Official Study Title:
Pre-Operative Immuno-Modulatory SBRT (POIMS Trial): A Pilot Trial in Early Stage NSCLC

NCT Number: [not yet assigned]

Document Description: Informed Consent Form

Document Date: July 1, 2021

Consent Research

RESEARCH CONSENT FORM

Pre-Operative Immuno-Modulatory SBRT (POIMS Trial): A pilot trial in early stage NSCLC

Protocol # IIT-2020-POIMS-Lung
Sponsor: University of Kansas Medical Center

Principal Investigator:

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Key Information: You are being invited to consider a research study. Research studies are always voluntary. The first section of this form is a short summary of the study. Please also read the Detailed Information that follows this summary before you make your decision.

Why are researchers doing the study?
We are doing this study to learn more about radiation effect on the tumor's immune response in people who have surgically removable non-small cell lung cancer. Patients will receive a short course of radiation treatment to the tumor which will be removed at the time of surgery. Tissue and blood samples will be collected to see the effect of the radiation on the tumor cells and the body's immune response.

What is involved in this study?
We are using three radiation treatments on the tumor itself followed by surgery several days later. We will collect blood and tissue samples to do laboratory studies.

Everyone in the study will receive radiation treatment for 3 days. Radiation treatments

will begin 5-7 days before surgery in patients with early stage non-small cell lung cancer who are fit enough to undergo surgery to get the tumor/cancer removed. The study schedule and the research procedures are discussed in Detailed Information below.

What are some reasons I might choose to volunteer?
Giving radiation treatment prior to surgery has been routinely used in other cancers and can improve surgical resection outcome and reduce cancer recurrence but has not been well studied in early stage lung cancers prior to receiving surgery. This may also help to reduce lung cancer recurrence. Furthermore, you will help to advance scientific knowledge about how the immune system can become activated following radiation treatment in lung cancer.

What risks are involved in the study?
Being in the study may pose risks. This study will give radiation treatment before surgery which is not normally done in early-stage lung cancer. Risks for participants include wound healing problems and longer post-operative recovery.

The risks listed in the Detailed Information section below has other risks you should consider.

Participating in this study is different than receiving regular care from your doctor. With regular care, you and your doctor decide on the treatment plan. There are additional tests/procedures that are required as part of this study that may cause discomfort to you.

What other things should I consider?
People who join the study must be willing to go through all the study procedures described in this form.

You can participate in the study if you are willing. The main study involves multiple visits (at least four extra visits) before your surgery to KUMC, some of which may last up to 2 hours. Before you sign up, please make sure this schedule will work for you.

Will being in this study help me?
If the study treatment works, you **might** have an improved likelihood that the cancer does not come back. No one knows yet if this will happen.

What are my choices if I decide not to be in the study?
Instead of being in this study, you can receive routine treatment that is already available or consider another research study. The study team will discuss various options with you.

DETAILED INFORMATION

This research study will take place at the University of Kansas Medical Center (KUMC) with Dr. Shalina Gupta-Burt and the rest of the study investigators which includes your surgeon and other cancer specialists as the study researchers. About 10 people will be in the study at KUMC.

Why is this study being done?
Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. Some patients with NSCLC are diagnosed early when the tumor can be removed by surgery and has not spread. Even with complete removal of the cancer, the likelihood for the cancer to come back remains high, greater than 30% in most studies. Some researchers have shown that the dose of radiation used in this study can stimulate immune cells to destroy cancer cells.

Because of this, the study researchers are studying how to use radiation treatment on the tumor just before it is removed in order to turn on your body's immune system. If there are a small number of unseen or hidden cancer cells, the body's immune response which has been alerted can look for and destroy those cells before they get a chance to grow. This may decrease the likelihood of the cancer coming back. This may have a positive effect on the outcome of patients with early stage NSCLC. We do not know if this will happen.

We are studying the effect of radiation on the tumor tissue and on your immune system.

How long will I be in the study?
You will participate in this study from the time you enroll until several months after surgery. After this time, we would like to continue monitoring your health with follow-up visits either to the study clinic or by telephone for up to 5 years.

What will I be asked to do?
Most of the tests and procedures you will have during your participation on this study are part of the usual approach for your disease (called your standard of care). These may include physical exams, lab tests, scans, and/or other procedures (such as biopsies). They will be performed in the normal way, and the information from them will be collected for research purposes on this study.

There will also be ***extra*** tests and procedures that you will have for research purposes or to monitor your health and safety because you are in a research study. Every effort will be made to minimize the time from your diagnosis to surgery. Often times, additional workup from time of diagnosis to surgery will require that you undergo testing and

evaluation to ensure you are an appropriate and fit candidate for surgery. During this time, you will be screened and undergo pre-operative radiation treatment which would represent no delay or a minimum delay getting to surgery. The projected additional time from diagnosis, determination of one's fitness for tolerating surgery to undergoing surgery if one were to participate in our trial is likely to be 0-2 weeks delay and is considered to be minimal impact on patient outcome or survival. If you decide to join the study, you will be asked to read and sign this consent form before any research procedures take place.

This study will be divided into the following 3 periods: Screening, Treatment, and Follow-up.

Screening: If you would like to be in this study, your study doctor will confirm that you are qualified. The procedures and tests performed during this period will determine if you are eligible to take part in the study. They may be performed over the course of 1 or more days.

If the results show that you can take part in the study, you will visit with a radiation cancer specialist who will discuss the study in detail and answer your questions. If you agree to be a part of the study, you will also undergo a radiation planning session. The radiation planning session is very similar to getting a CT scan. The process of seeing the radiation cancer doctor and completing the planning session can be done in one visit. This visit usually takes about 2 hours. You will then enter the Treatment Period.

If you chose not to participate, then the study doctor will arrange to have you go back to your surgeon to discuss other possible trials or proceed to surgery.

Treatment:
Patients following consultation and successful screening will undergo radiation planning. This will entail getting a planning CT scan in the department of Radiation Oncology for the purposes of radiation treatment planning. We will need about 5 days to plan the radiation treatment and perform necessary quality assurance checks. Once the radiation planning session is done, radiation treatment will be administered over a consecutive 3 day period (e.g., Monday, Tuesday, Wednesday). The type of radiation treatment you will receive is commonly known as stereotactic body radiotherapy (SBRT). This treatment is considered a high-precision radiation treatment that will provide a high-dose of radiation treatment to the tumor only over a short period of time while simultaneously minimizing radiation dose to all other body parts and organs.

The last dose of radiation treatment will be given 5-7 days before the scheduled surgery date. This will require you to come for four to five additional visits to KUMC.

Additional blood samples will also be collected after the radiation. You will then have the planned surgery.

Once you complete your surgery more blood samples will be collected. You will then enter the Follow-Up Period.

Follow-Up:
About 30 days after your End of Treatment Visit, a member of the study team will check your health and ask about any side-effects you may be experiencing. After the Safety Follow-Up Visit, you may be contacted every 3-6 months to check on your health. These Long-Term Follow-up Visits may be done in the clinic or by telephone.

On the following page is a table that lists all the procedures that will happen at each study visit, with the approximate amount of time each clinic visit may take. After the table, you will find more details about the ***extra*** tests done solely for this study.

Please talk to the study team if you have questions about any of the tests or procedures.

Table 1: Study Procedures and Tests for Screening & Treatment	Screening Period	Treatment Period												
		SBRT Schedule				Surgery	Post-Operative Follow Up							
		Day 0	Day 1	Day 2	Day 3	Day 8-10	24 Hours post-op	Day of Discharge	3-4 weeks post-op	3 months post-op	6 months post-op	1 year after surgery	15-18 months after surgery	2 years after surgery
Approximate time (in hours)	1-2	1	1	1	1	6	3-4	2	1	1	1	1	1	1
Review Medical History and Demographics	X	X				X								
Adverse Events (side effects)/ illnesses assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review your current Medications	X					X								
Physical Exam	X					X	X	X	X	X	X	X	X	
Performance Status						X								
CBC with Diff	X					x								
Blood Collection for Correlative Studies	X					X	X							
Tumor Tissue Collection	X					X								
Imaging of chest (+/- 4 days)	X								X		X	X	X	X
Simulation		X												
SBRT			X	X	X									

*There may be standard of care procedures (such as scans, labs, or biopsies) listed on the tables that may need to be done again to meet time point or eligibility requirements for this study. There may also be certain procedures that do not need to be repeated if they have already occurred within a certain timeframe. A member of the study team will let you know if any of these situations apply.

RESEARCH TESTS AND PROCEDURES

Below is a description of the tests and procedures that will be done for research purposes. You may be given separate information describing your standard of care tests and procedures before they occur.

Physical exams: The complete physical exam will include an evaluation of your body. The study doctor will also listen to your heart and lungs.

Tumor specimens for research testing: Tumor specimens from your biopsy and surgery will be collected for biomarker research testing.

Research blood tests: A needle will be used to draw blood from a vein in your arm. The total amount of blood collected for research purposes will depend on the number of cycles of treatment you receive. Approximately _6-8_ tablespoons of blood will be drawn each time these tests are required.

Your blood will be used for research purposes to test for:

- Flow cytometry: This test is done to detect the presence of any abnormal cells.
- Biomarkers: A biomarker is a substance measured in blood or tissue that may reflect the character or presence of cancer cells. Biomarker analysis may help determine how radiation may change the immune profile or characteristics of your cancer cells and your immune cells. This testing may also help researchers understand this interaction. Approximately 6-8 tablespoons of blood will be collected each time this test is required.
- Pregnancy (if applicable): Approximately 1 teaspoon of blood will be collected each time this test is required for all women who are able to get pregnant.
  If the pregnancy test is positive, you will not be able to participate in this study.

How will my samples be used and stored?

Some of your blood and tissue samples will be used for research purposes to conduct this study. These samples will be sent to a separate laboratory. Samples that are taken may be transferred to laboratories working for the study funder or its Affiliates. Collected samples may be stored indefinitely.

All samples collected as part of this research study will be labeled with a study identifier or code (such as numbers, letters, or combinations of both). This code is unique to you and will not be labeled or stored with names or other direct links to your identity. Results from any testing on your samples will also be labeled with your unique identifier code only.

The study doctor will have the link between your name and the code number. The link between your name and the code number will not be shared with the study funder, Varian Medical Systems. Only the code number and coded information will be sent to the study funder, Varian Medical Systems. The study funder will use your coded information for research only.

What are the possible risks or discomforts?
Radiation Treatment may cause side effects or other problems. You may experience none, some or all of the effects listed below. Please tell the study team about anything that is bothering you or about any changes in your health since your last study visit.

Radiation Risks
In addition to any scans you may have as a part of your normal medical care, you may have an additional CT scan. This scan is not needed for your medical care. You are exposed to radiation every day. This radiation comes from the sun and the earth. It is called background radiation. The amount of radiation in one year from the additional scans from this study could be up to 2 times the amount you are exposed to from background radiation.

The amount of radiation given to the tumor used in this study is well below what is normally used to treat patients with lung cancer. The most common short-term side-effects of radiation treatment for lung cancer is tiredness and dry cough. Many of these symptoms will self-resolve over a short period of time. The tumor which has received the radiation will be removed from your body. While we do not foresee any significant risks with this radiation dose before surgery, there may be an increase in wound healing problems, time in surgery, and longer post-operative recovery. The potential also exists for radiation irritation and/or scar to the lung. Again, most if not all of this lung tissue will be removed and therefore the likelihood of developing this symptom following surgery is likely to be quite low to zero.

Tumor Tissue Biopsy Risks
Possible risks related to a biopsy include pain or bleeding from the needles used to give anesthesia and the procedure itself. You may also have an allergic reaction to the local anesthetic that is used. There may be bruising at the site of the biopsy. Continuous bleeding and infection are rare and very often can be well controlled. Depending on the procedure used to perform the biopsy, there may be other risks involved. All of these risks will be discussed with you by your doctor.

CT Scan Risks
You may feel some discomfort or anxiety when lying inside the CT scanner. The contrast material (dye) will be injected into a vein and may cause a metallic taste in your mouth. The dye may make you feel warm and may cause nausea or vomiting. There is a rare risk of kidney failure due to the dye.

Blood Draw Risks
You may experience temporary discomfort from these periodic blood draws. These needle sticks may cause local pain, bruising and swelling, lightheadedness, dizziness and rarely, fainting and/or a local infection.

Pregnancy Risks
The procedures used in this study might hurt an unborn child or a child who is breast-feeding. You cannot be in this study if you are pregnant, nursing a baby, or if you are

trying to get pregnant. You will have a pregnancy test before the study starts [add, as applicable: and during the study].

You cannot be in this study if you are a man who is trying to father a child.

Men and women who are able to have children must agree to take appropriate precautions to avoid becoming pregnant or fathering a child. You must use two approved methods of birth control during the study and for 24 weeks after your last dose of radiation. The approved methods of birth control are:

- 1 Barrier method (cervical cap with spermicide plus male condom; diaphragm with spermicide plus male condom)

PLUS

- Hormonal method (oral contraceptives, implants, or injections) or an intrauterine device (e.g., Copper T).

The study doctor must approve the form of birth control. You must talk to your study doctor before changing any birth control methods you have already agreed to use.

There may be pregnancy risks that are not known yet. For this reason, you must tell the study doctor right away if you, or your partner, get pregnant during the study.

If you or your partner gets pregnant, the Sponsor, would like to collect information on the pregnancy and delivery. You (or your partner) will be asked to sign a separate consent form to collect this information.

Are there benefits to being in this study?
Researchers don't know if you will benefit from this study.

If the intervention is effective, you may experience a decrease in cancer recurrence. The tumor tissue and blood samples will help the study doctors by increasing our understanding of the radiation immune response.

Researchers hope that the information from this research study may be useful in the future of treatment of patients with non-small cell lung cancer.

Will it cost anything to be in the study?
All standard of care tests and/or procedures performed that are part of the usual approach to manage your disease, or are being done to monitor your health and safety while you are on this study, will be charged to you or your insurance (if applicable). Any other tests and procedures done for research purposes including radiation treatment will be paid for by the study.

If you have insurance it is possible that it will not pay for routine charges because they take place within a research study. You should talk to your insurance company and review your specific benefits and coverage before deciding to participate.

You will be responsible for normal co-pays, deductibles and non-covered services that are not the responsibility of the study. Some procedures require pre-authorization from your insurance company and representatives of the clinic or hospital will be helping you with that process. Pre-authorization is not a guarantee of payment. You may still be able to participate in the study even if your insurance denies coverage for your routine care costs, or if you are uninsured.

The University of Kansas Health System has a financial assistance program for patients who qualify. You will be charged for all costs that are not covered by the study, your insurance, or the financial assistance program. Financial Counselors from the University of Kansas Health System are available to review your expected costs, provide you with more information, and help you with any questions.

Will I get paid to participate in the study?
You will receive $25 for each study visit on your radiation treatment days. If you complete all regularly scheduled radiation visits, you may receive up to $100. If you leave the study early, you will be paid only for the visits you completed. You will not receive compensation for surgery or any follow-up visits.

You will be given a ClinCard, which works like a debit card. After a study visit, payment will be added onto your card by computer. The money will be available within 1 business day. You can use the ClinCard at an ATM or at a store. No one at KUMC will know where you spent the money. You will be given one card during the study. If your card is lost or stolen, please call (866) 952-3795.

The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to set you up in the ClinCard system. Study payments are taxable income. A Form 1099 will be sent to you and the Internal Revenue Service if your payments are $600 or more in a calendar year. If you do not provide a valid social security number or tax identification number, 30% of your payments will be set aside by KUMC and sent to the IRS for withholding on your behalf.

Your personal information will be kept on a secure computer. It will be removed from the computer after the study is over and the money on the card has been used. Your information will not be shared with other businesses. It will be kept completely confidential.

The specimens collected during this study will belong to the University of Kansas Medical Center. The research could lead to discoveries or inventions in the future. Participants will not be paid if a commercial product is developed.

Will the researchers get paid for doing the study?
The institution (KUMC Research Institute, Inc.) will receive payments from the study funder, Varian Medical Systems, for conducting this study. Payments will be used for

research purposes only.

What happens if I get hurt or sick during in the study?
If you have any problem during this study, you should immediately contact Dr. Shalina Gupta-Burt or her team at 785-295-7800

If it is after 5:00 p.m., a holiday or a weekend, you should call 913-588-3600 and ask for the radiation oncology attending physician on call. Please tell the physician that you are in this research study. A member of the research team will decide what type of treatment, if any, is best for you at that time.

If you have a physical injury as a result of participating in this study, treatment will be provided for you at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to your health insurance policy, your government program, or other third party. You will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

How will my confidentiality and privacy be protected?
The researchers will keep your identity confidential, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

Your study information will be labeled with your research ID number. The study team will keep a separate list that matches your name to the research ID number. These steps will lessen the risk that your personal identity and information will be seen by others who shouldn't have it.

If you sign this form, the research team will collect, use and share your private health information as described below. If you decide not to sign this form, you cannot be in the research study.

Study data includes information from your study activities and from your medical record. Your health care providers may release your private health information to Dr. Shalina Gupta-Burt and the research team. The team may use any and all of your information needed for the study. Your medical records may contain your name, address, phone, date of birth, social security number, or other identifiers. Others at KUMC might need to look at your research records. They include KUMC Research Institute, the Institutional Review Board or other committees and offices that review and monitor research studies.

Your participation in this study and your study information may be put into the University of Kansas Health System electronic medical record and combined with your health information from your clinical care. The health system may use and share this information for other purposes described in the Notice of Privacy Practices.

You may not be able to see your records relating to the study until after the study is over and the results are known. Any research information that is put in your medical record will be kept indefinitely.

The research team will share your study data with people outside KUMC. These groups or agencies may make copies of study data for audit purposes. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may not protect it. These groups may include:

- Federal agencies that oversee human research (if a study audit is performed)
- Varian Medical, Inc
- Experts who inspect the study information to see if the study is being done correctly and if it is still safe to continue
- Other groups that help manage or provide services to support the study
- Ethics committees that review the study for other locations

Your permission to use and share your health information will not expire unless you cancel it. To cancel your permission, please write to Dr. Shalina Gupta-Burt. The mailing address is MS 4033, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel your permission, you will be withdrawn from the study. The researchers will stop collecting any additional information about you about you unless they need information about a side effect of radiation treatment. They are permitted to use and share information that was gathered before they received your cancellation.

Will I be told about research results?
You will be told about any study results that directly affect your medical care.

At the end of the study, you will not be told about the research results of the study.

How will my research information and specimens be used in the future?
In the future, researchers at KUMC, the funding institution Varian, and other locations might re-use the information and blood samples from this study for other research. If that happens, information that could identify you will be removed first. You will not be asked if you agree to the future research that has identifiers removed. KUMC and other researchers working with KUMC or Varian or Varian's affiliates may use the information without identifiers to conduct research and development on radiation therapies and other related products, or to present regulatory submissions.

You won't be paid if money is made on the results of the future research.

Can I stop being in the study?
You may stop being in the study at any time. Stopping will not prevent you from getting treatment or services at KUMC. If you would be harmed by additional radiation treatments, then we will stop additional radiation treatments. We will discuss this plan with you. You might be asked to come back for a final study visit.

Who can I talk to about the study?
Dr. Gupta-Burt or other members of the study team should answer all your questions before you sign this form. They will also tell you if they learn anything new that might affect your decision to stay in the study. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints. If you have questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may contact the KUMC Institutional Review Board at (913) 588-1240 or IRBhelp@kumc.edu.

CONSENT
Dr. Gupta-Burt or the research team has given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

By signing this form, you say that you freely and voluntarily agree to be in this research study. You have read the information and had your questions answered.

You will be given a signed copy of the consent form to keep for your records.

_____

Print Participant's Name

_____ _____ _____

Signature of Participant Time Date

_____

Print Name of Person Explaining Consent

_____ _____ _____

Signature of Person Explaining Consent Time Date