Departments of Radiation Oncology and Hematology Oncology

A RANDOMIZED TRIAL OF CONSOLIDATIVE IMMUNOTHERAPY WITH VS WITHOUT THORACIC RADIOTHERAPY AND / OR STEREOTACTIC BODY RADIATION THERAPY (SBRT) AFTER FIRST-LINE SYSTEMIC THERAPY FOR METASTATIC NON SMALL CELL LUNG CANCER (NSCLC)

Informed Consent Form to Participate in Research
Michael Farris, M.D., Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to improve survival in patients who have lung cancer that has spread to other areas of the body. You are being asked to take part in this study because you have advanced non-small cell lung cancer that has spread to other areas of your body. To be eligible for this trial you have already completed standard of care immunotherapy and/or chemotherapy and now your scans show that the cancer has not progressed or gotten worse. Your participation in this research will involve multiple visits for treatment with immunotherapy, and possibly radiation therapy. There are two groups of participants in this study, as described below in detail.

On this trial, patients are randomly divided into two groups. One of the groups will receive targeted radiation to all areas of cancer in the body, and a total of two years of immunotherapy. The other group of participants will receive a total of 2 years of immunotherapy without any radiation.

Patients in both groups will be seen for routine follow up visits that typically last 1 - 2 hours. These visits will occur about every 3 months for 3 years then every 6 months for 2 years which is standard of care. These visits would happen even if you were not on the study.

All research studies involve some risks. A risk to this study that you should be aware of is possible pneumonitis. This is inflammation of the lungs. This can happen with standard chemotherapy, radiation, and immunotherapy. The chances of this happening may be increased when immunotherapy is given before or after radiation. The amount of risk depends on many factors and is not totally understood. There is the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include choosing not to receive extra treatment after you have completed your first four rounds of chemotherapy and immunotherapy. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The rest of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Michael Farris M.D. If you have questions, suggestions, or concerns about this study or you want to withdraw from the study his contact

information is:

Michael Farris, M.D.
Department of Radiation Oncology
Wake Forest University School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
[redacted]

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. Your participation is voluntary. Please take your time in making your decision as to whether you wish to participate or not. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out what effects (good or bad) may come with the addition of radiation treatments and immunotherapy for non-small cell lung cancer. This study is for patients whose lung cancer is not getting worse after they have completed 4 cycles of standard systemic therapy. Systemic therapy is chemotherapy and immunotherapy together, and these go throughout the entire body to treat cancer. In this trial, after patients have already completed 4 cycles of systemic therapy, and the cancer has not progressed at any locations in the body, they will be eligible to be participate. Patients will be randomized to receive either very precise targeted radiation to all sites of cancer and then 2 years of immunotherapy, or they will receive 2 years of immunotherapy without any radiation treatments. Some patients may receive a drug called pemetrexed if their lung cancer is a particular type of non-small cell lung cancer called adenocarcinoma. This would be given with their immunotherapy which is standard. Before going on this study you will have lung function tests which is a standard test to evaluate how well your lungs are working.

Radiation therapy to all sites in the body where cancer has spread is starting to become a common practice across the US. However, it is not the currently agreed upon standard treatment option once cancer has spread outside of the lungs. Right now, the standard care options for patients who have not gotten worse after their initial systemic therapy is either closely watching their cancer with scans or continuing with 2 years of additional immunotherapy.

We think there may be a better approach. There are still questions we need to answer to make sure these are safe and effective treatment options. After first-line systemic therapy, we do not know how many sites of cancer we should treat with radiation. Also, for patients who had a

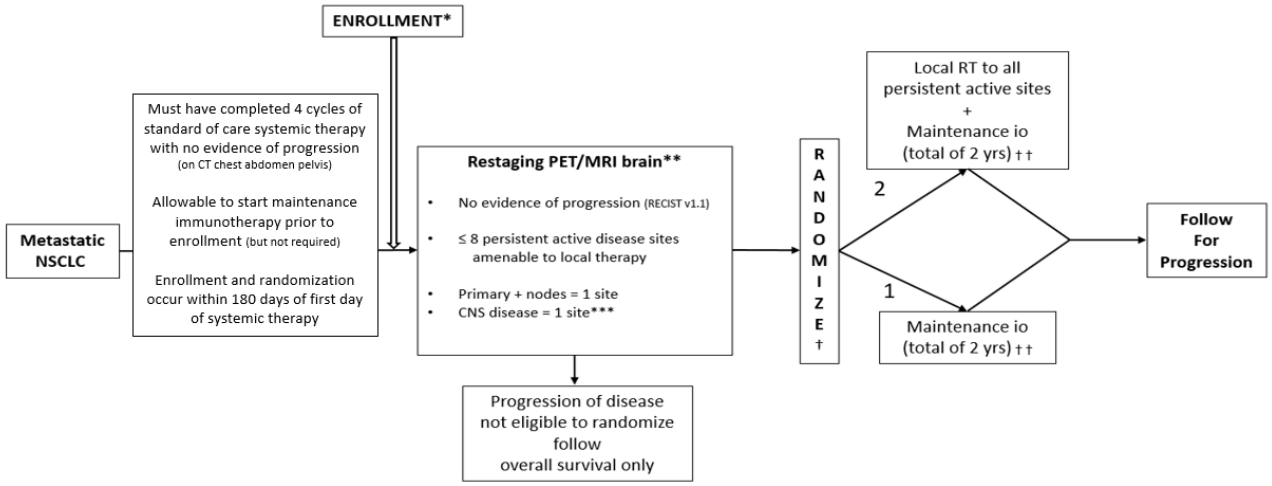
good response to first-line systemic therapy, we do not know if they should have radiation and more immunotherapy or just immunotherapy without the radiation.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be 125 people at Wake Forest Baptist University Hospital and its satellite sites in High Point and Statesville, will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

This is a diagram describing the study



*Enrollment may occur after 4 cycles of standard of care systemic therapy (usually this will consist of combination chemo immunotherapy, but in some cases may be chemotherapy or immunotherapy alone). Neither enrollment nor randomization may occur more than 180 days from the first day of cycle 1 of systemic therapy. Protocol directed therapy should occur within 21 days of randomization (i.e-The start of RT or the resumption of maintenance io)

** If a PET has been performed within 30 days of enrollment with no evidence of progression per RECIST v1.1, then this scan may be used and does not have to be repeated prior to randomization
If an MRI brain has been performed within 90 days of enrollment with no evidence of progression per RECIST v1.1, then this scan may be used and does not have to be repeated prior to randomization

*** Treatment of CNS disease with stereotactic radiosurgery or resection as appropriate per CNS team may take place prior to completion of first line chemotherapy, for stratification purposes this will still count as 1 site of disease

† Randomization will be stratified by number of metastatic sites (1-3, 4-6, or 7-8)
†† Total maintenance immunotherapy includes any maintenance therapy given prior to randomization
Treatment of non-squamous histology may include concurrent pemetrexed with immunotherapy consolidation

If you do qualify for the study, you will be asked to provide written informed consent (by signing this form) to join the study. When you are enrolled on this study, you will have a standard of care PET/CT scan and a brain MRI scan before you are randomized on the trial. These two scans help us make sure that the cancer has not grown or spread to new areas after the chemotherapy and immunotherapy that you already completed. If you have had a PET scan within 30 days of enrolling on this study, or an MRI brain within 90 days of enrolling on this study, then these do not need to be repeated. These scans would be done as a standard part of your care if we were considering radiation treatments and were not on this study.

If you do have evidence that cancer has grown or spread on your PET scan or MRI after enrollment on this study, then you will not be randomized to the two treatment arms, but you will be followed for overall survival every 3 months. Your doctors may still consider radiation or immunotherapy, in the choice of your treatment, but your treatment will not be directed by this study. This will not require extra effort or trips to the hospital on your part, but we may call you and monitor treatment records in the electronic medical record system to check on your status.

If you do not have any new sites of cancer, and if the sites that were known before starting chemotherapy and/or immunotherapy have not gotten worse, then you will be randomized into one of two treatment groups. Randomization means that you are put into a group by chance.

You will be randomized to receive either radiation to all sites of cancer, and then a total of 2 years of immunotherapy with the drug pembrolizumab (Keytruda®), or you will be randomized to receive a total of 2 years of immunotherapy without any radiation therapy. This medicine is given to you through your vein. The total amount of 2 years of immunotherapy in either of these randomized treatments will include any immunotherapy alone (also called maintenance immunotherapy), that you may have received prior to randomization.

Your pembrolizumab will be given every 3 weeks. Based on the specific type of non-small cell lung cancer that you have, your doctor may also give you a standard of care drug called pemetrexed (that is a type of chemotherapy) with the immunotherapy.

To summarize, if you take part in this study, you will have the following tests and procedures:
- Whole Body Positron Emission Tomography (PET/CT) to assess where cancer has spread
- Magnetic Resonance Imaging (MRI) of the brain to determine if cancer has spread to the brain
- Lung function tests
- NCI comorbidity index questionnaire
- Blood or urine pregnancy test for women who can become pregnant

The PET/CT scan and MRI brain scan are standard tests after finishing first line systemic therapy regardless of enrollment on this trial. The lung function tests are also standard tests that are done for lung cancer workup. These tests tell us how well your lungs function. The NCI comorbidity questionnaire helps us understand other health problems that you have at baseline and normally this would not be asked outside of the study. Physical examinations and blood tests will also be done before or during systemic therapy. This is a part of your normal care. It would happen even if you were not in this study. Blood or urine pregnancy tests are standard before radiation and chemotherapy because these treatments can cause severe harm or death to an unborn child.

If you are randomized to receive radiation therapy, before radiation begins, you will have a treatment planning session. This will take about one hour, you will lie in a specific position, possibly within a frame device or on a large plastic bag filled with tiny foam balls like a bean bag. The purpose of the frame or bag is to hold your body as still as possible for planning and treatment. After you are positioned, doctors will check your breathing and see how your organs move. The doctors will try to limit the effect of that movement on the position of your tumor by timing your breathing. They may use a device to control the depth of your breathing. They may use a device to monitor the rate and pattern of your breathing. This is so that they will be able to deliver the radiation to the tumor while accounting for the effect of breathing. In order to plan the radiation, you will have a CT scan that may or may not use contrast. Contrast would be given as an injection in the vein and sometimes helps us see the areas that we are trying to treat more clearly.

Radiation treatments will generally be given over the course of 5 – 10 treatments. This is often with one treatment per day given Monday through Friday. When radiation is given in this short

course and very focused to a small area of the body it is typically called stereotactic body radiotherapy (SBRT). Sometimes depending on the areas being irradiated, radiation may have to be more spread out and given at more times or "fractionated" over 15 – 30 treatments, and sometimes this radiation is given at the same time as low dose chemotherapy. This will be a discussion that is specific to the patient and will be decided on by you and your radiation oncologist.

You will have routine follow-up visits. If you are in the group receiving radiation treatments, then your first follow up visit will happen 1 month after you finish radiation. If you are in the group only receiving immunotherapy without radiation, then your first follow up visit will happen 1 month after you finish the second cycle of immunotherapy. You will have standard CT scans of your chest, abdomen, and pelvis every 3 months for the next 3 years and then every 6 months for 2 years that would be performed regardless of this trial. These CT scans may be performed with contrast that is given as in injection in the vein. You and your doctor will decide if contrast is needed. After this, you will likely continue to be followed by your oncologist for the rest of your life, but you will not continue to be followed for the purposes of the study.

Tumor Biopsies/Blood Collection for Future Research

Wake Forest (the sponsor) will conduct future biomedical research on blood and tumor tissue samples collected during this clinical trial. This research may include genetic analysis to be used for biomarker testing. The sponsor wants to use some of your blood to look at the DNA from your tumor. DNA is like an instruction book for each cell. Changes in your tumor's DNA may help to explain why your cancer cells do not behave like your normal cells, or how your cancer might respond to drugs and other treatments.

The biorepository is a place where human samples (e.g. blood and/or tissue) are stored. This sample will be used for future research and will be tested for markers that may aid research on lung cancer and related diseases and their diagnosis. In order to do this, a variety of techniques will be used. This research may include analysis of proteins, RNA and non-inheritable factors (factors that are not passed on in families) using tumor DNA. Future biomedical research related to genetic (heritable) factors (which could reveal information about your family members) may be conducted.

Storing samples for future studies is called "biobanking".

Common side effects of a biopsy or blood draw are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. Should your disease come back, an additional biopsy to confirm the pathology of disease is strongly recommended. In the event that a biopsy is performed, as part of your standard of care, a portion of the tumor sample will be sent to the Wake Forest Tumor Bank.

Blood samples will be stored indefinitely in secured wake forest tumor bank until analyzed. These samples will be identified by a unique code and the list that links the code to your name will be kept separate from your sample(s).

Two tubes of whole blood will be collected via routine blood draw prior to initiating any protocol treatment, and within 2 weeks of your one month followup. (In the radiation arm this is 1 month after completion of radiation, in the immunotherapy only arm this is 1 month after the 2nd cycle of immunotherapy). You would normally have your blood tested at these same time points to check your labs and blood counts, so these protocol blood draws will not require extra visits to the hospital, and can be done at the same time as your standard labs.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for a total of 5 years after completion of radiation therapy or your second cycle of immunotherapy. After this you will likely continue to follow with your oncologists but will not be specifically followed per this study protocol and results will not be collected past 5 years.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff.

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the radiation. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

Because subjects are being randomized into one of two different treatment arms, there is a chance that they could be randomized to an arm that does improve/benefit as much as the other arm. This is because investigators do not know which arm will perform best.

Risks and side effects related to the SBRT

The risks of SBRT depend heavily on the location of treatment in the body and the size of tumors treated, as well as how closely other organs lie near the tumors. Your doctor will have to discuss these risks individually with you. Your radiation oncologist follows recommended national guidelines to ensure the risks of toxicities with SBRT are as low as possible and all treatment plans are reviewed by physics staff and other radiation oncologist to ensure safety before any treatments are delivered.

<u>Likely</u>

- Damage to surrounding normal lung and/or collapse of a portion of treated lung
- Changes in the lungs as the tumor shrinks; these changes will be recognized by your radiation doctor on your x-rays or scans as expected "scarring" that is developing. In most patients, no noticeable symptoms will result from this lung damage.
- Fatigue

- Redness of irritation of the skin in the treatment area
- Hair loss in the treatment area
- Some soreness of the ribs with an increased risk of rib fracture.
    - Treatment for such symptoms usually consists of rest, heat, and pain medication.
- The following are likely if you have treatment to the bones of the spine in the neck:
    - Inflammation of the lining of the mouth and esophagus (passageway from mouth to stomach), which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur (your body does not have as much water and fluids as it should)
    - Inflammation of the back of the throat, which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur
    - Inflammation of the part of the airway that includes the vocal cords, which can result in hoarseness or loss of voice

Less Likely

- Cough
- Increased phlegm production
- Difficulty breathing
- Fever

Rare

- Fracture or compression of the treated bones of the spine, which can result in pain and which may need nonsurgical or surgical treatment.

Rare but Serious

- Some patients can have the following symptoms associated with lung scarring:
    - Shortness of breath, cough, fever, and/or pain in the chest wall.
    - These patients may require oxygen for a short time or permanently.
    - Lung damage can be life threatening.
- Damage to the lining of the heart, which can cause fluid accumulation around the heart and chest pain, shortness of breath, and/or irregular or rapid heart beat
- Damage to the heart muscle, which can cause heart attack, heart failure, or death
- Damage to the spinal cord, which can cause numbness, weakness, tingling, and/or inability to use the arms and/or legs
- Damage to the esophagus, which can cause problems with swallowing
- Damage to the stomach or bowel which can lead to ulceration or perforation with a risk of infection and death.
- Damage to the large blood vessels surrounding the heart, which could cause coughing up of blood and possibly death
- Severe pain or skin damage leading to an open wound.
- Radiation induced malignancy

Risks and side effects related to non-SBRT or more "fractionated" radiation to the chest:

Likely

- Difficulty, pain, or a burning sensation when swallowing, which is temporary
- Fatigue, which is temporary
- Tanning, redness of the skin, and hair loss within the treatment area, which is temporary

- Skin in the treatment area may remain permanently dry, and chest hair may not grow back
- Decrease in blood counts while undergoing treatment causing bleeding, and bruising
- Cough and some difficulty in breathing due to lung damage

Less Likely

- Narrowing of the esophagus causing difficulty swallowing meals (rarely requiring internal dilation or a feeding tube)

Rare but serious (late)

- Pericarditis – irritation of the heart sac causing a rapid heart rate, or chest pain.
- Myocarditis – irritation of the heart muscle causing shortness of breath, chest pain, or permanent heart muscle damage
- Transverse myelitis – irritation of the spinal cord causing weakness or paralysis
- Bleeding from the airway
- Narrowing of the airway causing shortness of breath
- Death from treatment complications above.
- Radiation induced malignancy

Additional risks with Pembrolizumab (Immunotherapy)
In general, immunotherapy has a risk (>10%) of developing autoimmune complication(s), such as inflammation of the thyroid (hypothyroidism or hyperthyroidism), colon (colitis), lungs (pneumonitis), liver (hepatitis), or pituitary gland (hypophysitis), which can lead to the symptoms noted below. Autoimmune complications can potentially be life-threatening or permanent. In some cases, they may be reversible with urgent administration of steroids and/or other immunosuppressant(s).

More common (>10% of patients):

- constipation
- depressed mood
- diarrhea
- dry skin and hair
- feeling cold
- flushing
- hair loss
- hoarseness or husky voice
- joint or muscle pain
- muscle cramps or stiffness
- skin rash or itching
- unusual tiredness or weakness
- stuffy or runny nose

Less common (<10% of patients):

- general feeling of discomfort or illness
- fever
- nervousness
- pain symptoms

- sensitivity to heat or cold
- slowed heartbeat
- stomach cramps
- sweating
- swelling of the face, feet, or lower legs
- tenderness
- cough or thickening of bronchial secretions
- trouble breathing, chest pain, or chest tightness
- trouble sleeping
- upper right abdominal or stomach pain
- watery or bloody diarrhea
- weight change
- yellow eyes and skin

Rare (<1% of patients)
- bloating
- dark, bloody, or cloudy urine
- blurred vision or other change in vision
- darkening of the skin
- dizziness
- drowsiness
- eye pain
- fainting
- fast heartbeat
- indigestion
- loss of appetite
- mental depression
- nausea or vomiting
- pains in the stomach, side, or abdomen, possibly radiating to the back
- redness or irritation of the eye
- sensitivity of the eye to light
- skin blistering, peeling, loosening, or tearing

Risks of pemetrexed

Likely > 20%
- Fatigue
- Nausea
- Anorexia (weight loss).

Less likely 20%
- vomiting
- changes in white blood cell counts and red blood cell counts
- constipation
- Inflammation of tongue, and mouth

Rare < 1%
- Fever from low blood cell counts
- Dehydration

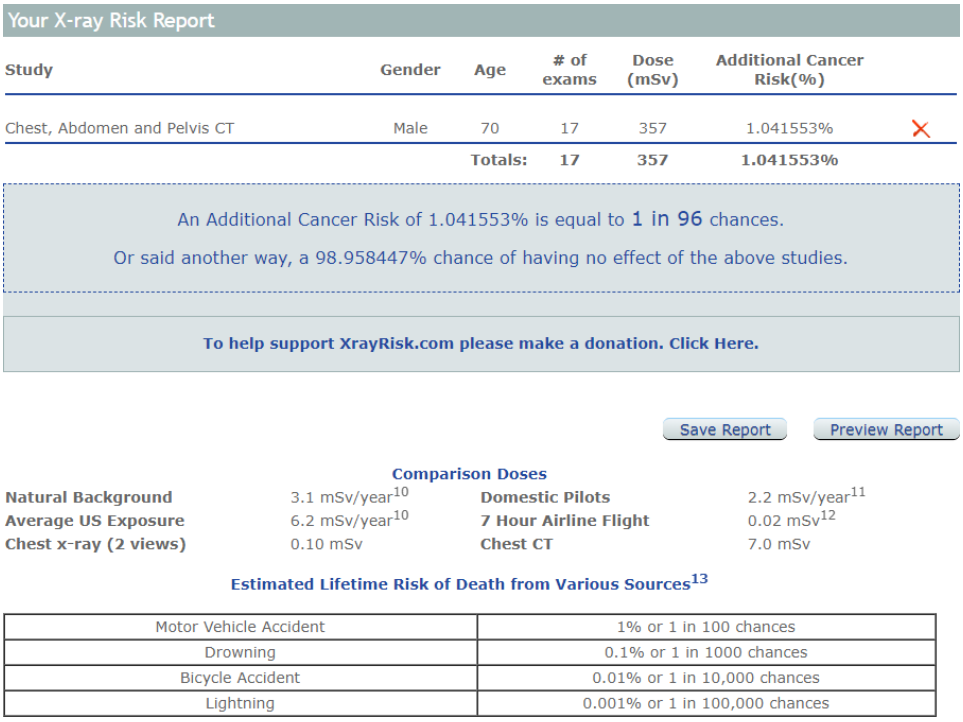
- Increased liver enzymes
- Decreased kidney function
- Heart arrhythmias
- Eye inflammation

Risks of Radiation Exposure

If you participate in this study, you will be exposed to amounts of radiation above what you would normally receive in daily life. To be sure that you do not receive an unhealthy amount of radiation from your participation in this study, you should let your study doctor know if you have had, or are going to have, any other scans or x-rays as part of your medical or dental care. It is very important that you let your study doctor know if you already are participating in, or plan to participate in, any other research study that involves radiation exposure.

After treatment, patients will receive a standard follow up computed tomography scan of the chest abdomen and pelvis at 1 month after completion of the last radiation treatment or in the immunotherapy alone arm, after the 2nd cycle of immunotherapy. After this first scan, additional computed tomography scans of the chest abdomen and pelvis would be performed every 3 months for 3 years then every 6 months for 2 years. In total, this equates to 17 = (1month scan + 3yrs x 4 scans per year + 2 yrs x 2 scans per year) CT scans over 5 years in accordance with NCCN guidelines. These are standard of care scans that would be obtained whether patients were included on this study or not. Below are calculated estimates of the extra radiation dose from these imaging studies which are standard of care.

The additional risks of secondary cancer from radiation therapy that is directed at your tumors are generally < 1% however this will depend on many factors and your physician will discuss this with you directly once your radiation plan has been made.



Your X-ray Risk Report

Study	Gender	Age	# of exams	Dose (mSv)	Additional Cancer Risk(%)	
Chest, Abdomen and Pelvis CT	Male	70	17	357	1.041553%	✕
		Totals:	**17**	**357**	**1.041553%**	

An Additional Cancer Risk of 1.041553% is equal to **1 in 96** chances.

Or said another way, a 98.958447% chance of having no effect of the above studies.

To help support XrayRisk.com please make a donation. Click Here.

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Comparison Doses

Natural Background	3.1 mSv/year[10]	**Domestic Pilots**	2.2 mSv/year[11]
Average US Exposure	6.2 mSv/year[10]	**7 Hour Airline Flight**	0.02 mSv[12]
Chest x-ray (2 views)	0.10 mSv	**Chest CT**	7.0 mSv

Estimated Lifetime Risk of Death from Various Sources[13]

Motor Vehicle Accident	1% or 1 in 100 chances
Drowning	0.1% or 1 in 1000 chances
Bicycle Accident	0.01% or 1 in 10,000 chances
Lightning	0.001% or 1 in 100,000 chances

Keep in mind, the overall lifetime risk of developing an invasive cancer is 37.5% (1 in 3) for women and 44.9% (1 in 2) for men regardless of imaging history. These statistics are averages and do not predict what is going to happen to you. They do not take into consideration individual risk factors including lifestyle (smoking, diet, exercise, etc), family history (genetics) or radiation exposure. The majority of cancers occur later in life and the average lifetime risk of dying from cancer is 25% (1 in 4).

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Risks Associated with Providing Confidential Information
Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. There is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Reproductive Risks and other Issues to Participating in Research

These therapies used in this protocol, including chemotherapy, immunotherapy, and radiation work by killing cells in the body that are dividing quickly. Since sperm cells divide quickly, they are an easy target for damage. Permanent infertility can result if all the immature cells in the testicles that divide to make new sperm (spermatogonial stem cells) are damaged to the point that they can no longer produce maturing sperm cells. This risk depends on patient age, areas in the body that are treated with radiation and the specific type of chemotherapy used and the amount of time that it is used. Your doctor will have an individualized discussion with you regarding these risks.
Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential. There could be a risk of radiation affecting sperm in men, and these sperm usually are replaced with healthy sperm in your body every 3 – 6 months. This could be harmful to any children that are fathered by men immediately after they receive radiation. We strongly encourage men not to father children for at least 6 months to 1 year following treatment with radiation.

Reproductive risks due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while Participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions. If you are a woman able to have children and are unwilling to use adequate birth control measures to prevent pregnancy, you should not participate in this study. If you should become pregnant or suspect that you have caused anyone to become pregnant while you are on this study, you must tell your study doctor immediately.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope that treatment of all visible areas of cancer will slow the overall disease but that is uncertain. We hope the information learned from this study will aid in the understanding of cancer and help in the development of new approaches to its treatment and benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. The usual treatment for your disease is the same chemotherapy but without the additional radiation treatments or immunotherapy.

You could be treated with the combination of chemotherapy, radiation therapy and immunotherapy even if you do not take part in the study.

WHAT ARE THE COSTS?

The costs of all medications, radiation treatment, x-rays, tests, physician's fees, diagnostic and laboratory studies, drug handling charges, transportation, and hospital or clinic visits will be billed to you. Some of these costs may or may not be covered by your insurance provider. In addition, the use of medications to help control side effects could result in added costs.

You will receive no payment for taking part in this study. Parking validation will be provided for all study-related visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest Baptist Comprehensive Cancer Center. The sponsor is providing money or other support to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the immunotherapy being studied.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of radiation treatment with pembrolizumab or pembrolizumab alone; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or

local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Michael Farris M.D. at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** History and physicals, pathology, labs, imaging and lung function tests.

If this research study involves the diagnosis or treatment of a medical condition, then Protected

Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

3) Representatives from government agencies such as the Food and Drug Administration (FDA), NCI (National Cancer Institute), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.
Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups, it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the

research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed, or it will be de-identified. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Farris that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Michael Farris M.D.
Department of Radiation Oncology
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form, you give us permission to use your Protected Health Information forthis study.
If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part, or you may leave the

study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is felt by the treating physician to be in your best medical interest, your condition worsened, new information becomes available, or you had an unexpected reaction. Additionally, this could occur because you failed to follow instructions, or because the entire study has been stopped

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Michael Farris MD Michael Farris M.D. at [redacted]

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].
You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature:_____Date:_____Time:_____am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____Date:_____Time:_____am pm