PRINCIPAL INVESTIGATOR: Anish Thomas, M.D.

STUDY TITLE:	Phase II Trial of Olaparib (LYNPARZA) plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas that Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors
STUDY SITE:	NIH Clinical Center
Cohort:	Affected patient
Consent Version:	03/11/2024

WHO DO YOU CONTACT ABOUT THIS STUDY?

Anish Thomas, MD, by phone at 240-760-6241 or email anish.thomas@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you had EGFR-mutated non-small-cell lung carcinoma (NSCLC) that was treated and now transformed to small cell lung carcinoma or another neuroendocrine tumor.

The purpose of this study is to see if combination of durvalumab and olaparib will cause your tumors to shrink.

The use of durvalumab and olaparib in this study is considered investigational which means this combination has not been approved by the U.S. Food and Drug Administration (FDA) to treat small cell lung carcinoma or other neuroendocrine tumors. However, the FDA has given us permission to use durvalumab and olaparib in this study.

Durvalumab has been approved by FDA to treat non-small cell lung cancer (NSCLC) and other cancers. Durvalumab is designed to boost the body's immune system by targeting a protein on tumor cells called PD-L1. PD-L1 usually helps the immune system work properly. In cancer, PD-L1 helps tumors avoid being seen and destroyed by the immune system. Durvalumab may increase the immune system's ability to find and destroy cancer cells.

Olaparib has been approved by FDA to treat other cancers besides the one that we are studying. Olaparib belongs to group of drugs called PARP inhibitors that target and block several pathways needed for cancer cells to grow and cause cancer cells to die.

There are other standard of care drugs and/or procedures that may be used to treat your disease, and these can be given to you by your regular cancer doctor if you are not in this study. For example: there is chemotherapy and radiation therapy. You can also participate in another clinical trial using drugs called immune checkpoint inhibitors (such as cabozantinib or pembrolizumab). The treatment given in this study and the known possible side effects may or may not be significantly different than if you were to receive standard care or taking part in another clinical trial. For example: chemotherapy and radiation therapy cause fatigue, hair loss, bruising and bleeding, infection, low blood cell counts. Immune checkpoint inhibitors may cause inflammation of the lung, intestines or liver, and kidney, heart, or problems of the nervous system. Any of these treatments can cause nausea, vomiting, diarrhea and rash.

The study drug durvalumab is a checkpoint inhibitor and has similar side effects to those listed above. The most common side effects of the other study drug, olaparib, include low blood cell counts, fatigue, nausea, vomiting, diarrhea, and infections.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- First, we will perform tests to find out if you fit the study requirements. We will do standard blood and urine tests and scans to test your health and see the status of your disease. These tests may be done under a separate protocol or on the study. We may also collect records from your outside physicians.
- If you fit the study requirements and decide to take part, you will start your treatment with durvalumab and olaparib. We will then send you home with a supply of olaparib that you will need to take. We will need to see you at the Clinical Center every 4 weeks while you are receiving treatment. There is one additional visit after 2 first weeks on treatment. You will not need to stay in the hospital for this study. Each visit should last no more than 8 hours.
- As described above and later in more detail in this consent form, you may have side effects if you take part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and see how your disease is responding. We will also collect samples from you (such as: blood and tumor tissues) for both clinical and research purposes. Some of the samples are required and some are optional.
- After the study treatment has ended we would like to see you in the Clinical Center approximately one month later to check on your health. After that we are planning to contact you by phone or e-mail to learn about your health status, and to see how you are doing, for the rest of your life or until the study is stopped. If you stop treatment for reasons other than worsening of your disease, we will continue to invite you for imaging studies approximately every 8 weeks until worsening of your disease. You can have these studies at home institution and send us the results.

This study may benefit you by shrinking your tumor or lessening your symptoms, such as pain, that are caused by the cancer. Even if you do not benefit from this study, the results from our research will help others in the future.

You are free to stop taking part in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this study is to see if combination of durvalumab and olaparib will cause your tumors to shrink.

We are asking you to join this research study because you had EGFR-mutated non-small-cell lung carcinoma (NSCLC) that was treated and now transformed to small cell lung carcinoma or another neuroendocrine tumor.

The use of durvalumab and olaparib in this study is considered investigational which means this combination has not been approved by the U.S. Food and Drug Administration (FDA) to treat small cell lung carcinoma or other neuroendocrine tumors. However, the FDA has given us permission to use durvalumab and olaparib in this study.

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Olaparib has been approved by the FDA to treat other cancers besides the one that we are studying. Olaparib belongs to group of drugs called PARP inhibitors that target and block several pathways needed for cancer cells to grow and cause cancer cells to die.

WHAT WILL HAPPEN DURING THE STUDY?

Durvalumab will be administered to you by IV (through an intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) on Day 1 of each cycle (1 Cycle = 28 days).

You will take olaparib by mouth every day of every cycle.

Olaparib should be taken 2 times a day. Try to space your doses out evenly throughout the day, so ideally, take a dose at 8 am and 8 pm with approximately 1 cup (240 mL) of water. You may take the tablets with a light meal/snack (i.e. 2 pieces of toast or a couple of crackers). If you need to take your olaparib earlier than scheduled or you missed a dose, you can take it in the time period of +/- 2 hours of the scheduled time. If you vomit after taking olaparib, please, do not immediately take another tablet unless the tablet is visible. You should simply proceed with next dose as scheduled.

If you have nausea or vomiting caused by olaparib, we will give you ondansetron to prevent or decrease the nausea and vomiting. You will need to take ondansetron by mouth with small meal or snack approximately 30 minutes prior to each dose of olaparib.

You will be given a Medication Diary to complete for each cycle. In the diary, you will be asked to record the date and time of each dose of olaparib. You will also be asked to record missed doses. Please bring the diary with you to every study visit.

At each visit, please also bring all empty bottles and any unused medication you may have.

If your doctor is convinced that you have unacceptable side effects caused by one of treatment drugs, this drug will be stopped, and you may continue treatment with the other drug if your study doctor finds that it is in your interest. Treatment will continue until you have unacceptable side effects (both drugs) or you are no longer benefiting from the study therapy.

Treatment and all study related procedures will be done during outpatient visits without planned hospitalization. However, we might still choose to keep your overnight if needed for biopsy and other situations that arise.

Before you begin the study

Before you begin this study, you will need to have standard clinical exams and tests to make sure you are eligible for this study. These tests may be done under a separate protocol or on the study. We may also collect records from your outside physicians.

These following tests and exams will need to be performed:

- Physical exam and medical history to check on your overall health
- We will check your heart through 3 electrocardiograms also called ECGs (a test that looks at electrical activity of your heart through electrodes/small stickers placed on your chest, arms, and legs).
- Routine clinical blood and urine tests to further check on your health status.
- As part of this study, we will do blood tests to check for infections with HIV (the virus that causes AIDS), Hepatitis B and C (viruses that infect the liver). If you are infected with any of these viruses, you will be able to take part in this study if you are getting treatment for these diseases and if the virus cannot be found through blood tests. We will tell you what the results of blood tests mean, how to find care, how to avoid infecting others, how we report these infections, and the importance of informing your partners at possible risk because of your HIV or hepatitis infection.

- If your doctor suspects it is needed, we may test you for tuberculosis a disease caused by germs that are spread from person to person through the air. A small amount of substance called purified protein derivative (PPD) is injected under your skin. If you have a red raised bump at the injection site, you may have been exposed to tuberculosis germs.
- Computer tomography (CT) or Magnetic Resonance Imaging (MRI) scan to see your cancer. A CT produces a series of x-ray images of different parts of your body. An MRI makes pictures of the inside of your body using strong magnets instead of x-ray energy. Either scan may take about 30 minutes.
- We will collect and review prior biopsy samples of your tumor and reports to confirm your diagnosis.
- We will check all the medications that you are currently taking.
- Pregnancy test (by blood or urine) if you are a woman who can have children.

You will be removed from the study if the results of the reviews/tests show that you are not eligible to participate.

You will be asked to provide documentation to confirm your diagnosis. If documentation is not available, we will perform a biopsy (collect a sample of your tumor) to confirm your diagnosis.

During the study

Ongoing procedures before treatment and with every cycle:

- Physical examination, including weight and vital signs.
- Review of your symptoms, medications and your ability to perform your normal activities.
- Discussion of any symptoms you might be having
- Routine blood and urine tests to find out if you are anemic, have low blood counts, and if your liver, kidneys, thyroid, clotting system and other organs are working well.
- Electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart.
- Pregnancy test if you are a woman who can have children.

On Day 15 of cycle 1:

- Physical examination, including weight and vital signs.
- Review of your symptoms, medications and your ability to perform your normal activities.
- Discussion of any symptoms you might be having
- Routine blood and urine tests to find out if you are anemic, have low blood counts, and if your liver, kidneys, thyroid, clotting system and other organs are working well.

Ongoing procedures before treatment and every 2 cycles:

- Imaging assessments/scans – either a CT scan or MRI of chest, abdomen and pelvis.

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of your body. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 30 minutes. You may be asked to lie still for up to 30 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time.

Additional research testing

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. The samples are being done to look at the effects of therapy on your immune system and markers of tumor activity. This will include collecting and testing tumor cells.

- Blood samples will be collected before treatment, on day 1 of every cycle and day 15 of cycle 1. Samples will be used to study how well your tumor responds to treatment, and to look at all of your genes and how well they are working.
- We will ask you to provide samples of your tumors from previous surgeries or biopsies if available. We also may perform three optional tumor biopsies: One before treatment, one on day 15 of cycle 1 and one if your disease gets worse. Please see Risks from Biopsy for the possible risks of biopsy. You will be asked to sign a separate consent each time you agree to have an optional biopsy. You can participate in the study even if you decide not to undergo the biopsy procedures. Samples will be used to study all of your tumor genes and how well they are working.

Tumor and blood samples collected for research purposes on this study may be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow. RNA (also called ribonucleic acid) carries the instructions from the DNA to the parts of your cells that make proteins.

To look at your DNA and RNA, we may use do what is called “DNA or RNA sequencing.” This is where we will do special tests in the lab to look at the sequence, or order, of how your DNA or RNA are put together. This is what makes you unique.

To determine which parts of the DNA or RNA have mutated, we will compare the DNA or RNA in your tumor cells to DNA or RNA from normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA or RNA that are common to a particular type of tumor.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There

may be exceptions to what we share with you and this is described later in this consent form in the section for "Return of research results".

When you are finished taking the drugs (treatment)

Approximately 30 days after you have finished taking the study drug, you will be asked to return to Clinical Center for a safety follow up visit. At this visit, you will be asked questions about your health, get a physical exam and undergo blood tests.

If you have been taken off treatment for reasons other than worsening of your disease, you will continue to have imaging studies approximately every 8 weeks until worsening of your disease. You can have these studies at home institution and send us results.

If you are unable to return for these visits, we will obtain the information from you by telephone or e-mail.

Once you stop coming to Clinical Center for safety visits and your scans, we will call or e-mail you every 6 months to ask you about your general well-being.

HOW LONG WILL THE STUDY TAKE?

You will come for study treatments every 28 days until your disease gets worse or you have unacceptable side effects at which time we will stop treatment.

Visits will range from 4-8 hours in length.

After stopping treatment, we would like to see you in the NIH Clinical Center one month later and follow you after that for the rest of your life by telephone or e-mail.

If you stop treatment for reasons other than worsening of your disease, we would like to invite you for imaging studies approximately every 8 weeks until worsening of your disease.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

About 14 people will take the study drugs at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

The drugs 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 be testing your blood and will let you know if changes occur that may affect your health.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last longer.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

- The study doctor may adjust the study drugs to try to reduce side effects.

Durvalumab

Most of the possible side effects listed below are mild to moderate. However, some side effects can be very serious and life-threatening and may even result in death. Some side effects do not need treatment while others generally get better with treatment. Some patients may need to delay doses of durvalumab to allow the side effects to get better. The most important possible side effects, which are listed below, may occur because of the way durvalumab works on the immune system and they have been seen in patients treated with durvalumab in clinical studies. Side effects like these have also been seen in clinical studies with other drugs that are very similar to durvalumab. Management of these side effects may require the administration of drugs such as steroids or other agents that can affect your immune system and reduce inflammation.

Very common, some may be serious **In 100 people receiving durvalumab, more than 10 may have:**
• Diarrhea, • Rash/dry itchy skin • Feeling tired • Nausea • Vomiting • Abdominal pain • Upper respiratory tract infections • Decreased appetite • Shortness of breath • Cough with or without mucus • Fever
Common, some may be serious **In 100 people receiving durvalumab, from 1 to 10 may have:**
• Liver problems: Increases in the blood level of substances called enzymes found within your liver cells. The enzyme changes are unlikely to make you feel unwell, however, if these blood enzyme levels become very high, your study doctor may need to stop the study medication. You may develop inflammation of the liver called hepatitis; however, this is uncommon. In some cases, this could be caused by your immune system attacking your liver. Signs and symptoms of this include yellowing of the skin or whites of the eyes, dark urine, severe nausea and vomiting, pain in the upper right side of your abdomen, skin itchiness, not feeling hungry and bleeding or bruising more easily than normal. • Inflammation in the lungs (pneumonitis): symptoms may include but are not limited to a new or worsening cough, shortness of breath possibly with fever. In some cases, this could be caused by your immune system attacking your lungs. Preliminary data

suggested that there may be the tendency of higher frequency and severity in Japanese patients compared with non-Japanese patients: tell your study doctor right away if you have any of these symptoms as it may need to be treated urgently.

- Low thyroid (Hypothyroidism): this is when the thyroid gland produces less thyroid hormone than it should which causes the metabolism to run too slow. Symptoms may include but are not limited to fatigue, increased sensitivity to cold, constipation, dry skin, unexplained weight gain, puffy face, muscle weakness, slow heart rate, thinning hair, impaired memory. The condition can be treated with replacement thyroid hormone.
- High thyroid (Hyperthyroidism): this is when the thyroid gland produces too much thyroid hormone. Symptoms include anxiety or nervousness, weight loss, frequent and loose bowel movements, breathlessness, feeling hot and possibly having heart palpitations. Depending on the severity of the symptoms, treatment may include just monitoring the symptoms, treating the symptoms themselves and/or giving medicine to block the thyroid hormone.
- Kidney problems: you may have an increase of creatinine levels in a blood test (creatinine is a protein marker that measures kidney function) but not have any symptoms or feel unwell. Uncommonly a patient may experience nephritis which is an inflammation of the kidneys that stops the kidneys from working properly.
- Nervous system problems: symptoms can include unusual weakness of legs, arms, or face, Numbness or tingling in hands or feet. In rare situations there is the potential for the inflammation of the nervous system to be severe and cause damage to the nerve cells or breakdown in the communication between nerves and muscles: tell your study doctor right away if you have problems swallowing, if you start to feel weak very quickly and you are having trouble breathing.
- Infusion Related Reactions: reactions may occur during or after the infusion of study medication. The reaction may cause fever or chills and a change in blood pressure or difficulty in breathing which might be serious. Tell your study doctor right away if you experience any of these symptoms even if it has been several days after the infusion has been completed.
- Inflammation of the intestine (colitis). It may cause abdominal pain and diarrhea with or without blood. Fever may be present. It may require you to receive additional fluids. If left untreated, in rare occasions this may lead to a tear in the wall of the intestine which can be serious and life threatening. Tell your study doctor right away if you have any of these symptoms.
- A hoarse voice
- Painful urination
- Night sweats
- Pneumonia
- Oral thrush
- Dental and oral soft tissue infection
- Pain in muscles and joints
- Influenza

- Accumulation of fluid causing swelling, especially in your hands and feet

Uncommon, some may be serious

In 100 people receiving durvalumab, 1 or fewer may have:

- Inflammation of the pancreas (pancreatitis). Pancreatitis usually causes symptoms of persistent upper abdominal pain (sometimes made worse by eating and drinking), nausea, vomiting and general weakness. Pancreatitis usually settles with simple measures but it can be a serious condition and can be fatal. You should immediately tell your study doctor if you develop any of these symptoms. You may get an increase of lipase and amylase levels in a blood test (related to the pancreas) but not have any symptoms or feel unwell. Lipase and amylase are enzymes or protein markers that measure the function of your pancreas. Uncommonly these increases may be associated with pancreatitis.
- Inflammation of the thyroid
- Allergic reactions: These can cause swelling of the face, lips and throat, breathing difficulties along with hives or nettle like rash. You should immediately tell your study doctor if you develop any of these symptoms.
- Problems with your adrenal glands (Adrenal Insufficiency): may cause stomach pains, vomiting, muscle weakness and fatigue, depression, low blood pressure, weight loss, kidney problems, and changes in mood and personality. These complications may be permanent and may require hormone replacement
- Problems with the pituitary gland (hypopituitarism): Hypopituitarism refers to decreased output of hormones from the pituitary gland in the brain and may be caused by inflammation of the pituitary gland (hypophysitis). Symptoms may include headaches, thirstiness, and trouble seeing or double vision, leakage of breast milk or irregular periods in women. These complications may be permanent and may require hormone replacement.
- Inflammation of the muscles or associated tissues, such as blood vessels that supply the muscles (Myositis/polymyositis). Symptoms can include muscle weakness and aches, tired feeling when standing or walking, muscle pain and soreness that does not resolve after a few weeks.
- Inflammation or sores in the lining of the small rectum that may be painful, bloody bowel movements, rectal bleeding or mucoid discharge

Rare side effects, some may be serious

In 1,000 people receiving durvalumab, 1 or fewer may have:

- Type 1 Diabetes mellitus which may cause increased blood glucose levels (called ‘hyperglycemia’): symptoms may include weight loss, increased urination, increased thirst, and increased hunger. Type 1 diabetes will require replacement of insulin through injection. Tell your study doctor right away if you have any of these symptoms.
- A disorder affecting how the body regulates salt and water which can result in intense thirst and heavy urination (diabetes insipidus).

- Problems with the pituitary gland (hypopituitarism): hypopituitarism refers to decreased output of hormones from the pituitary gland in the brain and may be caused by inflammation of the pituitary gland (hypophysitis). Symptoms may include headaches, thirstiness, and trouble seeing or double vision, leakage of breast milk or irregular periods in women. These complications may be permanent and may require hormone replacement.
- Inflammation of the heart muscle (myocarditis). Symptoms can include chest pain, rapid or abnormal heartbeat, shortness of breath and swelling of your legs. Tell your study doctor right away if you experience any of these symptoms.
- Inflammation of the membrane surrounding the heart
- Growths of tiny collections of inflammatory cells in different parts of the body
- Inflammation of the middle layer of the eye and other events involving the eye (e.g. inflammation of the cornea and optic nerves)
- Inflammation of the brain or the membranes that cover the brain and spinal cord
- Hardening and tightening of the skin and connective tissues and loss of skin color
- Pemphigoid (a rare autoimmune blistering of the skin and mucus membranes)
- Other hematological events (e.g., abnormal breakdown of the red blood cells and low levels of platelets, in some cases by your immune system)
- Inflammation of the blood vessels and rheumatological events (inflammatory disorder causing muscle pain and stiffness and autoimmune arthritis)
- Myasthenia Gravis which results in weakness and rapid fatigue of any of the muscles under your voluntary control.
- Inflammation of the bile duct system (cholangitis) that leads to scarring (sclerosis) and narrowing of the ducts. The bile duct system carries bile from your liver and gallbladder into the first part of your small intestine
- Inflammation of the bladder (cystitis)

In addition to the possible risks identified in patients treated with durvalumab, other immune-mediated side effects are possible that have not been observed and can result in inflammatory side effects in any organ or tissue.

Olaparib

Very common, some may be serious **In 100 people receiving olaparib, more than 10 and up to 100 may have:**
• Low red blood cell count (anemia) which may cause you to feel tired, weak, or have shortness of breath. In some instance, this decrease in red blood cell count may be serious and require blood transfusions (when you are given new blood or blood products from a donor).

- A decrease in white blood cells (specific type called neutrophils) with or without fever. In some cases, this decrease can be serious and lead to infection requiring antibiotic treatment and possibly hospitalization (neutropenia).
- A decrease in white blood cells in blood (leukopenia) which may be serious in rare cases.
- Dizziness
- Headache
- Changes in taste
- Cough
- Shortness of breath
- Constipation
- Heartburn
- Diarrhea, nausea, vomiting
- Tiredness (including weakness)
- Loss of appetite

Common, some may be serious
In 100 people receiving olaparib, from 1 to 10 may have:

- Bruising, bleeding which may be caused by a reduction in platelets (blood cells that help the blood to clot), and can lead to bleeding requiring platelet transfusions (thrombocytopenia).
- Lymphocyte count decreased (type of white blood cell that is part of the immune system) which may lead to an infection.
- Inflamed and sore mouth
- Upper abdominal pain
- Rash
- Blood creatinine increased (creatinine is a measure that tells us how well your kidneys are working). This may mean that your kidneys are not working well.
- A blood clot that starts in a vein (venous thromboembolism). These clots can also develop in deep veins in the arm, lower leg, thigh or pelvis and can in serious cases travel to the lungs.

Uncommon, some may be serious

In 1,000 people receiving olaparib, more than 1 but less than 10 may have:

- Irreversible abnormal blood counts and bone marrow damage, which may lead to leukemia (myelodysplasia).
- Undesirable reactions produced by the normal immune system (hypersensitivity)
- Swelling that occurs just beneath the surface of the skin (angioedema)

• Skin irritation or inflammation (dermatitis) • Increased blood cell size and volume • Cancer of the blood and bone marrow (the soft inner part of certain bones, where new blood cells are made) which may at time be serious (acute myeloid leukemia) • Blockage of an artery, typically by a clot of blood (embolism) • Blockage in one of the pulmonary arteries in your lungs (pulmonary embolism) • Inflammation of the lung tissue (pneumonitis), which may cause new or worsening symptoms of shortness of breath. This may be serious or life threatening.
Rare, and may be serious **In 10,000 people receiving olaparib, more than 1 but less than 10 may have:**
• Red blood cells that are larger than normal • Flat, firm, hot, red, and painful lumps that usually appear on the shins (erythema nodosum)

Getting medical treatment right away may keep these problems from becoming more serious. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Risks from Biopsy

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Risks of biopsy may include bleeding, injury to internal organs, and infection. Rarely, these complications from biopsy could result in hospitalization and require additional medical care. Risks of sedation will be described at the time of procedure.

Risks from Blood Collection

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop. About 22 tablespoons of blood may be collected at each visit with a maximum of 99 tablespoons in an 8-week period.

Risks from Urine Collection

There are no risks related to urine collection.

Risks from CT contrast

Itching, hives or headaches are possible risks associated with contrast agents that may be used during CT imaging. Symptoms of a more serious allergic reaction include shortness of breath and swelling of the throat or other parts of the body. Very rarely, the contrast agents used in CT can cause kidney problems for certain participants, such as those with impaired kidney function.

Risks from Electrocardiograms

Other than possibly experiencing some minor skin irritation from the electrodes, there are no anticipated risks related to complete the electrocardiogram and/or the echocardiogram.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You will need to use one highly effective birth control method and your partner will need to use a male condom or practice total/true abstinence throughout the study treatment and for at least 6 months after last dose of study drugs. Your study team will provide additional details on what methods may be used. If you become pregnant during this time, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible. If you plan to become pregnant in the future, please discuss with the research team how long you need to wait before becoming pregnant after completing the course of this study drug or procedures on this study.

You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

If you are a sexually active person with a partner capable of becoming pregnant, you will need to use a condom or total/true abstinence throughout the study and for at least 3 months after the last dose of study drugs. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must both agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted time period, please contact the research team member identified at the top of this document as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted time period, please discuss this with the study team.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from 3 CT guided biopsies and CTs every 8 weeks. The amount of radiation exposure you will receive from these procedures is equal to approximately 9 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called “background radiation.” This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CTs that you get in this study will expose you to the roughly the same amount of radiation as 27.3 years’ worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.9 out of 100 (0.9%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

Risks from MRI

You might be at risk for injury from the MRI magnet if you have some kinds of metal in your body. It may be unsafe for you to have an MRI scan if you have:

- pacemakers or other implanted electrical devices,
- brain stimulators,
- some types of dental implants,
- aneurysm clips (metal clips on the wall of a large artery),
- metal prostheses (including metal pins and rods, heart valves, and cochlear implants),
- permanent eyeliner,
- tattoos,
- an implanted delivery pump,
- or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye.

You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should tell us. You will be asked to fill out an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before you enter the MRI scan room.

If you are afraid of confined (small, cramped) spaces, you may get anxious during an MRI. If you have back problems, you may have back pain or discomfort from lying in the scanner.

The noise from the scanner is loud enough to damage your hearing, especially if you already have hearing loss. We will give you hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks from MRI Contrast (Gadolinium)

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein. These could cause pain and swelling.

Mild symptoms from gadolinium happen in less than 1% of people who get it. Symptoms usually go away quickly. Mild symptoms may include:

- your arm being cold during the injection,
- a metallic taste,
- headache, and
- nausea.

More severe symptoms have been reported in an extremely small number of people (fewer than 1 in 300,000 people). These symptoms include:

- shortness of breath,
- wheezing,
- hives, and

- lowering of blood pressure.

You should not get gadolinium if you ever had an allergic reaction to it. We will ask you about any allergic reactions before giving you gadolinium.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)." NSF always involves the skin and can also involve the muscles, joints, and internal organs. NSF has resulted in a very small number of deaths. We may do a blood test of your kidney function within 30 days before an MRI scan with gadolinium contrast. You will not get gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast will leave your body in the urine. However, the FDA has issued a safety alert that says small amounts of gadolinium may stay in your body for months or years. The long-term effects of the gadolinium that stays in your body are unknown. Some types of gadolinium are less likely to remain in the body than others. In this study, we will use the gadolinium that is less likely to stay in your body. We will also give you additional information called a "Medication Guide." If you ask, we will also give you individual information about any remaining gadolinium we see on your scans.

Privacy Risks Associated with Genetic Testing

It may be possible that genetic information from you could be used by law enforcement agencies or other entities to identify you or your blood relatives

Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because what we learn in this study may eventually be used to treat others with your disease.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether to be in this study, we will discuss the other options that are available to you. Instead of being in this study, you could:

- choose to be treated with surgery, radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

When we are examining your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings".

These include:

- Changes in genes that are related to diseases other than cancer.
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

Some of your samples may be tested in a laboratory that is certified to perform genetic testing. If this happens, we will offer to share the results for these tests.

Some of the analyses will be performed in our laboratory and will be nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. This means the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our

research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to provide a sample to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic healthcare provider to discuss the results.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop your therapy for the following reasons:

- if your disease worsens or comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if the durvalumab and olaparib become unavailable
- if new information shows that another treatment would be better for you
- if the study is stopped for any reason
- if you permanently lose the capacity to consent

In this case, you will be informed of the reason therapy is being stopped.

After the therapy is stopped, we would like to see you for a safety visit approximately one month after stopping therapy.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will Your Specimens or Data Be Saved for Use in Other Research Studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding small cell lung carcinoma or another neuroendocrine cancer, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will Your Specimens or Data Be Shared for Use in Other Research Studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

Will Your Genomic Data Be Shared Outside of This Study?

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and

ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

How Long Will Your Specimens and Data be Stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

AstraZeneca is providing Olaparib and Durvalumab for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some research partners not associated with the NIH working on this study who may receive payments or benefits, limited by the rules of their workplace.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, Center for Cancer Research of National Cancer Institute.
- Qualified representatives from AstraZeneca, the pharmaceutical company who provides durvalumab and olaparib.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for

research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Anish Thomas, M.D., anish.thomas@nih.gov, 240-760-6241. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness	Print Name of Witness	Date

NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.