INSTITUTE/CENTER: National Cancer Institute

PRINCIPAL INVESTIGATOR: A. P. Chen, MD

STUDY NUMBER: 19-C-0123

STUDY TITLE: DURVA+: Evaluation of the Safety and Pharmacodynamics of Anti-PD-L1 Antibody MEDI4736 (durvalumab) in Combination with Chemotherapy in Patients with Advanced Solid Tumors

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Cohort: Standard Adult

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WHO DO YOU CONTACT ABOUT THIS STUDY?

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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 to 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.

Overview and Key Information

What are you 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 advanced cancer.

Taking part in this study is your choice

You can choose to take part in this study or you can choose not to take part. 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 "*Clinical Trial Registration and Results Reporting*" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:
Is it safe to combine chemotherapy drugs with an immunotherapy drug?

Chemotherapy together with immunotherapy might improve how your immune cells respond to and attack cancer cells. We are doing this study because we want to find out if this approach is better or worse than the usual approach for your cancer. The usual approach is defined as the care most people get for advanced cancer.

What is the usual approach to your cancer?

The usual approach for patients who are not in a study is treatment with surgery, radiation, immunotherapy drugs, or chemotherapy drugs. There are no treatments that are proven to help patients with your health condition live longer.

What are your other choices if you do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different 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 you decide to take part in this study?

If you decide to take part in this study, you will be treated with the immunotherapy drug MEDI4736 (durvalumab) on its own or with one of six different chemotherapy drugs (capecitabine, carboplatin, paclitaxel, gemcitabine, doxorubicin, or nab-paclitaxel). All the study drugs are administered IV (through a vein in your arm), except for capecitabine, which is a tablet taken by mouth. Your study doctor will discuss these different study drugs with you. Treatment will be given in the outpatient setting, so you won't have to stay overnight in the hospital or clinic.

The drugs are given in cycles, which are either 4 weeks (28 days) or 6 weeks (42 days) long.

We will ask you for a tumor biopsy before you take any drugs and twice when you are on study. We may also collect a fourth biopsy (optional) before you leave the study.

You will continue to receive study drugs for as long as your cancer does not get worse, the side effects are tolerable, and you agree to stay on study.

In addition, you may be able to continue treatment with the study drugs if you are experiencing benefits and feeling better, even if tests suggest that your cancer is getting worse. In this case, your doctor will discuss with you whether you meet the criteria for remaining on treatment. However, it is not known at this time if continuing treatment once disease has gotten worse is actually beneficial for you.

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 will give you more information in the "*What are the risks and discomforts of being in the study?*" section.

If you choose to take part in this study, there is 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.

The study drug, alone or in combination with chemotherapy drugs, are NOT approved for treatment of any type of cancer and may be the first time used in humans.

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

- Diarrhea, nausea, vomiting
- Skin rashes and blisters
- Pain
- Tiredness, muscle weakness
- Fever

There are more serious side effects of the study drug up to and including potentially fatal risks. The potential benefits for taking part in this study do not outweigh the risks.

The combination of MEDI4736 (durvalumab) and chemotherapy drugs may also have some risks that the study doctors do not yet know about.

Benefits

This study is unlikely to help you. The knowledge gained from this study may help others in the future who have cancer.

Can you stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The 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.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If your disease comes back during treatment
- If you have side effects from the treatment that your doctor thinks are too severe
- If new information shows that another treatment would be better for you
- For women: if you become pregnant while on the study
- If the study is stopped by the sponsor, the IRB (people who review the research to protect the people taking part in the study), or FDA

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.

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?

The purpose of this study is to test the safety of combining one of six different chemotherapy drugs together with the immunotherapy drug MEDI4736 (durvalumab). We also want to learn if this combination of chemotherapy and immunotherapy might improve how your immune cells respond to and attack cancer cells.

MEDI4736 (durvalumab) works by unblocking your immune system, allowing your immune system cells to recognize and then attack your tumor cells. MEDI4736 (durvalumab) is approved by the Food and Drug Administration (FDA) for some bladder and lung cancers.

The chemotherapy drugs we will be using on this study are capecitabine, carboplatin, paclitaxel, gemcitabine, pegylated liposomal doxorubicin, and nab-paclitaxel. These chemotherapy drugs are all approved by the FDA for some types of cancers. However, MEDI4736 (durvalumab) and the chemotherapy drugs given together are considered experimental drugs in this study. Please ask your study doctor for more information about this.

WHAT WILL HAPPEN DURING THE STUDY?

Each patient taking part in this study in each study group (called arms) will receive MEDI4736 (durvalumab) on its own or with one of the six different chemotherapy drugs. If you decide to take part in this study, you will be assigned by the study doctor to one of these arms based on several factors. Your treatment history will determine which arms you are eligible for. Of the eligible arms, you will then be placed onto the arm with the smallest number of enrolled patients. The chemotherapy drugs on this study are capecitabine, carboplatin, paclitaxel, gemcitabine, doxorubicin, and nab-paclitaxel. Your study doctor will discuss these different arms and study drugs with you. If you have taken one of these chemotherapy drugs before for your cancer, you will be given a different chemotherapy with MEDI4736 (durvalumab) on this study.

Treatment will be given in the outpatient setting, so you won't have to stay overnight in the hospital or clinic. MEDI4736 (durvalumab) is administered IV (through a vein in your arm). The chemotherapy drugs carboplatin, paclitaxel, gemcitabine, pegylated liposomal doxorubicin, and nab-paclitaxel are also administered IV, while capecitabine is a tablet taken by mouth. The drugs are given in cycles, which are either 4 weeks (28 days) or 6 weeks (42 days) long. Your study doctor will explain how the drugs are given and when you will need to come to the Clinical Center for study tests and procedures.

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. CT scans or other imaging tests such as PET (an examination using a special injected dye) or MRI (an examination using magnetic field and radio waves) that detect your tumor will be done to monitor your disease, allowing your doctor to determine if you are having any benefit from the study drugs. These tests and scans are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study but may *not* be included in usual care.

You will need to have the following extra tests to find out if you can be in the study:

- An EKG (electrocardiogram) to check your heart (some patients will also need an echocardiogram, or ECHO)
- Pregnancy test in women who are able to become pregnant

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests. They are a necessary part of the research study but would not be included in usual care. Willingness to give blood and have tumors biopsied for research is required for taking part in this study.

- Blood tests to measure the effect of the study drug on immune cells in your blood. Blood will be drawn before you receive study drug at several times throughout the study. The total blood for all these tests will be about 4 tablespoons.
- Biopsies to measure the effect of the study drugs on your tumor cells and on the immune cells inside of your tumor. Tumor biopsies are a very important part of this trial, as it is the only way for study scientists to "see" if your immune cells are in the tumor and if they are attacking your cancer cells. We will collect a tumor biopsy before you take any study drugs and twice when you are on study. We may also collect a fourth biopsy (optional) before you leave the study, as specified in the section below. We are collecting these samples to study the effects of the study drugs and to search for any gene variations in your tumor that may help us understand how it responds to MEDI4736 (durvalumab) and chemotherapy.
    - **Genomic Sequencing**:

      One of the tests performed on your biopsy sample will be genomic sequencing. Your tumor tissue contains genes, which are made up of DNA (deoxyribonucleic acid) and serve as the "instruction book" for the cells that make up our bodies. Genomic sequencing will determine the exact order of the DNA building blocks in your tumor. To identify the genetic differences in your tumor compared to the genes you were born with, we will compare the genes in your tumor to the genes in your blood (germ line sequencing). We know that variations in some tumor genes play an important role in how cancers respond to drugs. Determining whether different tumor gene variations affect how MEDI4736 (durvalumab) and chemotherapy work together against tumors will help scientists understand which patients might respond best to these drugs.

      Most of the information collected from genomic sequencing of your tumor will be for research purposes only, and we will not give you any individual results from this sequencing or add this information to your medical records. However, if your cancer looks like it is getting worse and you choose to have a fourth tumor biopsy (optional) before leaving the study, we will perform a more specific, targeted sequencing test on this tumor tissue in a clinically approved laboratory. You and your doctor will receive the results of this test, and the results will be in your electronic medical record. Your doctor will discuss these results with you and tell

you about any gene variations that might make you able to take part in targeted therapy clinical trials in the future.

This consent form includes a study calendar that shows how often these tests will be done.

HOW LONG WILL THE STUDY TAKE?

You will continue to receive study drugs for as long as your cancer does not get worse, the side effects are tolerable, and you agree to stay on study.

In addition, you may be able to continue treatment with the study drugs if you are experiencing benefits and feeling better, even if tests suggest that your cancer is getting worse. In this case, your doctor will discuss with you whether you meet the criteria for remaining on treatment. However, it is not known at this time if continuing treatment once disease has gotten worse is actually beneficial for you.

Your doctor will continue to watch you for side effects and follow your condition for 3 months after you finish the study, or until any drug-related side effects you may have experienced during treatment get better.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

There will be about 115 patients taking part in this study at the NIH Clinical Center.

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

General Risks

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

Side Effect Risks

The study 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 test your blood and let you know if changes occur that may affect your health.

Here are important things to know 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 a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- 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 may include reducing or holding the dose of the study drugs at your study doctor's discretion.

This study is looking at a combination of the usual drugs 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 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. The combination of MEDI4736 (durvalumab) and chemotherapy may have some risks that the study doctors do not yet know about.

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

Inform your physician and study healthcare team about current medications including over the counter drugs, herbals, or natural medicines. We do not know if taking any of the study drugs will cause other drugs you may be taking to work differently. It is very important that you talk to a member of the research team before beginning any new drugs, over-the-counter medications, vitamins, or alternative therapies.

Let your study doctor know of any questions you have about possible side effects. You can ask your study doctor questions about side effects at any time.

If you experience diarrhea, or any other symptom listed in the "Rare, and Serious" categories below, it is important that you contact the study doctor immediately.

Possible Side Effects of MEDI4736 (durvalumab):

COMMON, SOME MAY BE SERIOUS

In 100 people receiving MEDI4736 (durvalumab), more than 20 and up to 100 may have:

- Cough

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving MEDI4736 (durvalumab), from 4 to 20 may have:

- 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
- Change in voice
- Increased sweating

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

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands). Signs and symptoms may include: 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 (including pneumonitis), symptoms may include: new or worsening cough, chest pain, shortness of breath
- Skin: itching; rash; patches of light skin color
- Reaction during or after infusion which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

RARE, AND SERIOUS

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

MEDI4736 (durvalumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may 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 heart failure. Symptoms and signs of heart problems 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 may include: diarrhea or increase in bowel movements, belly pain, bloody or dark, tarry, sticky stools
- 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
- Swelling of the brain, which may cause headache, blurred vision, stiff neck, and/or confusion
- 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
- Kidney problems, including 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

Possible Side Effects of Capecitabine

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, more than 20 and up to 100 may have:
• Swelling of the body • Blisters on the skin • Redness, pain or peeling of palms and soles • Pain • Diarrhea, loss of appetite, nausea, vomiting • Sores in mouth which may cause difficulty swallowing • Anemia which may require blood transfusions • Infection, especially when white blood cell count is low • Bruising, bleeding • Feeling of "pins and needles" in arms and legs • Tiredness • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, from 4 to 20 may have:
• Blurred vision, dry or itchy eyes • Muscle spasms, body aches • Abnormal heartbeat • Restlessness, irritability • Swelling of face, fingers and lower legs • Constipation • Difficulty with balancing

RARE, AND SERIOUS In 100 people receiving Capecitabine, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Difficulty speaking, walking or seeing • Internal bleeding which may cause blood in vomit or black tarry stools • Damage to the heart

Possible Side Effects of Carboplatin

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Hair loss • Vomiting, nausea • Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Belly pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, Constipation • Numbness and tingling in fingers and toes • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Changes in taste • Changes in vision

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Damage to organs which may cause hearing and balance problems

Possible Side Effects of Paclitaxel

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Anemia which may cause tiredness, or may require blood transfusions
- Pain
- Sores in mouth which may cause difficulty swallowing
- Diarrhea, nausea, vomiting
- Muscle weakness
- Numbness, tingling or pain of the arms and legs
- Hair loss

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Paclitaxel, from 4 to 20 may have:

- Abnormal heartbeat
- Blood clot which may cause swelling, pain, shortness of breath
- Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS

In 100 people receiving Paclitaxel, 3 or fewer may have:

- Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- A tear or a hole in the bowels which may cause pain or that may require surgery
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Gemcitabine

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, more than 20 and up to 100 may have:
• Flu-like symptoms of muscle pain, fever, headache, chills and fatigue • Nausea, vomiting • Rash • Hair loss • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Muscle weakness • Blood in urine • Feeling of "pins and needles" in arms and legs • Numbness and tingling of the arms and legs • Tiredness • Difficulty sleeping • Swelling of arms, legs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, from 4 to 20 may have:
• Swelling and redness of the area of radiation • Blisters on the skin • Diarrhea, constipation • Sores in mouth which may cause difficulty swallowing • Liver damage which may cause yellowing of eyes and skin, swelling • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Scarring of the lungs • Shortness of breath • Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles • Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness

RARE, AND SERIOUS In 100 people receiving Gemcitabine, 3 or fewer may have:
• Severe blood Infection • Anemia, kidney problems which may require dialysis • Blood clot • Blockage of the airway which may cause cough

Possible Side Effects of Pegylated Liposomal Doxorubicin (Doxil)

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS In 100 people receiving Doxil, more than 20 and up to 100 may have:
• Rash • Redness, pain or peeling of palms and soles • Vomiting, nausea, constipation or diarrhea • Sores in mouth which may cause difficulty swallowing • Weakness, tiredness • Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Bruising, bleeding • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Doxil, from 4 to 20 may have:
• Hair loss • Heart attack or failure which may cause chest pain, shortness of breath, swelling of ankles, cough • Swelling and redness at the site of the medication injection • Loss of appetite • Blockage of the stomach • Headache • Dry eye • Reaction during or following infusion of the drug

RARE, AND SERIOUS In 100 people receiving Doxil, 3 or fewer may have:
• Hepatitis, which may cause yellow eyes and skin • Severe blood infection • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelli of the face or throat • Cancer of bone marrow caused by chemotherapy

Possible Side Effects of Nab-Paclitaxel

Taking this drug? Yes/No

COMMON, SOME MAY BE SERIOUS In 100 people receiving Nab-Paclitaxel, more than 20 and up to 100 may have:
• Swelling of the body • Infection, especially when white blood cell count is low which can be serious • Bruising, bleeding • Anemia, which may cause tiredness, or may require blood transfusions • Diarrhea, nausea, vomiting, or loss of appetite • Numbness and tingling of the arms and legs, muscle weakness • Fever • Tiredness • Dehydration • Hair loss, rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Nab-Paclitaxel, from 4 to 20 may have:
• Heart stops beating • Mini stroke • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath • Cloudiness of the eye, visual disturbances • Pain • Constipation • Paralysis, weakness, headache • Numbness and tingling of the arms and legs • Hoarseness

What are the risks related to pregnancy?

You should not get pregnant, breastfeed, or father a baby while in this study because the study drugs could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. Birth control should be continued for 6 months after the last treatment. Patients who become pregnant while taking part in the study will be taken off the study. Effective forms of birth control include:

- abstinence
- hormonal (birth control pills, injections, or implants)
- vasectomy
- barrier methods (condoms)
- intrauterine device (IUD)
- tubal ligation

What are the risks related to blood sample collection?

Possible side effects from drawing the blood sample include mild pain, bleeding, bruising, and infection at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes.

What are the risks related to biopsy collection?

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur.

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

This research study involves exposure to radiation from up to 4 CT scans (used in biopsy collections). This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 3.2 rem, which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body. If you are pregnant, you may not participate in this protocol, as the fetus is more sensitive to radiation than children or adults.

What are the risks associated with genetic testing?

To identify the genetic differences in your tumor, we will need to compare the genes in your tumor to the genes in your blood (germ line sequencing). This analysis is investigational, not approved by the FDA, and for research purposes only. By performing a full genetic analysis of your blood cells, we may find information about your hereditary risk of developing disease, such as an increased risk of cancer or other serious illness. Because you share some genetic information with your children, parents, brothers, sisters, and other blood relatives, this information may also tell us about your blood relatives' risk of developing disease. The best way to protect your privacy and your family's privacy is to delink your personal information from your specimens before we do these research tests. This means that we will not be able to tell which patients have gene variations, and we will therefore not be able to give you any information we learn.

Even with these protections, there remains a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this genetic information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may increase in the future as people come up with 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. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance of these things will happen is very small but cannot promise that they will not occur.

WHAT ARE YOUR 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 6 months after your last dose of study drug.

WHAT ARE YOUR RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

This study is unlikely to help you. The knowledge gained from this study may help others in the future who have cancer.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different 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

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

Most of the results from this study will not be returned to you. However, if you choose to have the fourth tumor biopsy (optional) before leaving the study, you and your doctor will receive the results of the sequencing test, and the results will be in your electronic medical record. Your doctor will discuss these results with you and tell you about any gene variations that might make you able to take part in targeted therapy clinical trials in the future.

EARLY WITHDRAWAL FROM THE STUDY

You can decide to stop being in the study any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If your disease comes back during treatment
- If you have side effects from the treatment that your doctor thinks are too severe
- If new information shows that another treatment would be better for you
- For women: if you become pregnant while on the study
- If the study is stopped by the sponsor, the IRB (people who review the research to protect the people taking part in the study), or FDA

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 plan to use all of these specimens and data for the current study. If there are any specimens left over, we will try to use them for future research. 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. By agreeing to let us use your specimens and data, you give the NIH any rights you may have in the specimens and data.

Your specimens and data will be stored in our records without your name or any other kind of link that would help us to identify which specimens or data are yours. Therefore, even if we tried, we wouldn't be able to remove your specimens or data from use in future research studies because we will not be able to tell which yours are.

Please place your initials in the blank next to Yes or No for each of the questions below:

My specimens and data may be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

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. 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?

You will not receive compensation for taking part 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. Please ask your study team for more information about this.

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 you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays, or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. 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 Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

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.

The NIH and the research team for this study are using a drug developed by AstraZeneca through a joint study with your study team and the company. The company also provides financial support for this study.

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.

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).

PATIENT STUDY CALENDAR

Your exact schedule of treatments, exams, and tests will depend on which study group you are placed into. Your study doctor will explain this study calendar as it applies to you.

Day	Patient Activity
Before starting study drugs	*All patients:* • Check in at the Outpatient Clinic • Have a history taken of how you feel and undergo a physical examination by a Health Care Provider • Routine blood tests • EKG to test your heart (some patients will also need an ECHO) • Pregnancy test for women who are able to become pregnant • Tumor measurements by CT or MRI scans • Research blood samples will be taken • Tumor biopsy will be taken
Cycle 1, Day 1	*All patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *or* a chemotherapy drug (depending on which study arm you are on)
Cycle 1, Day 8	*All patients except those on MEDI4736 (durvalumab) alone:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples will be taken • Tumor biopsy will be taken for some patients • Receive MEDI4736 (durvalumab) *and* possibly a chemotherapy drug (depending on which study arm you are on)
Cycle 1, Day 15	*Some patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples may be taken • Receive MEDI4736 (durvalumab) *or* a chemotherapy drug (depending on which study arm you are on)
Cycle 1, Day 22	*All patients except those on MEDI4736 (durvalumab) alone:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and* possibly a chemotherapy drug (depending on which study arm you are on)

Day	Patient Activity
Cycle 1, Day 36 *Only applies to 6-week cycles*	*All patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and* possibly a chemotherapy drug (depending on which study arm you are on)
Cycle 2, Day 1	*All patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples will be taken • Receive MEDI4736 (durvalumab) *or* a chemotherapy drug (depending on which study arm you are on)
Cycle 2, Day 8	*All patients except those on MEDI4736 (durvalumab) alone:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and* possibly a chemotherapy drug (depending on which study arm you are on) *Some patients:* • Research blood samples may be taken • Tumor biopsy may be taken
Cycle 2, Day 15	*Some patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples may be taken • Tumor biopsy may be taken • Receive MEDI4736 (durvalumab) *or* a chemotherapy drug (depending on which study arm you are on)
Cycle 2, Day 22	*All patients except those on MEDI4736 (durvalumab) alone:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and* possibly a chemotherapy drug (depending on which study arm you are on) *Some patients:* • Research blood samples may be taken • Tumor biopsy may be taken
Cycle 3 and onwards, Day 1	*All patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests

Day	Patient Activity
	• Research blood samples will be taken • Receive MEDI4736 (durvalumab) *and/or* a chemotherapy drug (depending on which study arm you are on) • CT or MRI scans to determine how your tumor is responding to the drug every 2 cycles (less often if you have been on study for more than two years)
Cycle 3 and onwards, Day 8	*Some patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and/or* a chemotherapy drug (depending on which study arm you are on)
Cycle 3 and onwards, Day 15	*Some patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Research blood samples may be taken • Tumor biopsy may be taken • Receive a chemotherapy drug (depending on which study arm you are on)
Cycle 3 and onwards, Day 22	*Some patients:* • Check in at the Outpatient Clinic • Physical exam and routine blood tests • Receive MEDI4736 (durvalumab) *and/or* a chemotherapy drug (depending on which study arm you are on)
After finishing treatment	• You will be followed for 3 months after your last dose of drug is administered • Blood draws for research may be obtained • Tumor biopsy may be taken (optional)

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

Your privacy is very important to us and the researchers 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. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept in a central database for research. Your name or 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 inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor and drug companies (makers of the study drugs) supporting the study.
- The Institutional Review Board, IRB, a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, 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.

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

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 records 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 medical 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, Dr. Alice Chen, chenali@mail.nih.gov, (240) 781-3320. 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

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

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: _____.