THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Randomized Phase II Trial of Durvalumab (MEDI4736) and Tremelimumab Administered in Combination Versus Sequentially in Recurrent Platinum-Resistant Epithelial Ovarian Cancer
2016-0093

Study Chair: Amir A. Jazaeri

Participant's Name Medical Record Number

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This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by the MD Anderson Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to test 2 types of dosing schedules of tremelimumab and durvalumab to learn if one is more effective in patients with high-grade, platinum-resistant epithelial ovarian, peritoneal, or fallopian tube cancer. The safety of the dosing schedules will also be studied. Another goal is to see if a particular gene can predict how well ovarian or uterine cancers respond to treatment.

This is an investigational study. Neither durvalumab nor tremelimumab are FDA approved or commercially available for the types of cancer in this study. They are currently being used for research purposes only in these diseases. The study doctor can explain how the study drugs are designed to work.

Taking the study drugs may help to control the disease in patients with high-grade, platinum-resistant epithelial ovarian, peritoneal, or fallopian tube cancer. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may receive the study drugs for up to 13 cycles.

If you are in the combination group, you may receive the standard of care treatment after the study drugs for as long as the doctor thinks it is in your best interest or until the disease get worse.

If you are in the sequential group and you complete the full 13 cycles of the study drugs without the disease getting worse, you will have follow up visits until the disease gets worse or until you begin receiving treatment on another study.

Durvalumab and tremelimumab will be provided at no cost to you while you are on study. If you are in the Combination Group (described below) and the disease gets worse and you begin receiving a standard of care treatment, you and/or your insurance provider will be responsible for the costs.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to have tumor reduction surgery and/or laparoscopy without taking part in this study. You may choose to receive standard of care treatments outside of this study. The study doctor will discuss the possible risks and benefits of these treatments. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will be performed within 28 days before your first study drug dose to help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests (which may include cortisol testing, a type of hormone that may be related to inflammation), and to

check how well your blood clots, the functioning of your thyroid, and for hepatitis and HIV (the AIDS virus). If you can become pregnant, part of this sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.
- Urine will be collected for routine tests.
- You will have an EKG to check your heart function.
- You will have MRI or a CT scan to check the status of the disease.

Within 14 days before your first dose of study drugs, you will have a core tumor biopsy for immune system testing and for biomarker testing, which may include genetic biomarkers. If any additional standard of care biopsies are needed while you are on study, any extra tissue may be also be used for research on biomarkers. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs. To perform a core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

You will also complete 7 questionnaires about possible side effects, symptoms, quality of life, and your satisfaction with your care. Completing all 7 questionnaires should take up to 1 hour. The questionnaires will be completed on paper and can be completed in person or they can be mailed to you. If you prefer to be contacted by telephone, the study staff will call you, read the questionnaires over the phone, and record your answers. You will also complete these questionnaires at the time points described below. If your treatment is put on hold for any reason, these questionnaires may still be collected and repeated when your treatment has resumed.

You may be asked to participate in 1 or 2 interviews with the study staff. Each interview may take 25-45 minutes. During the interviews, you will be asked questions about any symptoms you had during the time when you were diagnosed, symptoms you are currently having, and any symptoms you had when you received previous treatments for cancer. If you participate in 2 interviews, you may be asked during your second interview how your symptoms have changed since the first interview.

The interviews will be held in a private conference room and will be digitally recorded. The study staff will transcribe (create a text copy of) the interview and will not record your name, medical record number, or any other identifying information. Only de-identified interview data will be shared with the sponsor, AstraZeneca, but the electronic files and transcription of the interview will be stored securely.

Study Groups

If you are found to be eligible to take part in this study you will be randomly assigned (as in the flip of a coin) to 1 of 2 study groups (the Combination group or the

Sequential group). This is done because no one knows if one study group is better, the same, or worse than the other group.

Each study cycle is 4 weeks.

Up to 175 participants will have screening tests to learn if they are eligible to take part in this study. Up to 120 participants that are found eligible will be enrolled in this study. All will take part at MD Anderson.

Combination Group
If you are assigned to the **Combination Group**, you will receive 4 cycles of tremelimumab and durvalumab together, followed by 9 cycles of durvalumab alone.

If your disease gets worse at any point you will begin a standard of care treatment chosen by the study doctor or you will be given the option to enroll on another study. If you receive a standard of care treatment, the study doctor will discuss the risks and procedures with you in detail. If you choose to enroll on another study, a separate consent form will be provided and you will be taken off this study.

Sequential Group
If you are assigned to the **Sequential Group**, you will receive 4 cycles of tremelimumab alone, and then if the disease gets worse, you will receive 9 cycles of durvalumab alone. The study doctor will discuss this with you.

Study Drug Administration
Each time you receive tremelimumab or durvalumab, it will be given by vein over about 60 minutes on Day 1 of each cycle.

Length of Study
You may receive the study drugs for up to 13 cycles.

If you are in the combination group, you may receive the standard of care treatment after the study drugs for as long as the doctor thinks it is in your best interest or until the disease get worse.

If you are in the sequential group and you complete the full 13 cycles of the study drugs without the disease getting worse, you will have follow up visits until the disease gets worse or until you begin receiving treatment on another study.

You will be taken off study if intolerable side effects occur, if you are unable to follow study directions, or if the study doctor thinks it is in your best interest.

Study Visits

Combination Group

All visits will occur on Day 1 of each 28-day cycle.

On Day 1 of Cycles 1-13:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, immune system testing, and to check the functioning of your thyroid. If you are able to become pregnant, the routine blood tests will include a pregnancy test during Cycle 1. **On Cycles 1 and 2 only**, additional blood (about 2 tablespoons) will be drawn for additional immune system testing.
- Urine will be collected for routine tests.
- You will complete the same questionnaires you did at screening. You will alternate among completing 7, 5, and 2 of the questionnaires each cycle.

During Cycle 1 only:

- You will return to the clinic for blood draws (3 tablespoon each time) for biomarker and immune system testing on Days 8, 15, and 22.

During Cycles 2, 4, 6, 8, 10, and 12 only, about 3 weeks after you receive the study drugs, you will have an MRI or a CT scan to check the status of the disease.

During **Cycle 3** only, you will have a core tumor biopsy for biomarker and immune system testing.

You may be asked to have 1 or 2 interviews at a point between Cycles 2 and 4 and/or Cycles 6 and 8. You may decline to take part in one or both of these interviews.

If the disease gets worse at any point you will begin a standard of care treatment chosen by the study doctor or you will be given the option to enroll on another study.

If the disease does not get worse after the 13 cycles of treatment with the study drugs, you will enter a waiting period. If the disease gets worse during the waiting period, you will then begin a standard of care treatment chosen by the study doctor or you will be given the option to enroll on another study.

During the waiting period, the following tests and procedures will be performed after 30 days and then at every 2 months until you begin the standard of care treatment chosen by your doctor or you leave the study:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests and to check the functioning of your thyroid.
- Urine will be collected for routine tests.
- You will complete the 7 questionnaires from screening.

If you receiving the standard of care treatment, you will follow the same study visit schedule that you did while receiving tremelimumab and durvalumab, except you will not have the blood draws and biopsy for biomarker and immune system testing.

Sequential Group

All visits will occur on Day 1 of each 28-day cycle.

On Day 1 of Cycles 1-4:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, immune system testing, and to check the functioning of your thyroid. If you are able to become pregnant, the routine blood tests will include a pregnancy test during Cycle 1. **On Cycles 1 and 2 only**, additional blood (about 2 tablespoons) will be drawn for additional immune system testing.
- Urine will be collected for routine tests.
- You will complete the same questionnaires you did at screening. You will alternate among completing 7, 5, and 2 of the questionnaires each cycle.

During Cycle 1 only:

- You will return to the clinic for blood draws (3 tablespoon each time) for biomarker and immune system testing on Days 8, 15, and 22.

During Cycles 2 and 4 only, about 3 weeks after you receive the study drugs, you will have an MRI or a CT scan to check the status of the disease.

You may be asked to have an interview between Cycles 2 and 4. You may decline to take part in this interview.

During **Cycle 3** only, you will have a core tumor biopsy for biomarker and immune system testing.

After **Cycle 4** or if the disease gets worse, whichever occurs first, you will wait at least 8 weeks to allow the tremelimumab to clear your system and then you will receive up to 9 cycles of durvalumab only **(Cycles 5-13)**.

About 1 month into the 8-week waiting period, you will have a study visit. The following tests and procedures will be performed:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests and to check the functioning of your thyroid.
- Urine will be collected for routine tests.
- You will complete the 7 questionnaires from screening.

You will begin receiving durvalumab on Day 1 of Cycle 5.

On Day 1 of Cycles 5-13:

- You will have a physical exam.
- Blood (about 1 tablespoon) will be drawn for routine tests and to check the functioning of your thyroid.
- Urine will be collected for routine tests.
- You will complete the same questionnaires you did at screening. You will alternate between completing all 7 of the questionnaires and only 4 of the questionnaires each cycle.

During Cycle 5 only, you will have an EKG to check your heart function.

During Cycles 5 and 6 only, an additional blood sample (about 1 tablespoon) will be drawn for immune system testing.

You may be asked to have an interview between Cycles 6 and 8. You may decline to take part in this interview.

During Cycles 6, 8, 10, and 12 only, about 2 weeks after you receive the study drugs, you will have an MRI or a CT scan to check the status of the disease.

End of Study Visit

After you have received your last dose of the study drugs or the standard of care treatment chosen by the study doctor, you will have an end of study visit. The following tests and procedures will be performed:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests and to check the functioning of your thyroid. If you can become pregnant, part of this sample will be used for a pregnancy test.
- Urine will be collected for routine tests.
- You will complete the 7 questionnaires from screening.

Follow-up

About 30 days after your last dose of the study drugs or standard of care treatment:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine and biomarker testing.
- Urine will be collected for routine tests.
- You will have an MRI or a CT scan to check the status of the disease.
- You will complete 7 questionnaires.

After the 30 day visit, every 2 months for 1 year, then every 3 months:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for immune system testing.

- You will have an MRI or a CT scan to check the status of the disease.
- You will complete 7 questionnaires (for the first 2 months only).

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Tremelimumab and durvalumab may each cause low blood cell counts (red and/or platelet).

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.

Tremelimumab Side Effects

The study drug tremelimumab works by boosting the immune system. Side effects as a result of stimulating the immune system have been reported in patients being given tremelimumab. These immune system side effects are included in the risks outlined below. Tremelimumab may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue.

Common (occurring in more than 20% of patients)

• fatigue (lack of energy) • dry/itchy skin	• skin rash • diarrhea	• nausea/vomiting • loss of appetite

Occasional (occurring in 3-20% of patients)

• fever • headache • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• high blood sugar (possible diabetes) • weight loss • constipation • dehydration • inflammation of the intestines • abdominal pain • abnormal digestive blood test (possible inflammation of the pancreas) • low red blood cell counts	• abnormal liver tests (possible liver damage) • numbness/tingling (hands/feet) • kidney inflammation (possible decreased kidney function) • abnormal kidney test (possible kidney damage) • difficulty breathing • cough

Rare but serious (occurring in fewer than 3% of patients)

• blood vessel inflammation (possible bleeding and/or bruising) • inflammation of the arteries around the temples (possible pain and/or double vision) • immune system damage to the nervous system (causing numbness, confusion, and/or paralysis) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • decreased production of adrenal hormones (possible weakness and/or low blood pressure)	• pituitary gland failure/inflammation (possible headaches, thirst, and/or irregular periods in women) • Type 1 diabetes • inflammation of the pancreas (possible abdominal pain) • holes in the intestines (possibly leaking contents into the abdomen) • digestive system bleeding • low blood cell counts (white/platelet) • liver damage (hepatitis)	• lung inflammation or fluid build up in the lungs (possible difficulty breathing) • weakness (arms/legs/face) • allergic reaction • infusion reaction (possible chills, fever, difficulty breathing, and/or change in blood pressure) • immune system disease (possible dry mouth/eyes, joint pain, fatigue, and/or organ damage)

<u>Durvalumab Side Effects</u>

Common (occurring in more than 20% of patients)

• swelling (hands/feet/limbs) • abnormal sensation including numbness/tingling of hands, feet or limbs • fatigue • fever	• headache • loss of appetite • nausea/vomiting • diarrhea • constipation • low blood cell counts (red/platelets/white) • back pain	• muscle spasms • cough • difficulty breathing • wheezing • infusion reaction (possible chills and/or hives) • infection

Daratumumab may cause a possibly life-threatening allergic reaction (possible difficulty breathing, low blood pressure, and/or organ failure). It is difficult to tell the difference between an infusion reaction and an allergic reaction, including serious reactions. Tell the doctor right away if you have low blood pressure, a skin rash, or any difficulty breathing.

Occasional (occurring in 3-20% of patients)

• high blood pressure • irregular heart beat • chills • fainting • difficulty sleeping • skin rash (possible change in color/texture of the skin) • itching • high blood sugar (possible diabetes) • low blood levels of calcium (possible weakness and/or cramping)	• dehydration • inflammation of the pancreas (possible abdominal pain) • low oxygen levels in the blood (possible dizziness) • lung inflammation (possible difficulty breathing)	• build-up of fluid in the lungs • stuffy nose • flu-like symptoms • worsening of physical health • weakness/lack of strength • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Rare but serious (occurring in fewer than 3% of patients)

• reactivation of hepatitis B infection (which may result in liver damage)	• abnormal blood test (possible anemia)	• immune reaction • cytomegalovirus (CMV) infection

Daratumumab treatment will interfere with blood type testing which is needed before blood transfusions can be given. You should tell the person doing any blood-related testing before an infusion that you are receiving daratumumab.

If you have light chain (AL) amyloidosis, you may be at risk for heart problems (which may be fatal). Tell the doctor right away if you have chest pain, swollen legs, difficulty breathing, an irregular heartbeat, or if you feel faint.

Durvalumab and Tremelimumab Side Effects

The study drugs, durvalumab and tremelimumab, work by boosting the immune system. Side effects as a result of stimulating the immune system have been reported in patients being given the study drugs. These immune system side effects are included in the risks outlined below. The study drugs may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue.

Common (occurring in more than 20% of patients)

• fatigue • skin rash / itchy or dry • constipation • diarrhea	• loss of appetite • pain (such as muscle / joint) • abdominal pain • difficulty breathing	• infection (possible upper respiratory infections, pneumonia, influenza, dental/oral infections) • cough

Occasional (occurring in 3-20% of patients)

• swelling (arms/legs) • fever • abnormal salts, minerals, and/or acids in the blood (which may cause weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • inflammation of the intestines • nausea/vomiting • dehydration • low blood cell counts (red/white) • infusion reaction (possible chills, fever, difficulty breathing, and/or change in blood pressure)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • · kidney inflammation (possible decreased kidney function) • lung inflammation (possible difficulty breathing) • hoarse voice • abnormal pancreas function tests •

Rare but serious (occurring in fewer than 3% of patients)

• heart inflammation	• pituitary gland	• low platelet count

• inflammation of the membranes around the spinal cord and brain (possible headache and/or coma) • immune system damage to the nervous system (causing numbness and/or paralysis) • inflammation of the blood vessels • hardening/tightening of the skin and connective tissue • loss of skin color • decreased production of adrenal hormones (possible weakness and/or low blood pressure)	failure/inflammation (possible headaches, thirst, and/or irregular periods in women) • Type 1 diabetes, which requires insulin • high blood sugar • hole in the intestines (possibly leaking contents into the abdomen) • inflammation of the pancreas (possible abdominal pain) • anemia due to destruction of red blood cells	• liver damage • immune response (causing joint, tissue, organ damage) • muscle inflammation • inflammation inside/around the eye (possible vision problems) • kidney failure • immune reaction (possible loss of drug function) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • allergic reaction

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study. There will be no personal identifying information connected to your questionnaire/interview answers.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you are able to become pregnant, you must use at least 2 effective methods of birth control from the time of screening until 90 days after your last durvalumab or tremelimumab alone or 180 days after your last combination dose. Stopping birth control after this point should be discussed with the study doctor. Male partners of a female patient must use a condom plus spermicide throughout this period.

Effective methods of birth control include barrier methods (male condom plus spermicide, cap plus spermicide, or diaphragm with spermicide), intrauterine device methods (Copper T, progesterone T, or levonorgestrel-releasing intrauterine system [e.g., Mirena®]), or hormonal methods (implants, hormonal shot or injection, combined pill, minipill, or patch).

If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedures #1: If you agree, you will have an additional core tumor biopsy collected at the end-of-study visit for biomarker testing, which may include genetic biomarkers, and immune system testing.

Optional Procedures #2: If you agree, you will have additional blood (about 1 tablespoon) drawn at the end-of-study visit for biomarker testing, which may include genetic biomarkers, and immune system testing.

Optional Procedures #3: If you agree, your information from the interviews and questionnaires along with related clinical information will be stored in a database at MD Anderson for use in future research related to cancer.

Before your data can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your data will be given a code number. No identifying information will be directly linked to your data. Only the researcher in charge of the database will have access to the code numbers and be able to link the data to you. This is to allow medical data related to the data to be updated as needed.

There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure Risks:
Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

MD Anderson and others can learn about cancer and other diseases from your banked interview data, questionnaire data, and related clinical information. MD Anderson will not be able to give you, your family, or your doctor the reports about the research done with your data, and these reports will not be put in your health records. If this information were released to you, your family, or third parties, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job. In the future, people who may do research with your data may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot ensure complete privacy. Sometimes your data may be used for genetic research about diseases that are passed on in families. If your data were used for this kind of research, the results would not be put in your health records.

If you withdraw your consent to the storage of your data in the research database, then the leftover data will no longer be collected for storage. Any of your data that remains in the research database will no longer be used for research and will be deleted from the research database.

However, if any of your de-identified data was already released for research purposes before you withdrew consent, MD Anderson will not be able to delete it.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Optional Procedure #1: Do you agree to provide an additional core tumor biopsy at the end of study visit for biomarker and immune system testing?

Optional Procedures #2: Do you agree to have additional blood drawn the end of study visit for biomarker and immune system testing?

Optional Procedure #3: Do you agree to allow your information to be stored in a research database at MD Anderson for use in future research related to cancer?

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or AstraZeneca-MedImmune for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Amir A. Jazaeri, at 713-745-1613) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of

benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, AstraZeneca-MedImmune, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: AstraZeneca-MedImmune.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Conflict of Interest

Dr. Amir Jazaeri (Study Chair) has received compensation from AstraZeneca UK Limited as a Consultant and Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Dr. Robert Coleman (Collaborator) has received compensation from AstraZeneca as a Consultant and Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Dr. Shannon Westin (Collaborator) has received compensation from AstraZeneca as a Consultant and Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- AstraZeneca-MedImmune, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Sidra Medical and Research Center
- Dr. Chiappinelli's research team at George Washington University (GWU)
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

To protect your identity, the samples collected from you will be labeled a unique number instead of your name or other identifying information. Only the study doctor or study staff will have access to the code that can link you to your samples.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ Date/Time: _____

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ Date/Time: _____

ASSENT OF MINOR