The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title: OSU-19132: An Investigator-Sponsored Phase II Single Arm Trial of Ramucirumab and Pembrolizumab in Patients with EGFR Mutant Non-Small Cell Lung Cancer

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Sponsor: The Ohio State University

Funders: Merck & Co., Eli Lilly and Company

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part in this clinical trial. Discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can always ask your study doctor for more information.

You are being asked to take part in this study because you have lung cancer that has continued to grow despite the treatment you have already received. The standard drugs used to treat your disease are no longer working. Your cancer has been confirmed by a pathologist (a person who studies diseases).

This clinical trial is testing a new drug combination – ramucirumab and pembrolizumab. Ramucirumab, also known as Cyramza, is a chemotherapy drug that treats cancer by blocking a signal for blood vessel growth. Ramucirumab is approved by the Food and Drug Administration (FDA) for the treatment of a variety of cancers, including lung cancer.

Pembrolizumab, also known as Keytruda, is an immunotherapy drug, meaning it stimulates the immune system to treatment cancer. Pembrolizumab is also approved by the Food and Drug Administration (FDA) for the treatment of a variety of cancers, including lung cancer.

The combination of these 2 drugs is not approved by the FDA. It is the combination of drugs that is experimental. Experiments in the laboratory suggest that using these 2 drugs together may be more effective in killing tumor cells than either separately.

If you agree to take part in this study, you will first be asked to sign this consent form. You will then have a series of tests done to determine if this study is a good fit for you. More information about what testing will be done can be found under the Screening heading in section 3, “What will happen if I take part in this study?”.

If you go on this study, you will then receive ramucirumab and pembrolizumab once every 3 weeks for up to 35 cycles, or approximately 2 years.

You will have other tests done to determine how well the study drug combination is fighting your cancer. These tests include CT scans, MRI scans, Blood draws, and urine tests. You may continue to receive the study drugs for as long as you continue to benefit from them.

If it is found that your tumor is growing, or if it is determined that you are not benefitting from the study drugs, you will be taken off study treatment. You will then have an End of Treatment Visit that assesses your cancer. More information about the End of Treatment Visit can be found under the End of Treatment heading in section 3, “What will happen if I take part in this study?”.

You will then be followed up with every 3 months for a year, and then every 6 months, to see how you are doing.

You may experience side effects while taking the study drugs (more information can be found on side effects in section 6, “What risks, side effects, or discomforts can I expect from being in the study?”).

Risks of Ramucirumab: Low white or red blood cell count, skin rash, elevated white blood cell count, blood clots, constipation, difficulty breathing, taste changes, heart rhythm abnormities, loss of hair, cough, abdominal pain, fluid retention with weight gain, numbness in your fingers and toes, vomiting, weight loss, mouth sores, nausea, dizziness, diarrhea, decreased appetite, fatigue/weakness, infection, vomiting, and allergic reaction.

Risks of Pembrolizumab: itchy skin, loose, watery stools, cough, joint pain, rash, fever, back pain, abdominal pain, loss of skin color, not enough thyroid hormone (resulting in tiredness, weight gain, feeling cold, or constipation), and low levels of salt in the blood (causing tiredness, confusion, headaches, muscle cramps, and nausea).

Your study doctor will help you manage any side effects you may have.

There are also risks with involved with blood draws, CT scans, MRI scans, and tumor biopsies. These are detailed in section 6, "What risks, side effects, or discomforts can I expect from being in the study?", and are the same as they would be if you were not a part of this research study.

You should not be pregnant, become pregnant, or impregnate a female sexual partner while you are taking the study drugs, as it is not known what effect they will have on an unborn child.

You can stop being in this study at any time, with no effect on your regular care.

1. Why is this study being done?

The major purposes of this study are:

- To test the safety of the study drugs and see what effects (good and bad) they have on you and your cancer
- To evaluate how the human body reacts to the study drugs in combination

2. How many people will take part in this study?

Approximately 51 subjects are expected to enroll in this study at The Ohio State University.

3. What will happen if I take part in this study?

Your participation in this study will be divided into different kinds of visit:

1. Screening
2. Treatment
3. Post-Treatment Follow-up

Different procedures will be done during each of these different visits as described below.

SCREENING

After your study doctor has answered all of your questions about the study and you have given written consent by signing this form, screening procedures will be done to make sure you are eligible to participate in the study. Many of the tests may be the same as those you have had in the past to diagnose and treat your cancer.

The Screening Visits will take place 7-28 days before you receive the study treatment.

The following will be performed during the Screening Visit:

- Your study doctor will ask you to sign this consent form before these tests or any other study procedures are performed.
- The study doctor or nurse will ask you about your medical history and obtain a list of all medications that you are currently taking and the previous treatments for your cancer you have received.
- A full physical examination will be performed and your height, weight and vital signs (heart rate, blood pressure, breathing rate, and body temperature) will be recorded.
- A computed tomography (CT scan - a computerized series of x-rays) or magnetic resonance imaging (MRI—images created with magnetic fields) will be performed within 4 weeks of starting the study treatment.
- Blood (about four teaspoons/20 ml) will be drawn for lab tests and for study-specific test and to check the status of your disease. These tests will be done within 10 days of study treatment.
    - A pregnancy test (blood test) will be done on part of the sample if you are a woman capable of becoming pregnant.
- Urine will be collected for lab tests.
- The study doctor will examine you and may order additional scans to show the extent of your cancer.
- A sample of your tumor will be requested for additional testing. This additional testing will be done on a piece of the tumor tissue you have already given during a previous surgery or biopsy. You will not need to have a separate biopsy for the purposes of this study. The information obtained from this test will not impact your care, but will be used to learn more about your disease.
- You may need to stop your current chemotherapy for a specified amount of time prior to starting the study treatment. This duration could be 1 week, 4 weeks, or longer depending on the half-life of your chemotherapy. A 7-day washout period or four half-lives after the last treatment dose, whichever is longer, is required for TKI. A 4-week washout period is required for cytotoxic chemotherapy.

All of these tests may be completed over several clinic visits. If a recent test result is already

available in your medical records, that test may not need to be repeated. Your study doctor or nurse will let you know if this is the case.

Once your eligibility is confirmed, you will be able to participate in the Treatment part of the study.

TREATMENT

Treatment visits are when you will receive the study drug.

Ramucirumab and Pembrolizumab will be given on the same day once every 3 weeks. (This 3 week period is referred to as a cycle.) You will receive the study drugs intravenously (into a vein/through an IV) once every 3 weeks. The treatment infusion will be 60-90 minutes although this may vary. If you only tolerate one of the study drugs well, you can still be on the study and take just that drug.

The following tests will be performed on the day you begin each cycle. The tests listed below will be completed over several hours during each Treatment Visit:

- The study doctor or nurse will ask you about any side effects you may have felt since your last visit and to list all medications that you are currently taking.
- The study doctor or nurse will review your symptoms and your ability to perform your normal activities.
- A physical exam will be performed and your body weight and vital signs (heart rate, blood pressure, breathing rate and body temperature) will be recorded.
- Blood (about four teaspoons/20 ml) will be drawn at visits, Cycles 1 and 3 for study-specific tests to check on the status of your disease.
- A sample of your urine will be collected for routine urinalysis.

The following tests will be performed on the 8th day of each cycle:

- A physical exam will be performed and your body weight and vital signs (heart rate, blood pressure, breathing rate and body temperature) will be recorded.
- A complete clinical chemistry (including liver function tests)
- A sample of your urine will be collected for routine urinalysis.

After you have been on the study for 2 cycles, you will receive a CT scan and/or MRI to determine if your cancer is changing. These assessments will then be performed approximately every 6-8 weeks while you remain on study in order to see if your tumor is shrinking, staying the same size, or growing.

You will receive ramucirumab and pembrolizumab for as long as you continue to benefit from them for up to 35 cycles (approximately 2 years). Your doctor will determine if you are benefitting from the treatment with testing. You or your study doctor can decide to stop treatment at any time, and your study doctor will help you do so safely.

If at any time your tumor is found to be growing, your study doctor will then discuss alternative treatment options with you. be
Patients who either stop treatment after showing no benefit from it, or are removed from the study for other reasons, will undergo the evaluations listed below.

END OF TREATMENT

If you stop study treatment after showing no benefit from it, or are removed from the study for other reasons, you will be asked to come back to the clinic for an End of Study visit. This visit will include a physical examination, blood draw, and CT Scan. These procedures will happen at least once about 30 days after your last dose of the study drug, and possibly more often if toxicities (side effects) are present.

The following will be performed during the End of Treatment visit:

- A physical exam, where your body weight and vital signs (heart rate, blood pressure, breathing rate, and body temperature) will be recorded.
- A review of your symptoms and your ability to perform your normal activities.
- A blood draw (about 4 teaspoons/20 ml) for routine lab tests and for study-specific tests to check the status of your disease.
- A tumor biopsy may be performed to assess the cancer – this is optional
- The study doctor or nurse will ask you to tell them about any side effects you may have felt since your last visit, and to give them a list of all medications that you are currently taking.

If it is found that your tumor is growing, you may have a biopsy done as part of the standard of care (what is usually done) treatment for your disease. You have the option of allowing the study team to take some extra tissue for additional research testing. These tests will look at specific biomarkers, which are substances in your body that signify the intensity of your cancer.

Taking part this optional tissue collection is entirely voluntary. No matter what you decide, it will not affect your participation in the main study or your medical care.

MAKING YOUR DECISION

_____ YES, I agree to give additional tissue at the time of disease progression biopsy.

_____NO, I do NOT agree to give additional tissue at the time of disease progression biopsy.

POST-TREATMENT FOLLOW-UP

Following this last visit, you will continue to be contacted every 3 months for one year, after which you will be contacted every 6 months.

STUDY CALENDAR

The study calendar can be found below:

Assessments	Screening/ Baseline			Cycle 1	Cycle 1	Cycle 2	Cycle 2	Cycle 3 +	End of Treatment
Visit window [days]	Within 28 days	Within 10 days	Within 7 days	Day 1	Day 8	Day 1	Day 8	Day 1	30 days
						+/- 3 days		+/- 3 days	± 14 days
Informed consent	X								
Medical History		X							X
Pregnancy test (if applicable)		X						X	
Physical examination			X	X	X	X	X	X	X
Urine Testing		X		X	X	X	X	X	X
Blood Testing		X		X	X	X	X	X	X
Tumor biopsy	X								X
Assessment of disease status	X							X	X
Ramucirumab dosing				X		X		X	
Pembrolizumab dosing				X		X		X	

4. How long will I be in the study?

You can receive ramucirumab and/or pembrolizumab for up to 35 cycles, or about two years, depending on how the study drug affects your cancer. If it causes you to have side effects that are either dangerous for you or that you cannot tolerate, your doctor may decide to have you stop taking the study drugs. . If you decide you wish to stop taking the study drugs due to side effects, your study doctor will help you do so safely.

The study doctor may also decide to stop your participation this study at any time without your consent if:

- You fail to follow the study doctor's instructions.
- You experience a serious adverse event (harmful side effect) that may require evaluation.
- Your disease does not respond to this treatment.
- You experience side effects that are not considered to outweigh benefits of your participation.
- You become pregnant.
- The research physician feels it is in the best interest of your health and welfare.
- If it is in your best interest.
- You do not consent to continue in the study after being told of changes in the research that may affect you.

The funders, the sponsor, the FDA, or The Ohio State University IRB (Institutional Review Board) may also end the study at any time without your consent.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

Study participation is voluntary. You can decide not to be in the study or you can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drug can be evaluated. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

If you withdraw from the study, we will ask to continue collecting clinical data from your medical records. If you stop taking the study drugs, additional blood (1-2 Tablespoons/15-30 ml) for laboratory tests may need to be drawn about 30 days after your last dose of study drug. Your doctor may also discuss a tumor biopsy if treatment stops working for the clinical study.

Leaving the study will not affect your medical care. You can still get your medical care from our clinic.

6. What risks, side effects or discomforts can I expect from being in the study?

RAMUCIRUMAB

Ramucirumab is known to cause the following side effects:

- Low white blood cell count (or types of white blood cells): (this can increase your risk for infection). Low white blood cells may be associated with fever
- Low red blood cell count (anemia)
- Elevated white blood cell counts
- Skin rashes
- Blood clots in legs or lungs
- Decreased blood oxygen
- Bleeding from the digestive tract
- Difficulty breathing
- Constipation
- Taste changes
- Heart rhythm abnormalities or EKG changes
- Liver blood test elevations
- Decreased or increased blood chemicals: potassium or sodium
- Increased blood chemical from bones
- Cough
- Abdominal pain
- Fluid retention with weight gain, swelling of the ankles or abdominal area
- Peripheral neuropathy (numbness in your fingers and toes may occur)
- Nausea
- Diarrhea
- Dizziness
- Decreased appetite or desire for food
- Weight loss
- Mouth sores or inflammation of the mouth lining
- Hair loss
- Fatigue and weakness
- Infection (including life threatening infection in the blood)
- Nail changes (color changes to your fingernails or toenails may occur. In extreme, but rare, cases nails may fall off. After you have finished treatments, your nails will generally grow back.)
- Vomiting
- Muscle/bone/joint pain (myalgias and arthralgias)
- Low platelet count (this can increase your risk of bleeding)
- Allergic reactions (rash, flushing, fever, lowered blood pressure).
- Infusion site reactions (Darkening of the vein, inflammation, redness or dryness of the skin, or swelling of the vein). Severe infusion reactions with trouble breathing, low blood pressure and possibly rash have occurred infrequently.

PEMBROLIZUMAB

Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, but may not be approved to treat your type of cancer. Overall, as of 03-Mar-2018, approximately 25,519 patients have been treated with pembrolizumab in clinical studies. Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab.

VERY COMMON

Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

COMMON

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back pain
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach

UNCOMMON

Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs so you may feel short of breath and cough
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside

of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection

RARE

Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the muscles so you may feel weak or have pain in your muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior,

difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling.

For more information about risks and side effects, ask your study doctor.

***You should talk to your study doctor about any side effects that you have while taking part in the study*.**

The study doctor will take steps to treat any side effects if they appear. If the study drug causes severe side effects or if your disease worsens, treatment with the study drug will be discontinued. In that case your study doctor will discuss other treatment options with you.

As with any study drug, unknown risks and side effects are also possible. You could experience a side effect that is more severe than those mentioned above or a side effect that has not been anticipated with this study drug. There is a chance that you could be allergic to the study drug or to one of the chemicals used in its formulation. There is also a chance that other medications you may be taking could interact with this investigational drug. For your safety, you must tell the study doctor or nurse about all medications you are taking before you start the study. Also, please tell the study doctor or nurse before starting any non-study medications while you are on the study, including any over the counter medicines such as cough and cold remedies or herbal supplements.

BLOOD DRAW

The risks of having blood drawn include pain, bruising, and rarely, infection. Blood will be drawn by experienced technicians, and whenever possible, it will be done at a time when blood is being drawn for other tests your study doctor has ordered, so you will not need to have an extra needle stick.

CT SCANS

The CT scanner is a free-standing machine with a large hole in the center (like a doughnut). You will be asked to lie on your back with your arms raised above your head on a narrow

table that slides through the hole in the machine. Subjects who have difficulty with enclosed spaces, like those found in some MRI scanners, do not usually have a problem with CT scans.

A dye (called "contrast") may be injected into your vein by IV to improve the images obtained from the CT scan. The radiologist will decide if this is necessary. Tell the technician or radiologist if you have any allergies or have had difficulty with prior CT scans. It is very important that you remain still throughout the exam and hold your breath when asked. This will allow for better images. The actual scan time is usually about two minutes, although the entire procedure usually takes much longer. If you have any concerns about this, you should discuss it with your study doctor.

CT scans use x-rays to allow your doctors to see images of your insides. During the study, you may have more scans than if you were receiving routine treatment and therefore you will be exposed to increased levels of radiation. The risk of radiation exposure adds up over a lifetime. If you have any concerns about this, you can discuss them with your study doctor.

MRI SCANS/IMAGING

Magnetic Resonance Imaging (MRI) is done with an imaging machine that uses a large magnet, a computer, and radio waves to look inside your body and to evaluate certain body parts. An MRI may be done to measure your cancer.

During the MRI exam, you will be lying on a large firm table for approximately 30-60 minutes. The inside of the machine is like a giant tunnel that is well lit and open on each end. The MRI makes a loud knocking noise while it creates the image. For your comfort, you will be given ear plugs or ear phones to listen to music during the exam. The test takes approximately one hour. When the test is finished, you are free to go.

Because a strong magnet is used in the MRI, patients who have pacemakers cannot have an MRI exam. Also, for your safety, you will be asked if you have any implanted medical devices such as cochlear implants, penile implants, aneurysm clips, artificial heart valves, or stents, have ever been hit in the eye or face with metal or metal shavings, or have ever been shot with a gun.

If you get an MRI, you may be asked to use a dye (called "contrast"). This dye will be injected into your vein by IV. This is a different type of dye than the one used during CT scans and is not known for causing allergic reactions. However, if you have an allergy to CT scan dye, tell your radiologist. Medical personnel will be available to treat any of these problems if they should occur.

ARCHIVAL TUMOR BIOPSY

There are no risks to you if previous tumor samples are used for testing because the sample was collected in the past.

TUMOR BIOPSY

Tumor biopsies may be collected before, and/or during and/or after study treatment. Your Study Doctor will inform you in detail about the risks associated with the place where your tumor is located, and with the biopsy technique chosen (tumor biopsies can be obtained by different techniques). Biopsies may cause pain, inflammation, bleeding, swelling, and/or infection at the site of the biopsy. If your doctor decides to use anesthetic, an allergic reaction may also occur.

PREGNANCY AND REPRODUCTIVE RISKS

There is not enough medical information to know what the risks of the study drug might be to you if you become pregnant, your breast-fed infant, or your unborn child. You cannot take part in this study if you are pregnant or lactating (breast-feeding). Therefore, all women who are sexually active and can become pregnant must use birth control measures while in this study. All men with female partners of childbearing potential must also use birth control measures while in this study, and avoid fathering a child for at least 120 days after receiving their last dose of the study drug. Breast-feeding mothers must stop breast-feeding to take part in this study.

The following birth control measures are considered acceptable:

- Birth control pills
- Contraceptive shots
- Contraceptive implants
- Condoms or a diaphragm.

Women who could possibly become pregnant must have a pregnancy test before taking part in this study. For the pregnancy test, a blood sample will be taken within 7 days before you receive your first dose of the study drug. You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study. Additionally, if you become pregnant during study participation, you will have to stop taking the study drugs immediately.

If you or your female partner becomes pregnant during your study participation, within 120 days after receiving your last dose of the study drug, or within 30 days of stopping the study drug if you start another anti-cancer drug, you must inform the study doctor immediately.

Your study doctor can give you more information about counseling and preventing pregnancy.

7. What benefits can I expect from being in the study?

If you agree to take part in this study, there may or may not be direct medical benefit to you. Your cancer may respond well to the study treatment, or it may get worse. The information obtained from this study may help doctors better understand cancers and this may eventually be helpful to future cancer patients.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled. Your other choices may include the following:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care (also called palliative care). This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly.
- Getting no treatment

Talk to your study doctor about your choices before you decide if you will take part in this study

9. What are the costs of taking part in this study?

The drug companies – Eli Lilly and Merck - will provide you with the study drugs – ramucirumab (Lilly) and pembrolizumab (Merck)—at no cost to your or your insurance provider. This does not include the costs related to giving the drug to you. In addition, the costs of tests, procedures and services performed solely for research purposes will be covered by the study. This includes the costs of research testing on blood and tissue by a central lab. Your study doctor or coordinator can tell you, specifically, which costs are covered by the study.

Most of the care you receive while participating in this study is considered routine for your disease. You or your insurance provider will be billed for the costs of routine doctor's fees, clinic visits, laboratory testing, medications, radiology procedures and other services performed during this study. This includes the costs of treating side effects or complications. You will be responsible for any deductibles, coinsurance or co-payments required by your insurance plan.

Participating in this research study may lead to additional costs to you. Some insurance companies and third party payers may not pay for routine costs if you are participating in a research study. Others may limit what they will pay. If your insurance company does not pay for these costs, you will be responsible for them. Before participating in this study, we recommend that you ask your insurance provider if there are any limitations to your particular

plan. Otherwise, you may experience unexpected medical costs.

If you are a Medicare Advantage Plan participant (HMO or PPO), or traditional Medicare is billed first for routine, study-related services while you participate in an approved trial. Your Advantage Plan is billed second for their share of your costs. You may or may not have additional out of pocket costs after Medicare or your Advantage Plan pays. Additional information can be obtained from your Advantage Plan and online at:

https://www.medicare.gov/Pubs/pdf/02226-Medicare-and-Clinical-Research-Studies.pdf

10. Will I be paid for taking part in this study?

You will not be paid for study participation

11. What happens if I am injured because I took part in this study?

OHIO STATE UNIVERSITY LIABILITY

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information (and bio-specimens) be used or shared for future research?

No.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors;
- The funders supporting this study, their agents, or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find information that significantly impacts your health, we **will** share it with you. For instance, if your disease is worsening, staying the same, or improving, the study doctor will inform you of this. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study in a timely manner.

When the study is completed at all the study sites, the data will be analyzed. You will have an opportunity to learn of the study results. You may ask your study doctor for the results and to have them explained to you

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 the website at any time.

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;

- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  Physical exams
  Laboratory, MRI, CT, PET scans, and other test results
- Records about any study drug you received

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.
- Others: Eli Lilly, Merck

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until after the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about this study, or if you feel you have been harmed as a result of study participation, you may contact **Asrar Alahmadi, MBBS at 614-293-6786 or 614-293-8000 (24 hours)**

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact :

HIPAA Privacy Manager
The Ohio State University Medical Center
600 Ackerman Road, Suite E2140
Columbus, OH 43202
Phone number: 614-293-4477

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the **Office of Responsible Research Practices at 1-800-678-6251.**

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact**: Asrar Alahmadi, MBBS at 614-293-6786 or 614-293-8000 (24 hours)**

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**AM/PM**
	Date and time

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time