NRG-LU004 Research Study Informed Consent Document for Patients Enrolling in Cohorts 5, 6, 7 and 8

Study Title for Participants: Testing the safety of adding either monalizumab (IPH2201) or oleclumab (MEDI9447) to durvalumab (MEDI4736) plus standard radiation therapy for locally advanced non-small cell lung cancer (NSCLC)

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol NRG-LU004, Phase I Trial of Radiotherapy Combined With Durvalumab (MEDI4736) Alone Plus Either Monalizumab (IPH2201) or Oleclumab (MEDI9447) in PD-L1 High Locally Advanced Non-Small Cell Lung Cancer (NSCLC) (ARCHON-1) (NCT03801902)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have non-small cell lung cancer that has not spread outside your lungs, and your cancer cells have a fairly large amount of a protein called PD-L1 that researchers have connected to a good response to immunotherapy treatment for cancer.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

In the first part of this study, we learned it is safe to give the immune therapy drug durvalumab with radiation therapy in your type of lung cancer that has a high level of PD-L1. The second part of the study is being done to answer the following question:

Is it safe to give a second immune therapy drug, monalizumab or oleclumab, along with durvalumab and the usual radiation therapy for this type of lung cancer that has a high level of PD-L1?
In studies on patients with more advanced NSCLC, immune therapy drugs like durvalumab have been shown to be as active or better than chemotherapy in people with PD-L1 high NSCLC, and combining two immune therapy drugs may be better than one drug alone.

Because the usual approach, chemotherapy given with radiation, can cause severe side effects, we are testing immune therapy given with radiation and without chemotherapy to learn if it is as good or better than the usual approach. The usual approach is defined as care most people get for non-small cell lung cancer.

What is the usual approach to my cancer?

The usual approach for patients who are not in a study is treatment with chemotherapy and radiation followed by immune therapy. There are several chemotherapy drugs approved by the Food and Drug Administration (FDA) that are commonly used with the radiation. The immune therapy commonly given after radiation and chemotherapy is durvalumab. Durvalumab is FDA approved for treating stage III non-small cell lung cancer after patients complete chemotherapy and radiation.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will receive durvalumab plus monalizumab or durvalumab plus oleclumab for about 1 year along with radiation for 6 weeks.

After you finish your study treatment, your doctor will continue to follow your condition every 3 months during clinic visits for the first year after treatment ends, and every 4 months for the second year after treatment ends (for a total of 3 years of participation in this study), and watch you for side effects.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that adding monalizumab or oleclumab to durvalumab and radiation is not as safe as the usual approach.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects of radiation that the study doctors know about are:

- Lung inflammation and scarring
- Esophageal irritation
- Fatigue

Some of the most common side effects of durvalumab combined with monalizumab or oleclumab that the study doctors know about are:

- Itching, rash, tiredness, constipation, abdominal pain, and nausea.
- There may be some risks that the study doctors do not yet know about.

Benefits

It may be possible that adding durvalumab and either monalizumab or oleclumab to radiation can delay the time until your disease progresses for the same or longer than the usual approach of chemotherapy and radiation. It is also possible that either of these treatment approaches (durvalumab with either monalizumab or oleclumab plus radiation) can have less side effects compared to the usual approach alone; however, we do not know if this will happen. The study may help the study doctors learn things that may help other people with lung cancer in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change, risk to your health, etc. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsors, National Cancer Institute and NRG Oncology. The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety of adding either monalizumab or oleclumab to durvalumab and radiation. We want to find out what effects the drugs combined with radiation have on people, if any. There will be about 24 people taking part in this study.

In the first part of this trial (now closed to patient enrollment), we tested the safety of adding durvalumab to 2 different radiation therapy schedules. We learned that durvalumab with radiation therapy was safe. You are now being asked to participate in this study to see if adding another immune therapy drug to durvalumab and radiation is safe. In both parts of the study, we also want to learn what effects immune therapy plus radiation has on the time, if any, until cancer gets worse.

What are the study groups?

Everyone participating in this part of the study will get the same doses of durvalumab and radiation, but one group will receive monalizumab combined with the durvalumab, and the other group will receive oleclumab combined with the durvalumab. People who enrolled in the first part of this study received only the durvalumab and radiation. There were 4 groups in that part of the study, and now there are 4 new groups for this part of the study. These 4 new groups are described below.

Group 5: The first 6 people taking part in this study will get durvalumab and monalizumab. These drugs are given through a vein in your arm. You will get durvalumab and monalizumab starting 2 weeks before radiation, every 4 weeks for as long as you can tolerate it, up to 13 cycles (1 cycle is equal to 4 weeks). Radiation starts 2 weeks after the first doses of durvalumab and monalizumab, and is given 5 days each week for 6 weeks. Durvalumab and monalizumab will continue for one year or until you have intolerable or serious side effects or your cancer gets worse, whichever comes first.

Group 6: The next 6 people who take part in the study will get durvalumab and oleclumab. These drugs are given through a vein in your arm. You will get durvalumab and oleclumab

starting 2 weeks before radiation. Durvalumab will be given every 4 weeks for as long as you can tolerate it up to 13 cycles (1 cycle is equal to 4 weeks). Oleclumab will be given every 2 weeks for the first 2 cycles of durvalumab. Starting with cycle 3 of durvalumab, oleclumab will be given every 4 weeks along with durvalumab for as long as you tolerate it up to a total of 13 cycles. Radiation starts 2 weeks after the first doses of durvalumab and oleclumab and is given 5 days each week for 6 weeks. Durvalumab and oleclumab will continue for 1 year or until you have intolerable or serious side effects or your cancer gets worse, whichever comes first.

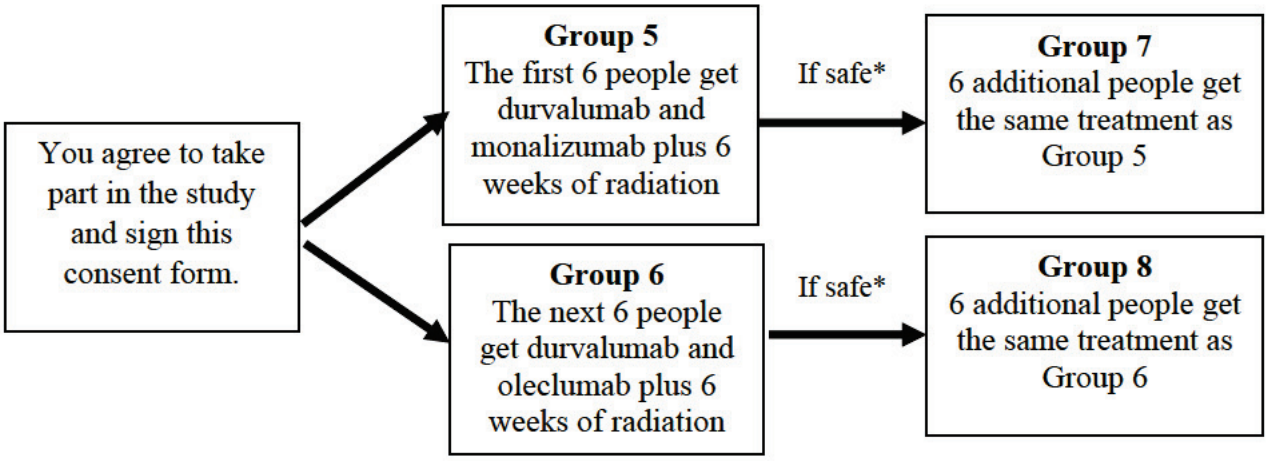
The study doctor will watch each group carefully for serious side effects and determine if one or both of the groups is safe. The next participants who join the study will receive the treatment considered safe. If only Group 5 treatment is considered safe, then the rest of the study participants will receive durvalumab and monalizumab plus radiation (called Group 7). If only Group 6 treatment is considered safe, then the rest of the study participants will receive durvalumab and radiation plus oleclumab (called Group 8).

Group 7: same treatment as Group 5 above.

Group 8: same treatment as Group 6 above.

If Group 5 and Group 6 are considered safe (there are no serious side effects of the drugs or the radiation), then the next 6 patients who take part in the study will be enrolled into Group 7, then the next 6 patients will be enrolled into Group 8. It means that your doctor will not choose and you cannot choose which study group you are in.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



*If unsafe, no patient will be enrolled to Group 7 or Group 8.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety

and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are tests that will be done for research purposes only.

You will need to have blood samples taken for the study. About 4 tablespoons of blood will be collected from a vein in your arm at the following times:

- Before you begin durvalumab treatment;
- Before you begin radiation treatment;
- During treatment after you've started radiation therapy (on Days 15 and 30); and
- At 3 months after you start durvalumab.

Researchers will use these samples to study cells in your blood (including white blood cells, immune proteins called "antibodies," and circulating tumor DNA or "ctDNA") to learn more about how your cells react to the study treatment. You and your study doctor will not get the results of this testing.

What risks can I expect from taking part in this study? (28-MAY-2024)

General Risks

If you choose to take part in this study, there is a risk that the study drugs plus radiation may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The treatments used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 3 months after you have completed the study.

To be part of this study, your cancer must make high levels of a protein called PD-L1. A nurse or doctor will take some of the tumor tissue and perform a test that tells us if your cancer has the protein and if so, how much of it. Although this test is FDA approved, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

Genetic Testing Risks

As part of this study, we are also studying a genetic test. The test is designed to find out if your tumor has the genetic changes that are needed for this study. If it does, we will assign you to a study group based on the genetic changes in your tumor.

Since this study is only testing tumor tissue, we will not know if a genetic change in your tumor is also in your normal tissue. If you want to find out if the change is in your normal tissue, then you will need to get other tests done outside of this study.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your study doctor will talk with you about what testing your normal tissue may mean for you and your family. He or she also may suggest that you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for any genetic tests and visits to a genetic counselor done outside of this study.

Side Effect Risks

The drugs and radiation used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study treatment.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual immunotherapy plus radiation used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 5 and Group 6 – Possible side effects of durvalumab are listed in the tables below. This immunotherapy drug is part of the usual approach for treating this type of cancer:

Possible Side Effects of Durvalumab (MEDI4736)
(CAEPR Version 2.5, February 29, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving durvalumab (MEDI4736), more than 20 and up to 100 may have:
• Cough

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving durvalumab (MEDI4736), from 4 to 20 may have:
• Anemia which may require blood transfusion • Pain in the muscles, joints • Diarrhea, nausea, vomiting • Swelling of the body • Tiredness, fever • Infections. Infections can be severe and involve jaws and fatty tissues • Loss of appetite • Painful urination • Shortness of breath • Changes in voice • Increased sweating Durvalumab (MEDI4736) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems include but are not limited to: • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting. • Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly. • Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath. • Skin: itching; rash, patches of light skin color

RARE, AND SERIOUS

In 100 people receiving durvalumab (MEDI4736), 3 or fewer may have:

- Pain and swelling of thyroid
- Reaction during or following a drug infusion which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Durvalumab (MEDI4736) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems include but are not limited to:

- Damage to blood cells that may cause bruises and bleeding
- Blood clots in small blood vessels, which may cause kidney failure, fever, and confusion
- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body or abnormal heartbeat
- A condition with high blood sugar (diabetes) which leads to tiredness, frequent urination or excessive thirst which may require treatment with insulin
- Swelling and redness of the eye
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Damage to the pancreas which may cause belly pain and hospitalization
- Problem of the muscle (myositis), which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Problem of the nervous system that can cause weakness and paralysis, which may include: numbness, tingling of hands and feet, and may also cause problems with breathing
- Swelling of the brain which may cause headache, blurred vision, stiff neck, and/or confusion
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Severe skin reactions with blisters and peeling which can involve mouth and other parts of the body

Study Groups 5 and 7 - In addition to side effects listed above, people who are in Groups 5 or 7 may also have some side effects from monalizumab. These side effects are listed below.

Possible Side Effects of Monalizumab (IPH2201)
(CAEPR Version 2.0, October 31, 2022)

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving monalizumab (IPH2201), from 4 to 20 may have:

RARE, AND SERIOUS
In 100 people receiving monalizumab (IPH2201), 3 or fewer may have:

Study Groups 6 and 8 - In addition to side effects for durvalumab listed above, people who are in Groups 6 or 8 may also have some side effects from oleclumab. These side effects are listed below.

Possible Side Effects of Oleclumab (MEDI9447)

Risk Profile for Oleclumab (MEDI9447)
(CAEPR Version 2.0, September 19, 2022)

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving oleclumab (MEDI9447), from 4 to 20 may have:

RARE, AND SERIOUS
In 100 people receiving oleclumab (MEDI9447), 3 or fewer may have:

Additional Drug Risks

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

Possible Side Effects of Lung Radiation

COMMON, SOME MAY BE SERIOUS In 100 people receiving lung radiation therapy, more than 20 and up to 100 may have:
• Swelling and redness, tanning, thickening, numbness, or peeling of the skin in the area of radiation • Difficulty and/or pain with swallowing • Hair loss in the treatment area, may be permanent • Shortness of breath • Cough with or without increased phlegm production • Tiredness • Diarrhea, nausea • Anemia, which may require blood transfusion • Infection, especially when white blood cell count is low • Bleeding, bruising • Rib pain, increased risk of rib fracture

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving lung radiation therapy, from 4 to 20 may have:
• Inflammation of the lung that may cause difficulty breathing and can be life-threatening • Narrowing of the throat which may cause vomiting, difficulty swallowing • Scarring in the lung • Lung collapse • Fluid around lungs • Bleeding from the lungs which may cause coughing up blood • Fever • Narrowing of the esophagus • Pain in chest wall

RARE, AND SERIOUS In 100 people receiving lung radiation therapy, 3 or fewer may have:
• Abnormal opening in internal organs which may cause pain and bleeding • Irritation of the heart causing heart failure, heart attack, chest pain, abnormal heartbeat, shortness of breath, swelling of ankles, cough or tiredness • Transverse myelitis – irritation of the spinal cord causing weakness, tingling or numbness of the lower body and legs, or paralysis of the lower half of the body • Brachial plexopathy – irritation of the nerves controlling the arm, causing weakness or paralysis • Bleeding from the airway (windpipe) • Narrowing of the airway causing shortness of breath • Death • Lung damage, may be life threatening • Damage to the large blood vessels surrounding the heart, which could cause coughing up of blood and possibly death • Sores and skin damage causing bleeding and severe pain and may lead to an open wound

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 3 months after your last dose of study drug. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within three months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, and procedures that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the radiation therapy

- the costs of getting the durvalumab, and either monalizumab or oleclumab ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for the durvalumab, monalizumab or the oleclumab (whichever you receive depending on the Group you are in) while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- NRG Oncology and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research, including the Cancer Trials Support Unit (CTSU).
- The NCI's National Clinical Trials Network and the groups it works with to conduct research, including the Imaging and Radiation Oncology Core (IROC).

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number, and email address if appropriate).*

For questions about your rights while in this study, call the _____ (*insert name of organization or center*) Institutional Review Board at _____ *(insert telephone number).*

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading this optional study hope the results will help other people with your cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the following study.

Optional sample collections for storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, a sample of tissue from your previous biopsy will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG Oncology and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. This is a publicly funded study. Samples from publicly

funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?
If you agree to take part, here is what will happen next:

1. A sample from the tissue that was collected at the time of your biopsy will be sent to the biobank.
2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?
Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?
You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?
There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?
If you decide you no longer want your samples to be used, you can call the study doctor, *(insert name of study doctor for main trial)* at *(insert telephone number of study doctor for main trial)*, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?
If you have questions about the use of your samples for research, contact the study doctor, *(insert name of study doctor for main trial)* at (*insert telephone number of study doctor for main trial).*

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:
I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

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

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

_____

Date of signature

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature

_____

Appendix I: Treatment Schedules

Groups 5 and 7

Cycle (=4 weeks)	Days	Radiation Therapy • Begins day 15 of Cycle 1 • Given for 6 weeks • Given for 5 consecutive days each week	Durvalumab	Monalizumab
1 (starts 2 weeks prior to start of RT)	1-7		1st day of cycle 1	1st day of cycle 1
	8-14			
	15-21	X		
	22-28	X		
2	29-35	X	1st day of cycle 2	1st day of cycle 2
	36-42	X		
	43-49	X		
	50-56	X		
3-13	57-343		Every 4 weeks x 11 cycles (given 1st day of each cycle*)	Every 4 weeks x 11 cycles (given 1st day of each cycle*)

Groups 6 and 8

Cycle (4 weeks)	Days	Standard RT • Begins day 15 of Cycle 1 • Given for 6 weeks • Given for 5 consecutive days each week	Durvalumab	Oleclumab
1 (starts 2 weeks prior to start of RT)	1-7		1st day of cycle 1	1st day of cycle 1
	8-14			
	15-21	X		15th day of cycle 1
	22-28	X		
2	29-35	X	1st day of cycle 2	1st day of cycle 2

	36-42	X		
	43-49	X		15th day of cycle 2
	50-56	X		
3-13	57-343		Every 4 weeks x 11 cycles (given 1st day of each cycle*)	Every 4 weeks x 11 cycles (given 1st day of each cycle*)