THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Randomized Phase I/II study of AVB-S6-500 in Combination with Durvalumab (MEDI4736) in Patients with Platinum-resistant, Recurrent Epithelial Ovarian Cancer
2019-0149

Study Chair: Amir A. Jazaeri

_____ _____
Participant's Name Medical Record Number

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.

STUDY SUMMARY

This study has 2 phases: Phase 1 (dose finding) and Phase 2 (dose expansion).

The goal of Phase 1 of this clinical research study is to find the highest tolerable dose of AVB-S6-500 that can be given in combination with durvalumab to patients with platinum-resistant epithelial, ovarian, peritoneal, or fallopian tube cancer that is recurrent (has returned after treatment).

The goal of Phase 2 of this clinical research study is to learn if the highest tolerable dose combination of AVB-S6-500 and durvalumab found in Phase 1 can help to control these cancer types.

The safety of this drug combination will also be studied in both parts.

This is an investigational study. AVB-S6-500 is not FDA approved or commercially available. It is currently being used for research purposes only. Durvalumab is FDA approved and commercially available for the treatment for certain types of urothelial cancer, but not for the types of cancer in this study. The use of the study drug combination in these disease types is investigational. The study doctor can explain how the study drugs are designed to work.

The study drugs may help to control the disease. 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

You may continue taking the study drugs for as long as the doctor thinks it is in your best interest.

While you are on study, AVB-S6-500 and durvalumab will be provided at no cost to you.

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. You may choose to receive standard of care treatments outside of this study. You may choose to receive other investigational therapy, if available. The doctor will talk to you to make sure you have considered all standard of care and investigational treatments 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 and test for viruses such as hepatitis and HIV (the AIDS virus). If you can become pregnant, part of this blood 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 an MRI or a CT scan to check the status of the disease. If the doctor thinks the disease may have spread to the brain, your brain will also be scanned.
- Tumor tissue from a previous biopsy will be collected for biomarker testing, which may include genetic biomarkers. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. If this tissue is not available, you will have a core tumor biopsy performed for biomarker testing. To collect a tumor biopsy, the affected area may be numbed with anesthetic and a small

amount of tissue is removed with a large needle or a small cut, depending on the location of the tumor.

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.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a phase depending on when you join the study. Up to 12 participants will be enrolled in Phase 1, and up to 24 participants will be enrolled in Phase 2.

If you are enrolled in Phase 1, the dose of the study drugs you receive will depend on when you join this study. Up to 2 dose levels of AVB-S6-500 will be tested in combination with durvalumab. The first group of participants will receive the highest dose level of AVB-S6-500. If intolerable side effects are seen, the next group will receive a lower dose level.

If you are enrolled in Phase 2, you will be randomly assigned (as in a roll of the dice) to 1 of 2 study groups:

- If you are assigned to the **AVB-S6-500 Cycle 0 Group**, you will receive 6 weeks of AVB-S6-500 before you receive the study drug combination.
- If you are assigned to the **Durvalumab Cycle 0 Group**, you will receive 6 weeks of durvalumab before you receive the study drug combination.

You will have a 75% (3 in 4) chance of being assigned to the AVB-S6-500 Cycle 0 Group. You will have a 25% (1 in 4) chance of being assigned to the Durvalumab Cycle 0 Group.

Up to 11 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle (except Cycle 0 for Phase 2, described below) will be 4 weeks long. You will receive AVB-S6-500 by vein over about 1 hour on Days 1 and 15 of each cycle. You will receive durvalumab by vein over about 60 minutes on Day 1 of each cycle.

If you are in Phase 2, your first cycle (Cycle 0) will be 6 weeks long. If you are in the **Durvalumab Cycle 0 Group**, you will receive durvalumab on Days 1 and 22 of this cycle only. If you are in the AVB-S6-500 Cycle 0 Group, you will receive it on Days 1, 15, and 29.

All participants will be given antihistamines before their first dose of AVB-S6-500 to prevent or reduce the chance of side effects. You will also be watched for 45 minutes after your infusion to watch for side effects. After the first dose, antihistamines and other drugs will only be given prior to dosing if you experienced side effects with the first dose.

You will no longer be able to take the study drugs if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Study Visits

Phase 2 – Cycle 0 Visits

On **Day 1 of Cycle 0**:

- You will have a physical exam.
- Blood (about 3 ½ tablespoons) will be drawn for routine tests. Some of this blood will also be used for biomarker and pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points.
- Urine will be collected for routine tests.
- If you can become pregnant, part of the above blood sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.

If you are in the AVB-S6-500 Cycle 0 Group, on **Day 15 of Cycle 0**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

If you are in the Durvalumab Cycle 0 Group, on **Day 22 of Cycle 0**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

For both study groups, on **Day 29 of Cycle 0**:

- You will have an MRI or a CT scan to check the status of the disease.
- You will have a core tumor biopsy for biomarker testing.
- If you are in the AVB-S6-500 Cycle 0 Group, you will also have a physical exam and blood (about 3 tablespoons) will be drawn for routine tests.

All Participants – Cycles 1 and beyond

On **Day 1 of Cycle 1**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests and biomarker testing. If you can become pregnant, part of this blood sample will be used for a pregnancy test.
- Urine will be collected for routine tests.
- Right before your dose, additional blood (about 3 ½ tablespoons) will be drawn for PK testing.
- If you are in Phase 1, additional blood (about 1 ½ tablespoons) will be drawn for PK testing about 1 and 4 hours after the dose.

On **Day 15 of Cycle 1**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

On **Day 1 of Cycle 2**:
- You will have a physical exam.
- Blood (about 3 ½ tablespoons) and urine will be collected for routine tests. If you can become pregnant, part of this blood sample will be used for a pregnancy test.
- Right before your dose, additional blood (about 3 tablespoons) will be drawn for PK testing.

On **Day 15 of Cycle 2**:
- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

Starting on Day 15 of Cycle 2, you will have an MRI or a CT scan to check the status of the disease **every 8 weeks**.

Just **before Cycle 3**, you will have a core tumor biopsy.

On **Day 1 of Cycle 3 and beyond**:
- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests and (at some of these visits) biomarker testing. If you can become pregnant, part of this blood sample will be used for a pregnancy test.
- Urine will be collected for routine tests.
- At Cycles 3 and 4 only, right before your dose, additional blood (about 3 ½ tablespoons) will be drawn for PK testing.

On **Day 15 of Cycle 3 and beyond**:
- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

End of Treatment Visit

Within 7 days after the last dose of study drug(s):
- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests and biomarker testing. If you can become pregnant, part of this blood sample will be used for a pregnancy test.
- Urine will be collected for routine tests.

Follow-up

If you are taken off study for any reason other than the disease getting worse, you will have follow-up visits **every 6 weeks** for at least 90 days or until you start another treatment:
- You will have a physical exam.
- Blood (about 3 tablespoons) and urine will be collected for routine tests.
- **Every 12 weeks**, you will also have an MRI or a CT scan to check the status of the disease.

If you are taken off study because the disease gets worse, **about 30 and 90 days after the last dose of study drug(s)**:

- You will have a physical exam.
- Blood (about 3 tablespoons) and urine will be collected for routine tests.
- On Day 90 after the last dose of study drug, additional blood (about 1½ tablespoons) will be drawn for antibody testing. Antibodies are created by the immune system and may attack foreign cells or substances, such as the study drug.

Other Instructions

You should not donate blood or receive a live vaccine while taking part in this study or for at least 90 days following the last dose of durvalumab or AVB-S6-500.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. 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.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. 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.

This is an early study of AVB-S6-500, so the side effects are not well known.
Based on early human studies, AVB-S6-500 may cause the following side effects.

• facial flushing/and or swelling • fast heart rate • low blood pressure (possible dizziness and/or fainting)	• fever • chills and/or cold sweats • headache • sweating	• abdominal pain • chest/back pain • difficulty breathing • tightness in the chest and throat

Durvalumab Side Effects

Durvalumab may cause side effects that are unknown. In previous studies people have had the side effects listed below. You may get none, some, or all of these. If you suffer any side effects or injuries, or your condition gets worse, it is important to tell your study doctor right away so you can receive appropriate care.

The study drug durvalumab works by boosting the immune system. Side effects as a result of stimulating the immune system have been reported in patients being given durvalumab. These immune system side effects are included in the risks outlined below. Durvalumab 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 • high blood sugar (possible diabetes)	• 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) • constipation • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)	• pain (such as muscle/joint) • lung inflammation (possible difficulty breathing) • cough • infections (upper respiratory infections, pneumonia, influenza, dental and oral soft tissue infections, oral thrush)

Occasional (occurring in 3-20% of patients)

• swelling (arms/legs) • fever • voice disorder/hoarse voice • night sweats • itching • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • loss of appetite • inflammation of the intestines • diarrhea • abdominal pain • nausea/vomiting • dehydration • difficult and/or painful urination	• low blood cell count (red, white) • liver damage/inflammation (hepatitis) • kidney inflammation or injury (possible kidney failure or decreased kidney function) • difficulty breathing

Durvalumab may occasionally cause a low blood cell count (red and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-

threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

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

• inflammation of the heart (or the membrane surrounding the heart) • inflammation of the brain or membranes around the spinal cord and brain (possible headache and/or coma) • immune system damage to the nervous system (causing weakness, numbness and/or paralysis) • inflammation of blood vessels • hardening/tightening of the skin and connective tissue • inflammation of skin (dermatitis) or patches of skin color loss • skin blisters • 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) • imbalance of body fluids and electrolytes (diabetes insipidus) • 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 • low platelet count • immune response (causing joint, tissue, and/or organ damage)	• inflammation and weakness of multiple muscles • inflammation inside/around the eye (possible vision problems) • immune reaction (possible loss of drug function) • lung damage • infusion reaction (possible chills, fever, difficulty breathing, and/or change in blood pressure) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • allergic reaction or over-activated immune system causing swelling of face, lips, or throat, fever, or shortness of breath

Durvalumab may rarely cause a low platelet cell count. 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.

Patients with head and neck cancer may have an increased risk of bleeding. Tell the study doctor right away if you experience any bleeding and about any drugs you are taking that may increase your risk of bleeding (such as aspirin, blood thinners, or NSAIDs).

Other Risks

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.

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.

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 can become pregnant, you must use at least 1 effective method of birth control from the time of screening until 180 days after your last dose of study drug(s). Stopping birth control after this point should be discussed with the study doctor. Your male 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).

Females: 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.

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, Aravive, or AstraZeneca 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, Aravive, AstraZeneca, 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: Aravive and AstraZeneca.

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.

Conflict of Interest

Dr. Amir Jazaeri (Study Chair) has received compensation from Aravive Biologics as a consultant. The financial interests are within the limits of the conflict of interest policy.

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

- Aravive and AstraZeneca, who are sponsors or supporters of this study, and/or any future sponsors and/or licensees of the study technology
- 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.

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.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2019-0149.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

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.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into _____ and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION