Study Title: **SICARIO: Split-Course Adaptive Radioimmunotherapy for Treatment of Oligometastatic Non-Small Cell Lung Cancer with Biologically-Adaptive Radiotherapy**
Version Date: **21 SEPT 2022** **NCT05501665**
PI: **Evan Osmundson, MD PhD**

Name of participant:_____ Age:_____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

You are being asked to participate in this research study because you have non-small cell lung cancer that has spread to limited disease sites outside of the lung (oligometastatic), and your doctor is recommending sites of observed cancer detected on imaging may possibly benefit from investigational treatment with radiation in combination with standard of care chemotherapy and immune therapy.

The addition of radiation therapy (as conducted in this study) to standard of care chemotherapy and immunotherapy is investigational. Investigational means combining radiation therapy with chemotherapy and immunotherapy has not been approved as a standard treatment by regulatory health authorities, such as the U.S. Food and Drug Administration (FDA).

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

The purpose of this study is to investigate whether combining investigational radiation therapy with standard of care chemotherapy and immune therapy will improve response to treatment.

You will be asked to undergo a total of five radiation treatments given once every 3 weeks to every site of the body involved by cancer on imaging. Also, you will be asked to undergo additional experimental imaging with positron emission tomography (PET) to evaluate how this imaging can be used to adapt your radiation treatment. Following completion of radiation therapy your treatment team will follow your progress with clinic visits, lab tests, and imaging studies at intervals up to 2 years.

The addition of investigational radiation treatment may improve disease control; however, it may contribute to increased treatment associated side effects. It is unknown if this study will help you. You may have side effects from the study treatment and feel worse. Your disease may or may not respond to this investigational study treatment.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may significantly affect the risks or benefits of this study, you will be told so that you can decide whether or not you still

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want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

If you choose not to participate in this study, you would typically be offered alternative treatment without radiation, consisting of guideline-recommend chemotherapy and immune therapy alone, with radiation therapy offered to patients who have a good response to initial chemotherapy or immunotherapy or who are in pain from their cancer.

In this study, we hope to determine if the addition of adaptive radiation therapy to standard of care chemotherapy and immunotherapy can improve disease control and patient outcomes in lung cancer. Approximately 25 patients are anticipated to enroll in this study at Vanderbilt.

Side effects and risks that you can expect if you take part in this study:

Radiation Risks:

This research study may involve exposure to radiation from up to 3 CT scans of the Chest, Abdomen and Pelvis, and 4 PET/CT scans. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you may receive by participating in this study about 110% more than the amount allowed in a year for people who are exposed to radiation as part of their work. Please tell your doctor if you have taken part in other research studies or received any other medical care recently involving radiation. If you are pregnant or breast feeding, you SHOULD NOT participate in this research study. To protect your bladder from the effects of the injected radioactive substances, you should drink plenty of fluids and empty your bladder every two hours for at least the first six hours after you have each PET/CT scan

The combination of radiation with chemotherapy and immunotherapy as performed in this study has not been previously tested, and thus may be associated with increased treatment side effects.

Radiation combined with immunotherapy has been demonstrated to be generally well tolerated based on previous studies, however, unexpected severe side effects could arise using this new approach. The side effects and risks will be based on the site of the body that is being treated with radiation therapy. Potential side effects of radiation could include, but are not limited to, pneumonitis (inflammation of the lung), esophagitis (irritation of the esophagus between the throat and stomach), fatigue, pain; or injury to bowel, spinal cord, kidney, or other organs.

Chemotherapy has known side effects including, but not limited to, reduced blood cell counts (can cause fatigue, bleeding and increased risk of infection), mucositis (lining of the digestive system becomes inflamed, often seen as sores in the mouth), esophagitis (irritation of the esophagitis), and fatigue.

Immunotherapy has known side effects including, but not limited to, pneumonitis (inflammation of the lung), thyroiditis (thyroid dysfunction) and colitis (inflammation of the bowel).

Radiation doses will be guided by acceptable national parameters of safe delivery doses thus we anticipate a minimal additional clinical risk of side effects from this treatment regimen.

Non-physical risks of participating in the study: include the potential loss of confidentiality.

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Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Other Risks: Gadolinium (Gadovist)

The contrast agent (i.e., dye) used for the MRI scan has been reported to cause a disease called nephrogenic systemic fibrosis (NSF) in individuals whose kidneys do not work normally. NSF is a disease that affects the skin, muscles, and internal organs and can make people very weak or cause death. The signs and symptoms of NSF include:

For the skin: burning or itching, reddened or darkened patches, swelling, hardening, or tightening of the skin

For the eyes: yellow raised spots on the whites of the eyes

For the bones, joints, and muscles: joint stiffness, stiffness and or reduced movement in the arms, hands, legs, or feet, pain deep in the hip bone or ribs, or muscle weakness.

This condition is known to be associated with unhealthy kidney function, and therefore we will ensure that your kidneys are healthy enough to receive the dye before the exam.

While most of the dye that you will receive will only remain in your body temporarily, it is possible that small amounts of the dye will remain in your body longer after the exam. This is not known to cause any health problems, but there may be risks that are unknown.

Good effects that might result from this study:

a) The benefits to science and humankind that might result from this study include demonstrating the efficacy of addition of adaptive radiation therapy to standard chemotherapy and immunotherapy in patients with oligometastatic non-small cell lung cancer
b) The benefits you might get from being in this study include possibly improving your chance for cancer control and clinical outcome

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Procedures to be followed:

You will undergo additional testing, imaging and follow-up before, during and after treatment on this study detailed in schedule of events for study as follows:

Procedure	# of times performed	Notes
Chest Abdomen Pelvis CT	3 + every 12 weeks during maintenance treatment	Imaging process
Brain MRI	2 + every 12 weeks during maintenance treatment	Imaging process
FSPG PET-CT	2	F-FSPG is a tumor-imaging agent for PET scans (imaging)
18F-deoxyglucose PET-CT	2	18F-FDG is a tumor-imaging agent for PET scans (imaging)
Physical Exam	7 + every 3 weeks during maintenance treatment	A medical practitioner examines you for any possible medical signs or symptoms of a medical condition.
Vital Signs	7 + every 3 weeks during maintenance treatment	Temperature, blood pressure, respiratory rate, pulse oximetry and pulse rate
Blood draw (labs)	7 + every 3 weeks during maintenance treatment	Lab work for CBC and Complete metabolic panel as well as others
Blood collection for Biobanking (completed during blood draw above)	9	Blood collected for research use to improve our understanding of health and disease
Urinalysis	1	Urine collection via urinating into a cup at the office.

Payments for your time spent taking part in this study or expenses:

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

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in this study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

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Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat the injury. You will be responsible for any copayments or deductibles associated with the treatment of that injury.

There are no plans for Vanderbilt to pay for the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact **Dr. Evan Osmundson** at [redacted] If you cannot reach the research staff, please page the study doctor at [redacted].

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at 615-322-2918 or toll free at 866-224-8273.

Reasons why the study doctor may take you out of this study:

Primary reason will be if there is an inability to establish proper follow-up with you or for some reason you are unable to complete standard of care treatment.

What will happen if you decide to stop being in this study?

If you decide to stop being part of this study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:

A description of this clinical trial will be available on 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 web site at any time.

Confidentiality:

Records and data collected in this study will be maintained in your Vanderbilt University Medical Center patient chart accessible by the medical staff that performed direct medical care for you. Data analyzed in this clinical trial will be stored in a secure online database and accessed by secure computers on the Vanderbilt network.

Vanderbilt may share your information, without identifiers, to others or use if for other research projects not listed in this form. Vanderbilt, Dr. Evan Osmundson and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study is supported by funding from Varian Medical. Sharing of information generated from this study with Varian will be governed by applicable policies from Vanderbilt University Medical Center and agreements between Vanderbilt and Varian.

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Information that must be reported by law, such as child abuse or some infectious diseases, is not protected under this confidentiality agreement. This agreement does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are not protected.

Privacy:

Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:

Records and data collected in this study will be maintained in your Vanderbilt University Medical Center patient chart accessible by the medical staff that performed direct medical care for you. Data analyzed in this clinical trial will be stored in a secure online database and accessed by secure computers on the Vanderbilt network.

Vanderbilt may share your information, without identifiers, to others or use if for other research projects not listed in this form. Vanderbilt, Dr. Ryan Whitaker, Dr. Evan Osmundson and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

Authorization to Use/Disclose Protected Health Information

What information is being collected, used or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?

The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example, if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the funder of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

You do not have to sign this Authorization, but if you do not, you may not join the study.

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How long will your information be used or shared?

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?

You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

You have the right to see and copy the protected health information we gather on you for as long as the study doctor or research site holds the data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer
Consent obtained by:	
Date	Signature
	Printed Name and Title

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Consent for Genetic Research

The purpose of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment.

You are being asked to give a blood for genetic research. What we learn about you from this sample will not be put in your health record. Your test results will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results.

A blood sample of 8 teaspoons will be drawn approximately 9 times. This will not add additional requirement of your time.

Blood samples – You may feel bothered or pained from the needle stick. You may have a bruise or the site may get infected. It is rare, but some people faint.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only treating physician and study team will have access to your name.

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

Your sample will be used to make DNA that will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

Your samples may be used to make new products, tests or findings. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Your samples and information about you may be shared with others to use for research. To protect your privacy, we will not release your name.

You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Giving samples for research is your free choice and you may be in the study even if you do not want your samples used or stored for gene research.

At any time, you may ask to have your sample destroyed. You should contact Dr. Evan Osmundson or study team at [redacted] to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

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Please check Yes or No to the questions below, regarding your decisions about participation in the required and optional parts of this study:

I agree that my blood/tissue/fluid samples and related health information may be used for current research in this study related to kidney cancer:

☐ Yes ☐ No

I agree that my blood/tissue/fluid samples and related health information may be kept in a biobank and stored/shared for future cancer research:

☐ Yes ☐ No

I agree that my blood/tissue/fluid samples and related health information may be kept in a biobank for use in future health research in other health problems (such as arthritis, heart disease, etc):

☐ Yes ☐ No

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future:

☐ Yes ☐ No

Signature: _____ Date: _____