Official Title: A Pilot Study of Combined Decompressive Spine Radiosurgery and Pembrolizumab in Patients With High-Grade Epidural Disease

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IRB Approval Date: 11/27/24

Wake Forest School of Medicine

COMPREHENSIVE CANCER CENTER
WFBCCC #03221

WAKE FOREST School of Medicine

Informed Consent

DEPARTMENT OF RADIATION ONCOLOGY

A pilot study of combined decompressive spine radiosurgery and pembrolizumab in patients with high-grade epidural disease

Informed Consent Form to Participate in Research
Christina Cramer, M.D., Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to study the combination of decompressive spine radiosurgery and the drug pembrolizumab in reducing the size of cancer that has spread near the spinal cord. You are being invited to be in this study because you have cancer that has spread or has the potential to spread near your spinal cord. Your participation in this research will involve 1-5 treatments of radiation, immunotherapy as prescribed by your medical oncologist, giving some blood, filling out some questionnaires, and getting three MRI scans of your spine.

Participation in this study will involve taking pembrolizumab and receiving radiosurgery. Radiosurgery involves radiation in a large dose to destroy your cancer. Radiosurgery is noninvasive, meaning it does not involve cutting your tumor out. All research studies involve some risks. A risk to this study that you should be aware of is the risks of the combination of the pembrolizumab and the radiosurgery. 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 receiving pembrolizumab and radiotherapy without being in a study. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder 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 Dr. Christina Cramer. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her phone number is [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].

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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. You are being asked to take part in this study because you have cancer that has spread or has the potential to spread near your spinal column. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. 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 and bad) pembrolizumab and radiosurgery have on you and your condition.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

10 people at Wake Forest Baptist Comprehensive Cancer Center will take part in this study. Wake Forest Baptist Comprehensive Cancer Center is the only site conducting this study.

WHAT IS INVOLVED IN THE STUDY?

First in this study, you will have a planning session for radiation treatment. This is called a simulation or mapping session and will take about an hour. Sometimes you will have contrast injected into your spinal canal by a radiologist prior to the scan to help your physician see the spinal cord better. Injecting the dye into the spinal canal feels like a lumbar puncture. During the planning session, your body will be positioned in the same way as when you receive your radiation treatment. Your body will be marked with some tiny tattoos and you will undergo a CT scan. The CT scan and an MRI scan will be used to design your radiation treatment. It will take roughly one and a half weeks after the planning until you receive treatment. Treatments will usually take about 30 minutes. The total number of treatments will depend on the exact shape of your cancer relative to your spinal cord. At most, you will receive five treatments. Usually you will have 1-2 days off in between treatments. Meaning that if you got your first treatment on a Monday, your second treatment would be on a Wednesday or a Thursday. After the radiation phase of your treatment is complete, you will start on immunotherapy (pembrolizumab) with your medical oncologist. This is a treatment given through a vein in your arm and is typically given every three weeks. Your medical oncologist may need to adjust the dose frequency or schedule for your particular needs.

If you take part in this study, you will have the following tests and procedures:

- Three MRI scans of your spine (before treatment, 2 months after treatment, and 6 months after treatment)

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- Answer questions about your pain and your quality of life before treatment, 2 months after treatment, and 6 months after treatment
- You will have approximately 2.5 teaspoons of blood withdrawn from a vein on three days. The total amount of blood withdrawn during the study will be approximately 7.5 teaspoons.

Your blood sample will be obtained in the Radiation Oncology or Medical Oncology Department at Wake Forest University Baptist Medical Center. The sample will be stored in the Shiozawa laboratory and it will be given only to researchers approved by Dr. Cramer. Some of your sample will be used immediately to look for markers in the blood that correlate with pain related to cancer. Some of your blood sample may be stored for future research. In order to participate in this study, you must be willing to provide this sample for future research. An Institutional Review Board (IRB) would have to approve any future research study using your sample. In the future, research on your specimen may involve whole genome sequencing.

The research that will be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you, which may occur as a result of the research.

Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES you many contact for future research studies
____NO I do not want to be contacted regarding future research studies.

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The future research may include studying your genetic information. At some point in the future, we may be required to share genetic data with federal repositories. The National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of genetic studies, especially when the research looks at all or large sections of individual's genetic code. This is often called whole genome sequencing. Genomic information relates to the structure and function of all of the genetic material in the body. These central banks will store your genetic information and give them to other qualified and approved researchers to do more studies. The data that we share with federal repositories will be coded in such a way that you would not be able to be identified. We will not share your name, birth date, or any other information that could directly identify you. The link to the code would be kept securely at the Wake Forest Baptist Health. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally. NIH prohibits people from trying to identify individuals whose genomic information is in an NIH-designated repository.

We do not think that there will be further risks to your privacy and confidentiality by sharing your genetic information with these banks. However, we cannot predict how genetic information will be used in the future. The genetic data could be used to study a wide variety of diseases.

In the future, research on your specimen may involve whole genome sequencing.

How Long Will I Be in the Study?

You will be in the study for about 7 months.

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. The primary risk of withdrawing from the study would be the risk of progressive disease near your spinal cord which could lead to: numbness or weakness in your arms or legs, paralysis, problems with use of your bladder or bowels.

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. Risks and side effects related to the pembrolizumab and radiosurgery we are studying include:

Pembrolizumab*:*

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

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<table>
<tr><td colspan="2">be reversible with urgent administration of steroids and/or other immunosuppressant(s).</td></tr>
<tr><td>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</td><td>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</td></tr>
<tr><td colspan="2">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</td></tr>
</table>

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Risks and side effects related to SBRT (stereotactic body radiation therapy):

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. SBRT is a cancer treatment that sends large, precise doses of radiation to your cancer and minimizes damage to healthy tissue. 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.

Common

- Fatigue
- Pain flare (pain getting worse in the area that gets treated because of some inflammation from the radiation)
- Sore throat (if the area that needs treatment is a bone in your neck or upper back)
- Hoarseness (if the area that needs treatment is a bone in your neck)

Less common

- Fracture of the bones being treated (about a 10% risk)

Very rare but serious

- Damage to the spinal cord or spinal nerves which could cause permanent numbness, weakness, or other neurologic damage
- Damage to the kidneys (only if the area that needs treatment is near the kidneys)
- Severe damage to the esophagus or bowels

There may also be risks to the combination of pembrolizumab and radiosurgery that we are not aware of.

In addition, 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 risks 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.

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.

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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.

You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

Reproductive Risks and other Issues to Participating in Research

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, OrthoEvra patch, NuvaRing, intrauterine devices (IUD), Nexplanon implant, 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 diaphragm with spermicide with Plan B used for any noticed condom or diaphragm failures. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because NO method of birth control is 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.

Contraceptive Measures for Males

Your participation in this research study may damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study and for 1 months afterwards. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should also promptly notify her doctor.

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 the information learned from this study will benefit other people in the future. The benefits of

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participating in this study may be reducing the amount of tumor near your spinal cord and improved pain relief. Based on experience with radiation and pembrolizumab, the study team believes that the combination of these treatments will be more effective than either treatment alone. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

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. Instead of being in this study, you have these options:

Your spine tumor could be treated with:

1. Surgery and radiation therapy
2. Radiation therapy or radiosurgery alone

Surgery followed by radiation or radiation alone are the most common treatments for your situation. The risks of surgery are bleeding, infection and other surgical risks. The benefit of surgery is that it reduces the amount of tumor near your spinal cord. The hope of the study team is that combining radiation and immunotherapy will effectively reduce the amount of tumor near your spinal cord without you having to do surgery but we do not know if it is going to be as effective as having surgery.

WHAT ARE THE COSTS?

You or your insurance company will be charged for all procedures that take place. These procedures are part of the standard of care for your condition, only the combination of the medication and the radiosurgery is unique.

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 pembrolizumab and radiosurgery; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

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WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study. However, you will receive a parking pass for your study visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the Wake Forest Comprehensive Cancer Center. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

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 Christina Cramer, MD at [redacted] (daytime) or [redacted] (afterhours emergencies only).

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**:** demographic information and medical information about your treatment for cancer.

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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 and the National Cancer Institute.

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

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research information not already in your medical record will either be destroyed or it will be de-identified

AND/ 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. Christina Cramer 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:

Dr. Christina Cramer
[redacted]

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 for this 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 clinically relevant 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

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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 in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

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

Clinically relevant research results will be disclosed to you. Standard of care procedures, like your blood tests and MRI results, will be part of your medical record. The research blood draw for future research results will not be disclosed to you.

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, Dr. Christina Cramer 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.

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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

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