PRINCIPAL INVESTIGATOR: Vladimir Valera Romero, M.D.

STUDY TITLE: A Phase I Single-Arm Study of the Combination of Durvalumab (MEDI4736) and Vicineum (oportuzumab monatox, VB4-845) in Subjects with High-Grade Non-Muscle-Invasive Bladder Cancer Previously Treated with Bacillus Calmette-Guérin (BCG)

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: 01/10/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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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). 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. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

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 research study is to obtain information on the safety and effectiveness of combination treatment with Durvalumab and Vicineum when given to participants with bladder cancer that has not spread to the muscle in the bladder.

If you join this research study, you will receive an investigational drug Vicineum. Investigational means that it has not been approved by the U.S. Food and Drug Administration (FDA) for treatment of your cancer.

Vicineum is a drug made of an antibody connected to a protein that can kill cells. This protein is a modified "pseudomonas exotoxin A." Vicineum is designed to attach to cells that have a different protein called EpCAM on the outside of the cell. After attaching to a cell, the modified pseudomonas exotoxin A can be released inside the cell causing the cell to die. It is thought that almost all bladder cancer cells have EpCAM on the surface of their cells.

Durvalumab is a drug designed to boost the body's immune system by targeting a protein on tumor cells called PDL-1. PDL-1 normally maintains the balance of the immune system. In cancer, PDL-1 helps tumors evade detection and elimination by the immune system. Durvalumab may increase the immune system's ability to identify and destroy cancer cells. Durvalumab, was recently approved by the FDA for metastatic urothelial/bladder cancer. Although it was FDA approved at a different dose than what is administered in this trial, there is safety data from several trials for the dosage used in this protocol.

There is some evidence in a mouse model that the combination of these two drugs can be more effective in shrinking your tumor. Therefore, we are evaluating both the safety of the combination as well as how well the combination works.

As of February 2021, Durvalumab is no longer approved in the US for metastatic urothelial/bladder cancer who have had their disease worsen on chemotherapy. This decision was made between the manufacturer of this drug and the FDA and was not based on any safety issues. Durvalumab is considered investigational and the FDA has given us permission to use it in this study. Early results from the current study provide data to support the continuation of this trial.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being invited to participate in a research study because you have been diagnosed with bladder cancer and your cancer has not spread to the muscle in the bladder. Your cancer may be spreading on the lining of the bladder (this is called carcinoma in situ [CIS]) and/or may look like a polyp (papillary disease). In the past, you were treated with BCG, and either your bladder cancer did not respond to BCG treatment or your bladder cancer returned after your BCG treatment was completed.

Currently, your bladder cancer is thought to be curable by having surgery to remove your bladder. By participating in this study, you agree to have treatments with Durvalumab in combination with Vicineum, an experimental therapy, rather than having surgery now to remove your bladder. You will be checked approximately every 3 months with a cystoscopy, by examining cells in the urine, and possibly bladder biopsies or bladder tumor resection while on treatment to see if your cancer seems to be getting better or worse. However, there is risk that by not having surgery to remove

your bladder now, your bladder cancer could progress to the point where it is no longer curable by removing your bladder or from any other types of treatment.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 40 people will be enrolled in this study.

DESCRIPTION OF RESEARCH STUDY

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

You will need to have some exams, tests and procedures to find out if you can be in the study. These exams, tests and procedures are usually a part of regular cancer care and may be done even if you do not join the study. However, there are some extra exams, tests and procedures that you will need to have if you take part in this study. Most of these tests will be done under a separate protocol for screening or records will be collected if you had these performed for another reason (such as standard of care or outside of the NIH). If you have had some of them recently, they may not need to be repeated.

During the study

Once it has been determined that you are eligible and agree to participate in the study, you will have additional blood (about 2 tablespoons) and urine tests and you will be asked again about any medications you have been taking. A sample of your tumor will be tested to measure the amount of protein called EpCAM on the surface of the cancer cells. You may also need to have some of the tests that were done at screening repeated depending on how much time has passed. Your study team will let you know if any of the above tests need to be repeated.

All participants in this study will receive Durvalumab and Vicineum. Vicineum will be administered using a Foley catheter placed in the bladder. You will hold the Vicineum for two hours and will have to change position every 15 minutes while sitting or lying in bed. After the two hours, the nurse will drain the Vicineum from your bladder.

Durvalumab is an infusion administered approximately over 1 hour by placing an IV or using a peripherally inserted central catheter (PICC) placed in your arm.

If you are not able to continue to take one of the study drugs for any reason (such as for side effects), the study treatment with both drugs will be stopped.

Treatments are given in two phases. The first phase is called the Induction Phase. In the Induction Phase, you will receive Durvalumab every 4 weeks and Vicineum once a week for 3 months. After the Induction Phase, if you have no evidence of cancer or if you have a less aggressive form of cancer, you will continue to the Maintenance Phase. In the Maintenance Phase, you will receive Durvalumab every 4 weeks and Vicineum once every other week.

During the treatment, you will see the doctor periodically to have many of the same tests done as were done in screening to see how you are doing – these include a physical exam and vital signs, blood samples (such as to check blood counts and organ function), and urine tests. You will also have an electrocardiogram (ECG or EKG) repeated at week 2 to check your heart function. An

additional sample of your tumor will be obtained every 3 months and a CT every year to determine whether your tumor has returned.

The research nurse will go over with you a study calendar that shows how often these tests, drug administration, and/or procedures will be done.

How long will I be in this study?

You will receive treatment for a total of 2 years as long as you are tolerating treatment and your cancer does not return.

While on treatment, if your bladder cancer hasn't returned, you will continue to be evaluated every 3 months. If your bladder cancer returns, your doctor will discuss your treatment options.

Research tests

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. These studies include:

- Urine: before you have received any study drug, first void after you have received your week 1 dose of Vicineum; first void the next morning after week 1 Vicineum; day 7 void prior to start of week 2 Vicineum; week 6, week 10, and week 13 before study therapy; 3 months; and 6 months.

- Blood: Research tests will be done on blood taken at various times (before you have received any study drug, at 2 weeks, 3 weeks, 5 weeks, 8 weeks, 3 months, 6 months) during your participation in this study. The NIH has set a limit on the maximum amount of blood that can be taken for research. This limit is based on your age. For adults, no more than 37 tablespoons can be taken over an 8-week period.

- Tumor biopsies: Any biopsies done on this study will be for clinical reasons to rule out tumor recurrence, however, extra biopsy material (if available) will be used for research purposes.

- Genetic testing: We will use your tissue sample to compare gene expression profiles in tumor cells before and after treatment with Vicineum and Durvalumab. This will help us better understand how the study drugs work inside the human body.

- Additional research testing: 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. While 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. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they may not be as accurate 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)

You will return to the clinic for monthly evaluations for up to 90 days after your last treatment, whenever that occurs. You will have the following tests done: physical exam, vital signs, routine blood tests (about 2 tablespoons of blood each time) and urine tests. If your bladder cancer hasn't returned, you will have a cystoscopy, biopsies of any areas of the bladder suspicious for cancer, and a urine test for cancer cells. If you have ongoing significant side effects, you will continue to be followed until the side effects end or they are not changing.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we do not know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice a highly effective form of birth control and a barrier method before starting study treatment, during study treatment, and for 120 days after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Please use effective forms of birth control or make sure your partner uses method from the list below:

Highly effective methods:

- Abstinence
- Intrauterine device (IUD)
- Hormonal [birth control pills, injections, or implants]
- Tubal ligation
- Vasectomy

Additional Effective methods:

- Male condom
- Diaphragm
- Cervical Cap

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

Durvalumab

The following are side effects observed in patients receiving Durvalumab alone:

Very Common

- Diarrhea
- Rash/itchy skin
- Abdominal pain
- Cough with or without mucus
- Fever
- Low thyroid function (hypothyroidism) which may cause fatigue, increased sensitivity to cold, constipation, dry skin, unexplained weight gain, puffy face, muscle weakness, slow heart rate, thinning hair, impaired memory.
- Upper respiratory tract infections

Common

- Increased liver enzymes
- High thyroid function (hyperthyroidism)which may cause anxiety or nervousness, weight loss, frequent and loose bowel movements, breathlessness, feeling hot and possibly having heart palpitations.
- Pain or difficulty urinating
- Night sweats
- Inflammation in the lungs (pneumonitis that can be fatal). In some cases, this could be caused by your immune system attacking your lungs.
- Hoarse voice
- Swelling of arms and legs
- Muscle pain
- Decreased kidney function (you may have an increase of creatinine levels in a blood test)
- During or after drug infusion having fever, chills, change in blood pressure or difficulty in breathing, which might be serious
- Pneumonia
- Oral thrush

- Dental and oral soft tissue infection
- Influenza

Uncommon

- Scarring of the lungs (interstitial lung disease)
- Inflammation to the liver (hepatitis), that can be fatal. In some cases, this could be caused by your immune system attacking your liver.
- Inflammation of the colon which can lead to abdominal pain and diarrhea with or without blood. If left untreated, this may lead to a tear in the wall of the intestine which can be serious and life threatening. In some cases, this could be caused by your immune system attacking your colon.
- Inflammation of the thyroid
- Inflammation of the kidney
- Dry itchy skin
- Inflammation of the muscles or associated tissues, such as blood vessels that supply the muscles which may cause weakness and aches, tired feeling when standing or walking, muscle pain and soreness
- 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
- Inflammation of the pancreas which may cause increased pancreas enzymes (lipase and amylase) and symptoms of persistent upper abdominal pain (sometimes made worse by eating and drinking), nausea, vomiting and general weakness.
- Inflammation or sores in the lining of the small rectum that may be painful, bloody bowel movements, rectal bleeding or mucoid discharge

Rare

- Type 1 Diabetes mellitus (high blood sugar)
- Allergic reactions, causing:
  - swelling of the face, lips and throat
  - breathing difficulties
  - hives or nettle like rash
- Pain, blistering, thickening, burning, and reddening at the site of injection.
- Problems with the pituitary gland (hypopituitarism/hypophysitis): 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.
- Thirstiness caused by an imbalance of fluids in the body (diabetes insipidus)

- New allergies to previously exposed substances, other than Durvalumab. For example, it is possible that you could develop an allergy to shellfish or IV contrast while taking Durvalumab. These allergies may be severe and life threatening
- Rash, blistering and ulcers on the legs, arms, and abdomen (pemphigoid)
- Inflammation of the blood vessels, heart and the tissue that surrounds the heart
- Inflammation of the brain or the tissues that cover the brain
- Inflammation of your heart causing fast or slow heart rate, chest pain and shortness of breath
- Problems with decrease number of platelets causing a rash or bleeding of your mouth, nose, gut and bladder (in some cases caused by your immune system)
- 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)
- Low white blood cell count which may caused by your immune system attacking these type of cells.
- Weakness in the arm and leg muscles, double vision, and difficulties with speech and chewing caused by a breakdown in communication between nerves and muscles (myasthenia gravis).
- Inflammation of the middle layer of the eye and other events involving the eye
- Growths of tiny collections of inflammatory cells in different parts of the body
- Hardening and tightening of the skin and connective tissues and loss of skin color
- 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.

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.

Vicineum

Likely

- Pain or difficulty urinating
- Blood in the urine
- Frequent urination
- Fatigue (tiredness)
- Urge to urinate quickly
- Bladder and urinary systems infection

- Frequent urination at night
- Uncontrolled leaking or passing of urine
- Bladder pain, spasm or discomfort

Less Likely

- Dizziness
- Flu-like symptoms
- Diarrhea
- Bone or joint pain
- Fever

Rare

- Kidney failure or acute kidney injury (kidneys suddenly stop working properly)
- Inflammation of the liver
- Allergic reaction

Tell your study doctor right away if you have any of these symptoms as they may need to be treated urgently.

A new drug may show an increase in side effects or unexpected effects as more studies are conducted. For your safety, you will be followed closely by your study doctor and the study staff for any undesirable or unexpected side effects during your participation in this study and each time you receive Durvalumab and Vicineum.

There may be other side effects of Durvalumab and Vicineum that are unknown. You will be told about any new findings that develop during this study that may affect your decision to stay in the study.

Risks from Blood Collection

The risks from drawing blood may include discomfort from insertion of the needle, bruising, pain, redness or swelling at site of blood drawing, fainting and rarely, infection at the site of blood drawing.

Risks from Bladder Procedures

Cystoscopy, TURBT, biopsies and catheterization may cause the following discomforts: burning when passing urine, blood-tinged urine, bladder infection or the need to urinate frequently following the procedures. The insertion of a catheter into the bladder through the urethra may be uncomfortable. You may be provided a local anesthetic (pain reliever put on your skin around where the catheter goes in) and sterile lubricant (jelly that makes the catheter easier to put in) at the time of the catheter placement. There is also a small risk that these procedures, particularly cystoscopy, TURBT and biopsies, could damage the lining of the bladder or cause a small hole in your bladder. This could lead to urine or drugs leaking out of the bladder causing severe side effects.

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.

Radiation Risk

During your participation in this research study, you will be exposed to radiation from CT scans. The amount of radiation exposure you will receive from these procedures is equal to approximately 1.4 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." 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 4.7 years' worth of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

CT contrast risks

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.

Electrocardiogram risks

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.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

You may or may not receive direct medical benefit from participating in this study. Even if treatment with Durvalumab and Vicineum demonstrates some efficacy such that some participants in this study are able to delay or avoid having their bladder removed, such a benefit cannot be guaranteed for all participants in the study. The possible benefit to other people with this condition includes learning more information about treatment in participants with bladder cancer that has not spread to the muscle in the bladder.

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.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, 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.

ALTERNATIVE APPROACHES OR TREATMENTS

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

You do not have to participate in this study to be treated for your cancer. Your doctor will discuss your treatment options with you. These may include:

- Having your bladder removed
- Receive additional treatment (with other approved or standard therapies) without being in a research study
- Taking part in another study

STOPPING THERAPY

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

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if your health status changes during the study such that receiving therapy might be too dangerous
- if you become pregnant
- 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
- if you are unable to follow the study requirements
- if the study is ended

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

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.

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 but they do not need to report their personal finances to the NIH.

The National Institutes of Health and the research team for this study are using drugs developed by AstraZeneca and Sesen Biotherapeutics through a joint study with your researchers and the company. The company also provides financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply

to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Genomic Data Sharing

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.

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. Someone will work with you to provide 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.

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 or their agent(s)
- Qualified representatives from AstraZeneca, the pharmaceutical company who produces Durvalumab and qualified representatives from Sesen Biotherapeutics, the pharmaceutical company who produces Vicineum

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 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, Vladimir Valera Romero at vladimir.valeraromero@nih.gov or 240-858-3947. 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 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: _____.