Title of Study: Phase II trial of concurrent, split course chemoradiation followed by Durvalumab (MEDI4736) in poor risk and/or elderly patients with newly diagnosed stage III non-small cell lung cancer

NCT04441138

Date of consent: 23Nov2023

RUSH

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

Site Principal Investigator: Gaurav Marwaha, MD

Department: Radiation Oncology

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Chicago IL 60612

Protocol Title: Phase II trial of concurrent, split course chemoradiation followed by Durvalumab (MEDI4736) in poor risk and/or elderly patients with newly diagnosed stage III non-small cell lung cancer

Sponsor(s): Dr. Gaurav Marwaha (with AstraZeneca as a collaborator/funder)

Name of Participant: _____

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to assess the safety and efficacy of a combined course of chemotherapy and radiation (chemoradiation) followed by immunotherapy (durvalumab) for poor risk or elderly patients with locally advanced non-small cell lung cancer (NSCLC). Combined chemoradiation followed by durvalumab is standard of care/FDA approved for

patients with locally advanced non-small cell lung cancer (NSCLC) with an excellent performance status (i.e. very "fit" patients). Several approaches are standard for poor risk/elderly patients with locally advanced non-small cell lung cancer (NSCLC): a combination of chemotherapy and radiation; chemotherapy followed by immunotherapy; or radiation followed by immunotherapy. If you agree to participate in this study, combined chemotherapy and radiation therapy, followed by durvalumab, would last 1 year at the most, and we would continue to follow your health to see how you are doing as long as the study is open.

During your follow-up visits, you will be asked to have a clinical assessment by your oncologists and research nurses, provide blood for standard laboratory tests, answer questions about your health, and have imaging scans (CT scans, MRI scans, and/or PET/CT scans). For a detailed list of study procedures, please see the "*What are the activities you will be doing if you participate in this study?*" section of this consent form.

There are risks to you for participating in this study, some of which may be serious, life-threatening or may not go away. In this study, risks depend on treatment modalities, and include but are not limited to: **Radiation related:** Fatigue, skin irritation, lung inflammation, swallowing discomfort; **Chemotherapy related**: fatigue, drop in blood counts (number of red blood cells, white blood cells, or platelets) infection, hair loss, neuropathy (pain or altered sensation in hands/toes); **Durvalumab related**: Inflammation in any part of the body (e.g. in bowel, causing diarrhea; in skin causing rash; in thyroid causing thyroid dysfunction, in lung causing cough/shortness of breath; in liver causing hepatitis) infusion-related reactions, allergic reactions and infections/serious infections. A serious infection is an infection that may cause hospitalization or death.

Based on experience with durvalumab, patients with the exact same diagnosis and stage of lung cancer have experienced an overall and progression free survival benefit, in addition to a reduction in risk for brain metastases. However, because individuals respond differently to therapy, no one can know in advance if it will be helpful for you.

There are other options available to you if you decide not to participate in this study. You may choose another form of treatment or care for your locally advanced lung cancer without being in a study such as chemotherapy + radiation without immunotherapy, radiation therapy alone, and/or systemic therapies alone (chemotherapy and/or immunotherapy). You should discuss other options with your study doctor.

<u>Detailed Information</u>: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

<u>Why are you being invited to participate in this study?</u>

You are being asked to participate in this study because patients with the same disease as you have experienced survival benefit from adding durvalumab after completion of chemotherapy/radiation. This regimen has not been used much in elderly patients and/or patients with other medical issues ("poor risk" patients), and we hope to see a similar benefit in elderly

subjects and/or subjects with other medical issues (“poor risk” subjects) .

How many participants will take part in this study?

Approximately 30 participants are expected to take part in this study at Rush University Medical Center.

What are the activities you will be doing if you participate in this study?

If you agree to be in this study, you will be asked to participate in the following activities:

Screening Activities

- Physical exam
- Vital signs (height, weight, temperature, blood pressure, etc.)
- ECG (electrocardiogram) – a test that measures the electrical activity of your heart
- Blood and urine tests to make sure you are healthy enough to participate
- Thyroid tests
- If you have known HIV disease or active hepatitis or tuberculosis you will not be allowed to participate. If we discover during the study that you have tested positive for a reportable infectious disease (tuberculosis, HIV and/or hepatitis), we will be required to report such findings to the Illinois Department of Public Health, according to applicable Illinois laws. The study doctor will refer you to a doctor for counseling and treatment. The Sponsor, Dr. Marwaha with AstraZeneca, will not cover the cost of this treatment or further care. This means that along with the test result your personal information (name, birth date, phone number and address) will be released to the public health authorities.
- Pregnancy test for women who are able to have children (if positive, patient will be excluded)
- Performance status. Performance status is a score that estimates your ability to perform certain activities of daily living (ADLs) without the help of others and general well-being.
- PET/CT imaging
- MRI brain or CT chest/abdomen/pelvis, brain
    - Magnetic resonance imaging (MRI) scans (brain):
      MRI scans use powerful magnets. Some MRI scanners are very narrow. Talk to the study doctor if you have metal in your body or if you are uncomfortable in small spaces. With a certain type of dye used for MRI scans, some participants with kidney disease may have a severe reaction. This could include skin thickening, joint pain and/or swelling, and, in rare cases, lung and heart problems, and even death.
    - Computed tomography (CT) scans (chest/abdomen/pelvis, brain):
      Some people can have allergic reactions to the dye put in their veins for these tests. The allergic reactions can cause itching or rash. More serious allergic reactions can cause difficulty breathing, dangerously low blood pressure, or kidney damage. X-rays and CT scans use radiation. Please talk to the study doctor about the amount of radiation from these scans.

- Tumor biopsy for PD-L1 testing. A previously collected sample may be used if the existing sample is not older than 3 years old. Your doctor will discuss with you whether a new tumor biopsy is needed or whether an existing sample is enough.
- Pulmonary function testing – tests to show how well the lungs are working
- Complete a quality of life (QOL) that require you to answer questions about your health

Study Visits

A "cycle" of chemotherapy and radiation consists of 21 days. Radiation will occur daily on weekdays for either 7 or 8 consecutive weekdays per cycle, for a total of 30 radiation treatments over the entire 4 cycles. Once a week during radiation therapy, you will meet with the Radiation Oncologist for a clinical check in/physical exam. You will receive FDA approved chemotherapy regimen ("chemotherapy" refers to therapy involving drugs) in combination with radiation therapy ("radiation therapy" refers to therapy involving radiation) such as carboplatin pemetrexed (carbo pem), carboplatin paclitaxel (carbo tax) and carboplatin etoposide (carbo etoposide).During chemotherapy weeks, you will meet with the Oncologist for routine lab work (blood counts and chemistries (serum, plasma or hematology tests), and a clinical visit/physical exam. These visits are all consistent with standard of care, or what we would do for patients not on a clinical study.

Once you have completed four cycles of chemoradiation, you will have "restaging scans," consisting of CT chest/abdomen/pelvis as well as routine lab work. If your disease has not spread or progressed, and you are believed to remain a candidate for immunotherapy (as deemed by your Medical Oncologist), you will go on to receive durvalumab as an IV infusion (through a needle into your vein) every 4 weeks (i.e. 28 days, also known as a cycle) for up to a maximum of 12 months (up to 13 doses/cycles).

<u>Durvalumab Cycles 1-12, Day 1</u>

- Targeted physical exam based on symptoms
- Vital signs
- ECG, if your doctor thinks an ECG is needed
- Blood tests to make sure you are healthy enough to participate
- Pregnancy test for women who are able to have children
- ECOG performance status.
- Durvalumab will be infused over the course of one hour
- You will complete a quality of life (QOL) questionnaire

<u>Durvalumab Cycles 1-3, Day 14</u>

Clinical follow-up with Medical Oncologist

<u>Follow-up after completion of treatment</u>

Visits every 3 months with blood work and imaging (possibly more frequently if any concerns) for 1 year after completion of treatment, then per standard of care less frequent follow-up thereafter (every 4 months for years 3-5, then every year for years 5+). We would continue to follow your health to see how you are doing as long as the study is open.

Imaging Scans
To see how your disease is responding to the study treatment, CT scans will be done every 3 months for the first 48 weeks, and then every 3-6 months thereafter. Brain MRIs will be performed annually in follow-up or for new neurological symptoms.

What are the radiation risks of participating in this study?
CT scans deliver a low dose of radiation, considered to be safe and per standard of care for locally advanced NSCLC. MRIs are also considered to be safe and per standard of care for surveillance of NSCLC. MRI may affect the accuracy or optimal use of any metallic devices that are implanted in your body. The radiology department can provide additional details regarding risks associated with these imaging modalities should you desire to know more at (312) 942-5751.

Will you be contacted about participating in future research?
If you agree, we may contact you after your participation in this study about participating in future research. Please initial and date one of the following options:

_____ _____ Yes, I agree to be contacted about future research.
Initials Date

_____ _____ No, I do NOT agree to be contacted about future research.
Initials Date

What are the risks and discomforts of participating in this study?
There are risks to you for participating in this study, some of which may be serious, life-threatening or may not go away.

Radiation risks are generally mild. Most participants experience some fatigue (exhaustion), dry cough, difficulty or pain with swallowing certain foods/drinks, and/or skin irritation over the chest/back. Some risks that are more rare are severe fatigue, symptomatic lung inflammation and/or lung fibrosis, damage to the heart/cardiac vessels, spinal cord injury, and bleeding events.

Chemotherapy risks include fatigue, drops in blood counts (number of red blood cells, white blood cells, or platelets), infection, hair loss, neuropathy (pain or weakness in fingers, toes), fevers, nausea/vomiting, changes in taste, mouth ulcers, kidney injury, and hearing loss.

Risks with durvalumab include, but are not limited to,

- Lung problems (pneumonitis). Signs and symptoms may include new or worsening cough, shortness of breath, and chest pain.

- Liver problems (hepatitis). Signs and symptoms may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.

- Intestinal problems (colitis). Signs and symptoms may include diarrhea or more bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.

- Hormone gland problems (especially the thyroid, adrenals, pituitary, and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches; extreme tiredness; weight gain or weight loss; dizziness or fainting; feeling more hungry or thirsty than usual; hair loss; feeling cold; constipation; your voice gets deeper; urinating more often than usual; nausea or vomiting; stomach-area (abdomen) pain; and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.

- Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include decrease in the amount of urine, blood in your urine, swelling of your ankles, and loss of appetite.

- Interstitial lung disease (ILD) is an umbrella term used for a large group of diseases that cause scarring (fibrosis) of the lungs. Uncommon side effects (affects between 1 and 2 in 1,000 patients treated)
    - Scarring of lung tissue (interstitial lung disease): May cause breathlessness, a cough that does not go away, and feeling tired all the time

- Skin problems. Signs may include rash, itching, and skin blistering.

- Guillain-Barre (gee-YAH-buh-RAY) syndrome is a rare disorder in which your body's immune system attacks your nerves. Weakness and tingling in your hands and feet are usually the first symptoms.

- Inflammation inside your eye known as Uveitis. This usually happens when your immune system is fighting an eye infection — but it can also happen when your immune system attacks healthy tissue in your eyes. This usually occur in 1 out of 1000 patients.

- Inflammation or swelling of the joints also known as Immune-mediated arthritis. Which means that your immune system attacks healthy cells in your body by mistake, causing inflammation (painful swelling) in the affected parts of the body. (Uncommon side effects affects between 1 and 2 in 1,000 patients)

- Problems in other organs. Signs and symptoms may include neck stiffness; headache; confusion; fever; chest pain, shortness of breath, or irregular heartbeat (myocarditis); changes in mood or behavior; low red blood cells (anemia); excessive bleeding or bruising; muscle weakness or muscle pain; blurry vision, double vision, or other vision problems; and eye pain or redness.

- Severe infections. Signs and symptoms may include fever, cough, frequent urination, pain when urinating, and flu-like symptoms.

- Severe infusion reactions. Signs and symptoms may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling like passing out, back or neck pain, and facial swelling.

There may be other risks that may happen that we cannot predict.

What are the reproductive risks of participating in this study?

Women
If you are pregnant or breastfeeding, you cannot take part in this study. A pregnancy test is required and will be given before you start treatment and throughout the study. You are responsible for using an effective birth control method such as birth control pills, barrier method (such as condoms or diaphragms), intrauterine device (IUD), hormone implants or surgical sterility while you are taking part in this study. Once you have completed treatment, you may discontinue birth control after 12 months after completion of your study treatment. If you become pregnant, you must notify the study doctor immediately.

Interactions with some drugs, including antibiotics can affect birth control pills. You should discuss with the study doctor a second method of birth control during the study, if birth control pills are used.

Men
You are responsible for using an effective birth control method, such as the ones listed above. If you are a male and your female partner becomes pregnant, you must notify your study doctor immediately. Once you have completed treatment, you may discontinue birth control after 12 months after completion of your study treatment.

What if there is new information that may affect your decision to participate in this study?
During this study, you will be told about important findings (either good or bad), such as changes in the risks or benefits of participation in the study or new choices to participation that might cause you to change your mind about being in the study. If new information is shared with you, you may be asked to sign a revised consent form in order to continue participating in this study.

Will you receive your individual results from the study?
Generally, activities performed for research purposes are not meant to provide clinical information. We may learn things about you from this study which could be important to your health or treatment. If this happens, this information will be shared with you. The therapies involved may impact your overall health, blood work, and or imaging scans. These are all part of routine follow-up regardless of whether or not you are enrolled on the study, and all of these results will be shared with you.

Can you leave or be removed from this study?
You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to leave this study. If you leave this study

before the final study visit, the study doctor may ask you to complete the final steps. Risks to withdrawal could compromise your overall outcomes from your disease. Withdrawal from the study can otherwise happen immediately.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the instructions;
- The study is cancelled for any reason.

What about confidentiality of your medical information?

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Marwaha, Dr. Fidler, their study team, and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Marwaha and his study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may use or disclose for this research includes: all information in the medical record.

Dr. Marwaha and his study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers
- The study Sponsor, and to AstraZeneca and its representatives
- Monitoring agencies such as the Food and Drug Administration (FDA).

While you participate in the study you will have access to your medical record, but Dr. Marwaha and Dr. Fidler and study team are not required to release to your study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed above.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Marwaha at 500 S. Paulina, Chicago, IL 60612. If the authorization is revoked, you will no longer be allowed to participate in the study and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law. Names will be replaced by coded identification numbers.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. This research study can be found by searching for the following Clinical Trial Registry Number (NCT#): NCT04441138.

What are the costs to participate in this study?

There are no additional costs to you for participating in this research.

You or your insurer will be responsible for paying for the cost of the following: chemotherapy, radiation therapy, and immunotherapy.

If you have health insurance the insurance may or may not pay for the costs associated with your participation in this study. You will have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires. Our Social Work team will work with your insurance company to verify coverages.

If you do not have insurance, you will be billed for the amount you have to pay.

Will you be paid for your participation in this study?

You will not be paid for being in this study.

What if you are injured as a result of your participation in this study?
If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact a member of the study team as soon as possible. Dr. Marwaha's office phone is (312) 942-5751. Dr. Fidler's office phone is (312) 942-5904.

You should let any health care provider who treats you know that you are in a research study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What other information should you know about?

Investigator Financial Disclosure
This research study is supported by money from AstraZeneca, LP. Drs. Fidler and Bonomi (investigators on this study) receive extra money from AstraZeneca, LP for activities that are not a part of this research. The activities are for consulting and speaking engagements for AstraZeneca, LP. It was determined that the relationships are considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Drs. Fidler and/or Bonomi at (312) 942-5904.

Who can you contact for more information about this study?
Questions are encouraged. If you have further questions about this study, you may call any of the following:

Research Nurses: 312-CANCER-1
Thoracic Medical Oncology Nurses: 312-563-4880
Radiation Oncology: 312-942-5751

Who can you contact if you have concerns about your rights as a study participant?
Questions about the rights of research participants may be addressed to the Rush University Medical Center Office of Research Affairs at 1-800-876-0772.

What are your rights as a study participant?

Taking part in this study is voluntary. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected.

If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Marwaha in writing at the address on the first page. Dr. Marwaha may still use your information that was collected prior to your written notice.

SIGNATURE BY THE PARTICIPANT

By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent form. You will be given a signed copy of this consent.

Name of Participant	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Signature of Individual Obtaining Consent	Date of Signature

SIGNATURE BY WITNESS/INTERPRETER:
I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the and the person signing the form has done so voluntarily.

Name of Witness/Interpreter	
Signature of Witness/Interpreter	Date of Signature