMENS BE USED? Your blood, urine, tissue and cell samples will be used to study the effects of leucoselect phytosome treatment on various biomarkers related to lung cancer. Your samples will be stored with a coded label that does not identify you.

HOW WILL MY PRIVATE INFORMTION BE PROTECTED? We will make every effort to protect your confidentiality and make sure that your identity does not become known without your specific consent; however, we cannot guarantee confidentiality of all study data. Your identity will not be used in any reports about the study. In records that leave the VASDHS you will be identified by a study code only. All information associated with this study will be kept in Dr. Mao's research office in a locked file cabinet behind locked doors. Electronic information will be stored on a secure VA network computer drive. Only designated staff members will have access to the data. Study records will be stored according to the VA Record Retention Schedule in a secure environment with limited access on the VASDHS campus. Information that directly discloses your identity will remain only with the Principal Investigator and her designees. Information that could be used to "link" your identity will not be released without your knowledge or consent unless required by law or regulation, or if necessary to protect your rights or welfare (e.g. if you are injured and need emergency care).

Study Title: Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer

Principal Investigator: Jenny T. Mao, M.D.

VA Facility: VA San Diego HealthCare System

You understand that by agreeing to participate in this study, anonymized information about you will be provided to the sponsor of this research study. All of your reports and samples are collected only for the purpose of research and will be identified only by a coded number to maintain confidentiality.

Information contained in your study records is used by study staff. The VASDHS IRB that oversees human subject research, federal agencies such as the Department of VA Office of Research Oversight, VA Clinical Science Research and Development (VA CS R&D), Office of Inspector General, Office of Human Research Protection, Government Accounting Office, Food and Drug Administration, and/or other VA entities such as VA research and safety monitors may need to review records of individual subjects. As a result, they may see your name, but they are bound by rules of confidentiality not to reveal your identity to others. Your name will not be used in any published reports about this study. A copy of this consent will be kept with your study medical record.

Identifiers might be removed from the identifiable private information or identifiable biospecimens that are collected. After that removal, the information or biospecimens could be used or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative. We will include information about your study participation in your study medical record.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. 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.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY You have been informed that you do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of your VA or other benefits.

Dr. Mao and/or her study Associates have explained the study to me. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

By signing this document below, I voluntarily consent to participate in this study. I also confirm that I have read this consent, or it has been read to me. I will receive a copy of this consent after I sign it. A copy of this signed consent will also be put in my study medical record.

I agree to participate in this research study as has been explained in this document.

_____ _____

Participant's Signature Date

_____ _____ _____

Signature of Researcher obtaining consent Name (print) Date

Study Title: Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer

Principal Investigator: **Jenny T. Mao, M.D.**

VA Facility: VA San Diego Healthcare System

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this document, you provide your permission called your 'authorization,' for the access, use, and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect and use information learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, allergies, lab, imaging and other diagnostics results, and genetic test results,

The research team may also need to share your health information and the information it collects to other entities as part of the study progress. Other VA entities may include the VA Office of Research Oversight (ORO), VA Clinical Science Research and Development (VA CS R&D), Office of Inspector General, Office of Human Research Protection, Government Accounting Office, Food and Drug Administration, and/or other VA entities such as VA research and safety monitors.

Your health information disclosed outside the VA as described in this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you may (a) write to the Release of Information Office at this facility; (b) ask a member of the research team to give you a form to revoke the authorization; or (c) send your written request to the Principal Investigator for this study at the following address: Jenny T. Mao, M.D., Pulmonary & Critical Care Section (111 J), VA San Diego Healthcare System, 3350 La Jolla Village Dr. San Diego, CA. 92161-0002.

If you revoke this authorization, Dr. Mao and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

While this study is being conducted you will not have access to your research-related health records.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization.

Unless you revoke (take back) your permission, your authorization to allow us to use and/or disclose your information and any information that has been placed into a repository to be used for future research will not expire.

Study Title: Leucoselect Phytosome for Neoadjuvant Treatment of Early Stage Lung Cancer

Principal Investigator: **Jenny T. Mao, M.D.**

VA Facility: VA San Diego Healthcare System

AGREEMENT TO AUTHORIZE USE AND RELEASE OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION

By signing this document below, I give my authorization (permission) for the use and disclosure of my individually identifiable health information as described in this document. This authorization has been explained to me and I have been given the opportunity to ask questions. If I believe that my privacy rights have been compromised, I may contact the VHA facility Privacy Officer to file a verbal or written complaint. I will be given a signed copy of this document for my records. A copy of this signed document will also be put in my study medical record.

_____ _____ _____

Participant's Signature | Last 4 of SSN | Date

_____

Legally Authorized Representative (print)

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

You have been asked to participate as a subject in medical research.
You have the right to know:

1) The nature and purpose of the study.
2) The procedures in the study and any drug or device to be used.
3) Discomforts and risks reasonably to be expected from the study.
4) Benefits reasonably to be expected from the study.
5) Alternative procedures, drugs, or devices that might be helpful to you and their risks and benefits.
6) Availability of medical treatment should complications occur.
7) You may ask questions about the study or the procedure.
8) You may quit the study at any time without affecting your future care at the VA.
9) You should be given a copy of the signed and dated written consent form for the study.
10) Your consent to participate must be given freely, without being obtained through deceit, force, or coercion.

If you have any questions or concerns about your rights as a research subject please contact the VASDHS Research Compliance Officer at (858) 642-3817 or RCO@vapop.ucsd.edu. You may leave an anonymous comment at the VASDHS research compliance hotline at 858-642-6311.

REF: California HSC 24170-24179.5

A copy of this document will be provided to the research participant.