THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

TITLE:	A phase 2 study to assess the effect of BALSTILIMAB (AGEN2034) on viral clearance in HPV-positive oropharyngeal cancer patients with persistent HPV detection in plasma cfDNA after definitive therapy
PROTOCOL NO.:	2021-1077 WCG IRB Protocol #20221801
SPONSOR:	MD Anderson Cancer Center
INVESTIGATOR:	Luana Guimaraes de Sousa, MD 1515 Holcombe Blvd. Houston, Texas 77030 United States
STUDY-RELATED PHONE NUMBER(S):	832-728-7849 713-606-1524 (24-hours)

_____ _____
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.

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

STUDY SUMMARY

The goal of this clinical research study is to learn if balstilimab (AGEN2034) can help to clear persistent human papillomavirus (HPV) circulating-free (cf)DNA in blood of patients who have received treatment for HPV-positive oropharyngeal cancer (OPC). Persistent means that the virus has not cleared (gone away).

This is an investigational study. The study drug, balstilimab, is investigational and is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can explain how the study drug is designed to work.

Balstilimab may help to clear persistent HPV cfDNA in the blood of patients, which has been suggested to be associated with higher risk of relapse. 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 should also know that receiving balstilimab after treatment for HPV-positive OPC may increase toxicity and your risk of developing side effects, and there may be no additional benefit compared to standard treatment.

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

You will receive balstilimab by vein over about 30 minutes on Days 1 and 15 of each cycle (every 2 weeks). You may receive balstilimab for up to 6 months (6 cycles).

Balstilimab will be provided to you at no cost during this study.

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 help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 1-2 teaspoons) will be drawn for routine tests.
- If you can become pregnant, part of the above blood sample will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

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.

Up to 20 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle is 28 days. You will receive balstilimab by vein over about 30 minutes on Days 1 and 15 of each cycle (every 2 weeks). You will stay at the clinic for about 60 minutes after each dose to be monitored for side effects.

If the study doctor thinks it is needed, you may be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

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

Study Visits

On **Day 1 of each cycle**:

- You will have a physical exam.
- Blood (about 7-8 teaspoons) will be drawn for routine tests and for circulating cell-free DNA (cfDNA) testing to check for HPV DNA. cfDNA testing measures the amount of DNA traveling in your blood, outside of a cell.
- In Cycles 2 and beyond, if you can become pregnant, part of the above blood sample or a urine sample will be collected for a pregnancy test.
- You will answer a quality of life questionnaire named EORTC30. This questionnaire is like a survey about different parts of your life during treatment. You'll answer questions about how you feel physically, emotionally, and socially. It helps your doctors understand your overall well-being, so they can plan treatments and support that fit your needs. It's also used for research to improve cancer care for everyone.

Every 3 months during treatment:

- You will have a CT or PET/CT scan of neck to check the status of the disease.

Follow-Up

If there is no sign of cancer after your last dose of study drug, every 3 months after your last dose for up to 2 years:

- You will have a physical exam.
- Blood (about 1-2 teaspoons) will be drawn for routine tests.
- At the first two follow-up visits (3 months and 6 months after your last dose) blood (about 6 teaspoons) will be drawn for cfDNA testing to check for HPV DNA.

You will also have a CT or PET/CT scan of neck to check the status of the disease. The imaging schedule will follow the standard of care guideline.

If you receive at least 1 dose of study drug***,*** every 6 months after your last dose for up to 3 years, the study staff will check on how you are doing and if you have started any new treatments. This may be done by calling you, your family or caretaker, and/or your treating doctor. If you are called, each call will take about 10 minutes.

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.

Balstilimab Side Effects

Like all medicines, balstilimab may cause adverse events. The Trial Doctor will observe you closely to monitor adverse events which can be managed quickly. Adverse events can be mild and short lived-, or they can become serious and long-lasting. Adverse events can cause a risk to life or may require a stay in hospital. Adverse events are considered serious if they are life-threatening- or require a stay in hospital.

Balstilimab is a new investigational medicine, so the Sponsor does not know all the adverse events it might cause. However, the most common adverse events experienced by study participants which the Trial Doctors (Investigators) considered to be related to treatment with this medication are listed below. You too may experience one or more of these adverse events. It is also possible that you may experience other adverse events that are not listed below.

If you experience an adverse effect, or any new or worrying symptoms, please tell the Trial Doctor or clinic staff right away.

1.1. POSSIBLE ADVERSE EVENTS OF BALSTILIMAB

As of 21 December 2024, below adverse events were reported in Agenus-sponsored clinical study programs for balstilimab monotherapy.

1.1.1. Adverse events reported as related to balstilimab in 20% or more of patients:

None

1.1.2. Adverse events reported as related to balstilimab in 5% to less than 20% of patients:

Fatigue	Feeling tired, tiredness or weakness
Diarrhea	Diarrhea is a disorder characterized by loose and watery stools.
Nausea	Feeling sick to the stomach
Decreased appetite	Loss of appetite
Pruritis	Itchy skin
Anemia	The number of red blood cells below normal.
Rash	Skin condition characterized by redness, itching, and irritation. It can occur in one area or spread to multiple parts of the body
Increased aspartate aminotransferase (AST)	An enzyme found in the liver, heart, and other tissues which levels are found increased in bloodstream
Asthenia	Weakness
Arthralgia	Joint pain
Hyperthyroidism	Overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating).

1.1.3. Serious adverse events reported as related to balstilimab in 1% or more of patients:

Immune-Mediated Enterocolitis	Immune –mediated enterocolitis is an inflammatory process that affects the small intestine and colon.
Pneumonitis	Pneumonitis is an inflammatory process affecting the lung parenchyma. It is a milder form of lung inflammation compared to pneumonia.

1.1.4. Additional serious adverse events reported as related to balstilimab in less than 1% of patients:

Diarrhea	Diarrhea is a disorder characterized by loose and watery stools.
Adrenal Insufficiency	Adrenal Insufficiency is a disorder characterized by the adrenal cortex not producing enough of the hormone cortisol and in some cases, the hormone aldosterone.
Immune-Mediated nephritis	Immune-mediated nephritis is an inflammation of renal tissue
Colitis	Colitis is an inflammatory bowel disease involving the mucosal surface of the large intestine and rectum.
Vomiting	Throwing up
Nausea	Feeling sick to the stomach
Hypokalemia	Reduced potassium in the blood leading to weakness, cramping, tiredness, constipation or irregular heartbeats
Hepatitis	Inflammation of the liver

Immune thrombocytopenic purpura	Blood cells called platelets are reduced leading to easier bruising, bleeding from the nose or gums or small red or purple spots on the skin (called purpura)
Psoriasis	The skin cells grow too fast leading to thick, scaly, itchy or sometimes painful patches of skin,

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.

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, which may result in a loss of confidentiality. All study data will be stored in password-protected computers and/or locked file cabinets for 2 years after the study ends and will continue to be stored securely after the study. Only the study doctor and research team will have access to study data.

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, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active. The study doctor will discuss appropriate birth control methods with you.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy during the study or within 3 months after your last dose of study drug.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant during the study or within 30 days after your last dose of study drug, you must tell your doctor right away. The study doctor will ask for information about the outcome of the pregnancy and the health of the baby for up to 30 days after birth.

Getting pregnant will result in your removal from this study.

3. COMPENSATION FOR INJURY, 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. There are no plans made by MD Anderson to reimburse you for expenses or to compensate you financially for this injury.

If you suffer a study-related injury, you may contact the Chair of the study, Dr. Luana Guimaraes de Sousa, at 832-728-7849, or 713-606-1524 (24-hours) with any questions you may have. 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 billed 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.

ALTERNATIVES

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard clinical monitoring for persistent HPV. You may choose to receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. You may choose not to have treatment for HPV or cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

If you decide that you don’t want any more active treatment; one of your options is called “comfort care.” Comfort care includes pain medication and other support. It

aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

Additional Information

4. You may ask the study chair any questions you have about this study, if you have any questions, concerns, or complaints about the research, or if at any time you feel you have experienced a research-related injury or a reaction to the study drug. You may contact the study chair, Dr. Luana Guimaraes de Sousa, at 832-728-7849, or 713-606-1524 (24-hours).

   If you have questions about your rights as a research subject or if you have questions, concerns, or complaints about the research, you may contact:

   WCG IRB
   Telephone: 855-818-2289
   E-mail: clientcare@wcgclinical.com

   WCG IRB is a group of people who perform independent review of research.

   WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

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 to which you are otherwise entitled.

   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, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or WCG IRB.

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 supported by: Agenus Inc.

   Agenus Inc. supports the study by providing the study drug, balstilimab.

10. In a medical emergency, call 911 and contact your study doctor, Dr. Luana Guimaraes de Sousa, at 832-728-7849, or 713-606-1524 (24-hours) as soon as possible.

Future Research

Data

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

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research 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 research samples are used for future research. If future 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 research 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.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

Genetic Research
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. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

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.

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:
   - Agenus Inc. (and/or any future supporters of the study)
   - Any future licensees of the study technology
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - WCG IRB
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require 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. If the results of this study are made public, information that identifies you will not be used.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI and it may be re-disclosed.

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 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 voluntarily agree to participate in this study. I authorize the release of my medical and research records for the purpose of this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed and dated copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

PERSON OBTAINING CONSENT

I have discussed this clinical research study with the participant, 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