INFORMED CONSENT FORM

Official title: INNATE: Immunotherapy during neoadjuvant therapy for rectal cancer, a phase II randomized multi-center trial with and without APX005M, an anti-CD40 agonist

NCT number: NCT04130854

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Consent to be part of a Research Study
To be conducted at
The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

Key Information about this Study

You may be eligible to participate in this research study because you have been diagnosed with locally advanced rectal cancer. The standard treatment for this condition involves radiation and chemotherapy followed by surgery and more chemotherapy afterwards. In this study, we are testing whether adding the study drug, APX005M (also known as Sotigalimab), to standard of care treatment may more effectively treat the rectal cancer. The study drug, sotigalimab, is a type of immunotherapy. These type of medications aim to help treat cancer by strengthening your own immune system. In order to participate in the trial, you must meet all of the inclusion criteria, have none of the exclusion criteria, and have provided written informed consent before the conduct of any screening tests not performed routinely in the treatment of your condition.

The study has two arms: Arm 1 and 2. Eligible participants consenting to this study will be randomized to either receive the study drug, sotigalimab, as part of their chemoradiation therapy regimen (radiation therapy + chemotherapy) in Arm 1 or receive only the chemoradiation therapy regimen in Arm 2. All patients will have surgery. Participants will go through screening procedures that include a physical exam, imaging assessments such as MRI and CT scans EKG, blood work and completion of a performance status questionnaire to assess your overall health status. Once screening is complete and you are considered eligible for the study, you will start the treatment either on the experimental arm (Arm 1) or the comparator arm (Arm 2) depending on the randomization.

Treatment will be administered on an out-patient basis. Starting on Day 1, all study participants (both Arm 1 and Arm 2) will undergo treatment with short-course radiation therapy for 5 consecutive days (i.e., 5 fractions of radiation with a dose of 5Gy for each fraction). Approximately 14 days after the last dose of planned radiation therapy, all participants will receive up to 6 cycles of mFOLFOX (regimen (standard-of-care chemotherapy treatment for participants with locally advanced rectal cancer), with each cycle lasting 2 weeks. Participants on Arm 1 will receive the study drug, sotigalimab, on day 3 of radiation and on day 3 of cycle 1-5 of mFOLFOX chemotherapy. Participants on Arm 2 will receive short-course radiation therapy and mFOLFOX regimen and no study drug (sotigalimab). After completing the last planned dose of mFOLFOX, participants will be considered off-protocol directed therapy and undergo planned total mesorectal excision (resection of the tumor with surrounding fascia/soft tissue and regional nodes), a standard surgery for this type of cancer, per institutional standards, and proceed to the follow-up portion of this study.

Participants will be followed every 3-6 months per standard of care after discontinuing protocol-directed therapy or up to 3 years after last dose of study treatment, whichever occurs first. Study visits will occur 3 months (± 1 month) after surgery and then yearly after completion of treatment up to 3 years (± 3 months for study visits). Participants that discontinue their study therapy due to progression, toxicity, or desire for alternative non-protocol therapy or other trials will be followed for disease status (up to 3 years after the last dose of study drug, ± 1 month). Participants need to undergo H&P (history and physical) and bloodwork every 3-6 months for the first two years then every 6 months for 5 years. In addition, for stage II and III patients imaging should occur every 6 months (± 1 month) from the last scan for 2 years then yearly up to 5 years. Visits can be synchronized to last imaging interval, but yearly study visits should be within the window specified.

There are risks associated with your standard treatment procedures and receiving the study drug. Most of the possible side effects are mild or moderate, however some side effects can be very serious and life-threatening such as cough, administration site skin reaction, acute liver injury, chest pain, hemorrhage (bleeding), dyspnea

(shortness of breath), tachycardia (fast heart rate), insomnia (sleep disorder), hyperthyroidism (overactive thyroid), muscular weakness, acute respiratory distress, hepatitis (inflammation of liver), inflammation of the lung (pneumonitis), facial pain, skin hypopigmentation (light patches of skin), inflammation of the pancreas, hepatic failure (liver failure), infusion related reactions (detailed below), and cytokine release syndrome (detailed below). Taking part in this research study may or may not make your health better. We hope the information learned from this study will benefit others with rectal cancer in the future. Information gained from this research could lead to better treatment of rectal cancer.

If you are interested in learning more about this study, please continue to read below.

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Todd Aguilera, MD PhD, Department of Radiation Oncology at the University of Texas Southwestern Medical Center.

Funding
Apexigen America, Inc., is funding a portion of this study. Apexigen America, Inc. is providing money to UTSW so that the researchers can conduct the study.

Conflict of Interest
There are no conflicts of interest to disclose.

If you require further information regarding the financial arrangements, you should discuss the matter with the Study Doctor and/or Principal Investigator.

Purpose – "Why is this study being done?"

You are asked to participate in this research study of newly diagnosed locally advanced rectal cancer. The overall goal of this study is to determine if the addition of sotigalimab, the study drug to FOLFOX (standard of care chemotherapy for this type of cancer) and short-course radiation therapy could improve response rates and long-term outcomes in treatment of locally advanced rectal cancer patients.

With the increasing incidence, decreasing age, and inadequate cure from definitive treatment there is a critical need for new approaches to rectal cancer to improve long term survival. Sotigalimab has shown promise when used as a single agent as well as in combination with other chemotherapeutic agents in advanced solid tumors. Therefore, researchers hope to learn if radiation and chemotherapy when combined with sotigalimab could overcome the limited response observed after chemoradiation in rectal cancer. Our approach on this study involves treatment with short-course radiation therapy followed by FOLFOX chemotherapy which is then followed by definitive total mesorectal excision with the addition of sotigalimab at the end of the radiation course and after the first two cycles of chemotherapy. If efficacious, the treatment would offer an opportunity to extend survival in rectal cancer.

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.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you have been diagnosed with locally advanced rectal adenocarcinoma.

How many people are expected to take part in this study?
There will be a total of 58 people participating in this research study. This study also is taking place at a number of other medical facilities across the United States. UT Southwestern Medical center and its affiliates plans to enroll 35 participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will receive 5 fractions of radiation therapy which is followed by 6 cycles of mFOLFOX chemotherapy. Participants randomized to Arm 1 will receive the study drug, sotigalimab, on day 3 of radiation and on day 3 of cycle 1-5 of mFOLFOX chemotherapy. Ideally the clinic visit and all the study requirements should be performed on Day 1 of each cycle, but may be performed within 5 days before or after that day. Each cycle is 14 days. After completing the last planned dose of mFOLFOX, participants will be considered off-protocol directed therapy and undergo planned total mesorectal excision and adjuvant chemotherapy up to 6 months total therapy per institutional standards, and proceed to the follow-up portion of this study. You will be followed every 3-6 months per standard of care after discontinuing protocol-directed therapy or up to 3 years after last dose of study treatment. Study visits will occur 3 months (± 1 month) after surgery and then yearly after completion of treatment up to 3 years (± 3 months for study visits). Participants that discontinue their study therapy due to progression, refusal, intolerable toxicity, or desire for alternative non-protocol therapy or other trials will be followed for disease status (up to 3 years after the last dose of study drug± 1 month).

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. Many of the procedures are

described below as "**standard care**" and would be done even if you do not take part in this research study. You will be told which ones are for "**research only**".

Screening Procedures

- Informed consent **(research only)**
- Eligibility criteria **(research only)**
- Physical exam with vital signs (temperature, pulse, respiration, blood pressure, height and weight) and medical history
- Demographics information: age, gender, race, ethnicity
- Concomitant medications
- Endoscopy
- MRI pelvis
- CT CAP or PET-CT
- ECG
- Lab (CBC, CMP, CEA)
- Disease assessments
- Performance status
- Pregnancy Test, If you are capable of becoming pregnant, a pregnancy test will also be done before you receive study treatment.
- Quality of life questionnaires **(research only)**
- Toxicity assessment **(research only)**
- Tissue collection **(research only)**
- Research blood collection **(research only)**
- Stool collection **(research only)**

Baseline/screening evaluations are to be conducted within 45 days of randomization. The research procedures will add approximately 45 minutes to the length of a routine care visit.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you and will discuss other possible options.

Assignment to Study Groups –

When it is determined that you are eligible for the study, you will be assigned by chance (like flipping a coin) to one of two study groups: Arm 1 or Arm 2

You will be randomized in a 3:2 ratio to the experimental arm (Arm 1 – sotigalimab) or the comparator arm (Arm 2). Randomization to treatment assignment should occur following the completion of all screening assessments and after confirmation of your eligibility.

Study Procedures - as a participant, you will undergo the following procedures:
Prior to the start of your treatment, a Planning CT Scan will be performed which provides accurate images for your Radiation Oncologist to help plan how to treat your tumor. This is the same Planning CT Scan that you would get if you were not involved in this research study.

Starting on Day 1, all study participants (both Arm 1 and Arm 2) will undergo treatment with short-course radiation therapy comprised of 5 Gy per day for 5 consecutive days (i.e., 5 Gy x 5 fractions). Approximately 14 after the last dose of planned RT, all participants will receive up to 6 cycles of a modified FOLFOX (mFOLFOX) regimen (given every other week). Each mFOLFOX treatment cycle consists of oxaliplatin 85 mg/m2

(intravenous [IV]) with leucovorin 400 mg/m2 IV over 2 hours, fluorouracil (5FU; IV bolus 400 mg/m2) () and 5FU 2400mg/m2 infusion over 46 hours all given/started on Day 1 (Table 1). At the completion of the planned mFOLFOX regimen, participants will be considered off-protocol directed treatment and proceed with subsequent total mesorectal excision (removal of a significant length of bowel around the tumor) and adjuvant chemotherapy up to 6 months total therapy, per institutional standards.

A. Arm 1

Starting on Day 3 of short-course radiation therapy, participants will receive a single dose of sotigalimab. On Day 3 of Cycles 1-5 of each mFOLFOX treatment, participants will receive another dose of sotigalimab. In Cycle 6, participants will receive only mFOLFOX. After completing the last planned dose of mFOLFOX, participants will be considered off-protocol directed therapy and undergo planned total mesorectal excision (removal of a significant length of bowel around the tumor), per institutional standards and adjuvant chemotherapy up to 6 months total therapy, and proceed to the follow-up portion of this study.

B. Arm 2

Participants randomized to Arm 2 will receive short-course radiation therapy and mFOLFOX regimen, except that participants will not receive any of the study drug. After completing the last planned dose of mFOLFOX, participants will be considered off-protocol directed therapy and undergo planned total mesorectal excision (removal of a significant length of bowel around the tumor), per institutional standards and adjuvant chemotherapy up to 6 months total therapy, and proceed to the follow-up portion of this study.

The following procedures will be done during treatment:

- Medical history and physical exam with vital signs
- Labs (CBC, CMP, CEA)
- Endoscopy (if biopsy is collected)
- Tissue collection **(research only)**
- Research blood collection **(research only)**
- Stool collection **(research only)**

Treatment will be given on an outpatient basis. This means that you will not have to stay in the hospital overnight.

Table 1. Summary of Study Regimen

Drug	**Dose**†	**Route**‡	**Dosing Interval**	**Cycle Length**	**Planned Duration**
APX005M/ sotigalimab*	0.3 mg/kg	IV over 1 hour	Day 3 of radiation, and Day 3 of Cycles 1-5 of chemotherapy	Every 14 days	6 doses
Oxaliplatin**	85 mg/m^2	IV over 2 hours (up to 6 hours is allowed)	Day 1 of each cycle		6 cycles
Leucovorin**	400 mg/m^2	IV over 2 hours (can be infused with oxaliplatin)	Day 1 of each cycle		

5-FU**	400 mg/m^2	IV bolus recommended over 2-4 minutes immediately following oxaliplatin/leucovorin infusion	Day 1 of each cycle		
5-FU**	2400 mg/m^2	Continuous infusion through portable infusion pump over 46 hours following 5FU bolus injection	Day 1 of each cycle, given over 46 hours		

† Other standard-of-care FOLFOX regimens are permitted at the discretion of the investigators
‡ Infusion times and schedule may be changed per institutional guidelines and patient scenario
** Pre-medication may be changed per institutional guidelines and patient scenario. Recommended premedications for mFOLFOX include:
- Fosaprepitant 150mg IV 30 minutes before chemotherapy
- Ondansetron 8mg IV once 30 minutes before chemotherapy
- Olanzapine 5mg PO once before chemotherapy then 5mg qhs days 2-5
- No ice chips or iced drinks/food allowed

You will have an MRI of your tumor. For this procedure, you will lie still on your stomach inside a large, doughnut-shaped magnet, also called the MRI scanner. The MRI technologist can see and hear you during the procedure. You will also be given a squeeze ball to use for communication. You will be inside the MRI scanner for approximately 60 minutes. You will complete an MRI for study eligibility and may be asked to complete another one at least four weeks after the last chemotherapy cycle.

For the MRI procedure, you may receive a contrast agent. The contrast is used to highlight organs or tissues during imaging. For administration of the contrast, an intravenous catheter will be placed in your arm or hand. You will also have a blood test to measure your kidney function. For this test, approximately one teaspoon of blood will be drawn from your arm or hand.

Please let your doctors and the researchers know if you have a known allergy to any type of contrast.

Follow-up procedures

Participants will be followed via medical charts after completion of study therapy. Additional radiology reports, clinic evaluations, surgery reports, and pathology reports may be collected. Additional telephone and electronic communications may be required for study-related issues that may have arisen since study treatment ended. Participants will be followed every 3-6 months per standard of care after discontinuing protocol-directed therapy or up to 3 years after last dose of study treatment, whichever occurs first. Study visits will occur 3 months (± 1 month) after surgery and then yearly after completion of treatment up to 3 years (± 3 months for study visits). Participants removed from protocol therapy for unacceptable AE (s) will be followed until resolution or stabilization of the AE.

Participants that discontinue their study therapy due to progression, refusal, intolerable toxicity, or desire for alternative non-protocol therapy or other trials will be followed for disease status (up to 3 years after the last dose of study drug ± 1 month).

It is recommended per NCCN guidelines that patients undergo H&P and CEA every 3-6 months for the first two years then every 6 months for 5 years. In addition, for stage II and III patients Imaging should occur every 6

months (± 1 month) from the last scan for 2 years then yearly up to 5 years. Visits can be synchronized to last imaging interval but yearly study visits should be within the window specified.

The following procedures will be done:

- Medical history and physical exam with vital signs
- Performance status assessments
- CT CAP or PET-CT
- Lab (CBC, CMP, CEA)
- Quality of life questionnaires **(research only)**
- Adverse event evaluation **(research only)**
- Tissue collection **(research only)**
- Research blood **(research only)**
- Stool collection **(research only)**

Sample Blood and Stool Collection for Correlative studies

As part of this research study, the researchers would like to take extra blood and stool samples from you for correlative studies. It is entirely up to you whether you donate these extra samples or not. You can still take part in this research study, even if you do not agree to donate these extra samples.

If you agree, we will take approximately 50 mL (about 10 teaspoons) at each visit. We will also collect stool using a standard at home stool collection kit. This will include at the time of radiation simulation pretreatment baseline, prior to sotigalimab infusion on day 3 of radiation, after radiation therapy, prior to each cycle of mFOLFOX chemotherapy, on the day of surgery, and 3 months after completing treatment. The research using your blood will look at your immune cells and circulating antigen, DNA, or tumor cells and compare it with some or all your personal information collected in this research study. Stool will be collected for exploratory studies that aim to associate the microbiome with therapeutic response to treatment. This testing may help us to understand diseases better. It may help find better ways of diagnosing diseases, or may help to choose the right medicines for different people.

The primary storage of blood samples will be at Dr. Todd Aguilera Lab in UTSW Medical Center. Your blood sample will de-identified with a study number and collection date.

If you decide to stop taking part in the study please tell the Study Doctor if you want to change your mind about using donated sample(s). If you change your mind after a sample has been taken but before your blood or stool sample has been tested, the Study Doctor will arrange for it to be destroyed.

I agree to donate extra blood samples. *Yes* ☐ *No* ☐

Patient Initials: _____ *Date:* _____

I agree to donate stool samples. *Yes* ☐ *No* ☐

Patient Initials: _____ *Date:* _____

Tumor biopsies for additional study research
These samples may be used to characterize cellular and molecular disease status of the rectal cancer and microenvironment. It is entirely up to you whether you donate these extra sample(s) or not. If you agree to donate extra sample(s), we will take tumor biopsies at the time of screening, approximately 14 days (+/- 7 days) after completion of radiation and prior to starting FOLFOX chemotherapy, and at the planned total mesorectal resection (removal of a significant length of bowel around the tumor). You can still take part in this research study, even if you do not agree to donate the extra biopsy samples. If you decide to stop taking part in the study, please tell the Study Doctor if you want to change your mind about using extra biopsy sample(s) for further research.

In addition to the tumor biopsies, we will take biopsies from normal tissue 2cm away from the tumor, and biopsies of the normal rectum. Our goal is to compare the pre and post treatment inflammatory response.

I agree to donate extra tumor samples for additional study research *Yes* ☐ *No* ☐

Patient Initials: _____ *Date:* _____

I agree to donate normal rectal tissue samples for additional study research *Yes* ☐ *No* ☐

Patient Initials: _____ *Date:* _____

Your tissue contains DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests. The testing on your tissue samples might include genetic testing called whole genome sequencing. Whole genome sequencing looks at all the known genes in your cells. This type of testing can provide useful information to researchers. It can also present risks if the test results became known to others, for example you could have problems with family members or insurance companies. There is also a risk that these test results could be combined with other genetic information to identify you.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your data and/or tissue samples.

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:
- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Risks – "What are the risks of participation in the research?"

Risks from the specific research procedures (drug(s), interventions, or procedures)
There are risks to taking part in this research study. One risk is that you may have side effects while on the study.

Many side effects go away shortly after the treatment is stopped (acute adverse events), but in some cases side effects can be serious, long-lasting, or permanent (chronic adverse events). It is also possible that your cancer may not respond to radiation therapy or could return after you have completed your treatment and may require additional treatment. It is also possible that side effects from the study treatment may result in a delay of your surgery.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to each your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

The majority of side effects reported by patients have been mild to moderate in severity and reversible. Since sotigalimab is an agent designed to stimulate the body's inflammatory immune response that may help the immune system to attack your cancer, some side effects may be similar to symptoms seen when your body is fighting an infection. Below is a list of side effects that have been reported in patients treated with sotigalimab alone or in combination with other agents. Some of the side effects were also reported to be related to other agents using the combination treatment such as chemotherapy or immunotherapy agents approved and used as standard of care for underlying cancer. If your treatment includes a combination of sotigalimab with an agent not previously examined, other side effects not reported here may occur.

Side effects observed and considered possibly related to Sotigalimab:

Side effects seen in more than 20% of patients:

- Fever
- Chills
- Fatigue
- Nausea (feeling sick to your stomach)
- Pruritus (itchy skin)
- Abnormal liver function as seen on blood tests (transaminases [ALT and/or AST]) increased in blood
- Vomiting

Side effects seen in >10% to 20% of patients:

- Infusion-related reaction (see details below)
- Rash
- Headache
- Diarrhea
- Asthenia (lack of energy or strength)

- Decreased appetite
- Blood gamma-GT increase
- Cytokine release syndrome (see details below)

Side effects seen in >5% to 10% of patients:

- Blood alkaline phosphatase increased
- Anemia (low red blood cells which may make you feel tired or short of breath)
- Hypotension (low blood pressure)
- Dyspnea (shortness of breath)
- Hypertension (high blood pressure)
- Arthralgia (joint pain)
- Blood bilirubin increased
- Myalgia (muscle pain)
- Flushing
- Thrombocytopenia (reduction in the number of blood cells called platelets that may result in bruising or bleeding)

Side effects seen in >2% to 5% of patients:

- Tachycardia (fast heartbeat)
- Abdominal pain
- Amylase increased (increased levels of amylase in blood)
- Cough
- Lipase increased (increased levels of lipase in blood)
- Weight loss
- Constipation
- Dizziness
- Dysgeusia (changes in taste)
- Influenza-like illness
- Urticaria (hives)
- Malaise
- Lymphopenia/leucopenia/ (low white blood cell count)

Other Important Serious Side Effects seen in less than 2% of patients:

- Inflammation of pancreas (<0.4%)
- Hepatic failure (<0.4%)

Infusion Related Reaction/Cytokine Release Syndrome:

Certain side effects with sotigalimab have been observed either during the infusion or within 48 hours after the infusion. Study doctors have reported some of these side effects or combinations of them as infusion-related reactions or cytokine release syndrome.

An infusion-related reaction (IRR) is a type of hypersensitivity (or immune) reaction that can develop during or shortly after administration of a drug. Signs and symptoms may include itching, hives, fever, rigors/chills, sweating, difficulty in breathing, and (if severe) collapse.

Cytokine release syndrome (CRS) is an acute systemic inflammatory syndrome due to release of chemicals within the body that causes fever and other symptoms and can occur, for example, with therapeutic antibodies like sotigalimab. It can develop during the infusion or may occur later (usually not later than 24 hours after the infusion). It can be difficult to determine whether a patient is experiencing an IRR or a CRS. Patients who were

reported to have experienced CRS after sotigalimab infusion had symptoms including chills, tiredness, rigors, fever, rash, nausea, diarrhea, headache, cough, joint pain, rash, vomiting, muscle aches, back pain, fast heart rate, shortness of breath, and low blood pressure. Some of these patients who experienced CRS with sotigalimab had serious symptoms and had to be treated with medications or even admitted to the hospital until the symptoms resolved. In its most severe form, CRS may be fatal, however no fatal case of CRS has been observed with sotigalimab.

Your study doctor will give you certain medications prior to the infusion to lower the risk or severity of these possible side effects (called premedication). You will be carefully monitored for these potential side effects by your study team during the infusions and for at least 4 hours following the first 2 infusions. If you suspect you are experiencing IRR or CRS, inform your study doctor immediately.

Abnormal liver function - transaminases and bilirubin increase:

Transient elevations in liver enzymes (transaminases [AST, ALT]) and less frequently in bilirubin in the blood were observed in patients after receiving sotigalimab infusion, especially in those patients with preexisting liver metastases. These events were generally mild to moderate in severity and resolved to baseline by the time of the next infusion.

Two serious events of hepatic failure (identified by high liver enzymes in blood) were reported. One patient had metastatic pancreatic cancer with extensive liver metastases who received sotigalimab in combination with chemotherapy, experienced liver abnormalities, and later died. The events were complicated by the presence of extensive metastases and recent treatment with chemotherapy known to have potential liver toxicity. A second case occurred in a patient with a brain tumor who develop cytokine release syndrome and liver abnormalities. In this case, the liver dysfunction was transient (resolving in days) and the subject recovered. In all cases the cause of the liver failure remained unclear.

Your liver function will be carefully monitored by your study doctor, and if necessary, the study drug may be held and/or dose reduced.

Decrease in platelets and white blood cells:

Several patients experienced reductions in their blood cell counts, particularly in platelets (which may increase your bleeding risk) or in a type of white blood cell called lymphocytes (which may increase your risk of infection). These changes were generally mild or moderate and resolved usually within a week or two. Your blood counts will be monitored carefully by your study doctor, and if needed, study drug will be held and/or dose reduced.

For more information about risks and side effects, ask one of the researchers or study staff.

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Risks of FOLFOX chemotherapy

FOLFOX chemotherapy is used in many gastrointestinal cancers. The most commonly used regimen in the US is modified FOLFOX, which consists of oxaliplatin, leucovorin, and FU.

Toxicities of oxaliplatin include:

- Peripheral sensory neuropathy (weakness, numbness, and pain from nerve damage, usually in the hands and feet)

- Diarrhea
- Stomatitis (inflammation of the mouth and lips)
- Neutropenia (low white blood cell count which can make it easier to become sick)
- Thrombocytopenia (low level of platelets which can make it harder for your blood to clot)
- Anemia (low red blood cell count which can make you feel tired)
- Nausea
- Increase in liver enzymes (which can indicate liver damage)
- Vomiting
- Tiredness

The most common toxicities of 5-FU are:

- Diarrhea,
- Hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)
- Mucositis (mouth blisters/sores)
- Neutropenia (low white blood cell counts)

The most common toxicities of leucovorin are:

- Stomatitis (inflammation of the mouth and lips)
- Nausea
- Leukopenia (low white blood cell counts)
- Diarrhea
- Vomiting
- Alopecia (loss of hair)
- Dermatitis (inflammation of the skin)
- Anorexia
- Fatigue
- Thrombocytopenia (low level of platelets which can make it harder for your blood to clot)
- Infection
- Constipation

Risks and side effects of Radiation Therapy for rectal cancer:

Short-Term Reactions

Common:
In 100 people, approximately 50 or more may have:
Tiredness
Burning on urination
More frequent urination
Cramping & diarrhea
Skin reddening and irritation
Decreased blood count

Rare:
In 100 people, approximately 10 or more may have:
Nausea

Extremely Rare:
In 100 people, approximately 5 or more may have:
Severe diarrhea and dehydration requiring hospitalization

Long-Term Reactions

Common:
In 100 people, approximately 50 or more may have:
Males: Sterility
Females:
Sterility
Menopause, if premenopausal
Decreased vaginal secretions

Uncommon:
In 100 people, approximately 25 or more may have:
Bowel spasms & diarrhea
Bladder irritation
Females: Scarring of vaginal wall
Males: Erectile dysfunction

Rare:
In 100 people, approximately 10 or more may have:
Bowel complications requiring surgical procedure
Pelvic and hip fractures

Extremely Rare:
In 100 people, approximately 5 or more may have:
Rectal or urinary bleeding requiring transfusion or surgery
Cancers caused by radiation

Risks of Radiation – Diagnostic Test
The radiation dose that you will get from diagnostic tests (such as CT scans) is medically indicated for your condition and it is the same that you would get if you were not involved in this research study.

Risks of Rectal Biopsy
Potential risks of the rectal biopsy include bleeding at the biopsy site, pain at the biopsy site, and bruising. Rarely, an infection may occur.

Risks of Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

For more information about risks and side effects, ask one of the researchers or study staff.

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Genetic Informational risks
This research study includes genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members.

Releasing this information to you could cause psychological distress, anxiety or family problems. Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information is released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study early, please discuss your decision with the principal investigator. The researcher may ask you to complete study withdrawal procedures at a final study visit. If a participant withdraws consent, they will be specifically asked if they are withdrawing consent to:

- All further participation in the study including any further follow-up (e.g., telephone calls)
- Withdrawal of consent to the use of their study generated data
- Withdrawal to the use of any biological samples

There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

Reproductive Risks

Concerns for sexually active men and women: Women should not become pregnant and men should not father a baby while taking part in this study because we do not know how the study drugs/procedures could affect a man's sperm (for some drugs/procedures, the concern may be that the sperm might be affected and in some cases, drugs could being carried by the semen into the vagina and cause harm) or a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant or if you believe your female partner has become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed. Participants who are sexually active with a non-sterilized male partner or partners of male participant must use highly effective method(s) of contraception for up to 90 days after last dose of study drug and 9 months after the last dose of oxaliplatin for females of reproductive potential. Males with female partners of reproductive potential must use highly effective method(s) of contraception for 6 months after the last dose of oxaliplatin. Highly effective methods of contraception for female participants or their male partner include:

1. Established use of oral, intravaginal, or transdermal combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation.

2. Established use of oral, injectable, or implantable progestogen-only hormonal contraception associated with inhibition of ovulation or permanent sterilization method (hysterectomy, bilateral oophorectomy, or bilateral salpingectomy. The participants of childbearing potential should start using these forms of birth control from time of enrollment and throughout the study period up to 90-days after completing on study therapy.

3. Placement of intrauterine device (IUD) or Intrauterine hormonal-releasing system (IUS)

4. Barrier methods of contraception: male condom with either cap, diaphragm or sponge with spermicide (double barrier methods). The use of double barrier methods should always be supplemented with the use of a spermicide. Female condom and male condom should not be used together.

5. Vasectomized partner: Provided the partner is the sole sexual partner of the FOCBP trial participant and that the vasectomized partner has received medical assessment of the surgical success.

6. Sexual abstinence: Refraining from heterosexual intercourse during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and with the preferred and usual lifestyle of the participant. Periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of birth control

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the treatment might affect a developing fetus. We will do a pregnancy test before you start treatment to make sure you are not pregnant.

If you or your partner become pregnant during your participation in this research study or within 120 days of the last dose of study drug, please inform your treating physician immediately. If you become pregnant during the study, we will ask to follow your pregnancy, and to follow your newborn baby for at least 8 weeks. Information about the pregnancy and the newborn baby will be collected and communicated to the UTSW research team and Apexigen America, Inc. The identity of the mother and her child will remain confidential.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs/procedures might have on their breast milk.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section “Contact Information” for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – “How could you or others benefit from your taking part in this study?”

You may not receive any personal benefits from being in this study. We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

There are other options available to you. Your other choices may include:

- Standard radiation treatment
- Chemotherapy
- Surgery
- Palliative/Comfort Care
- No treatment

Payments – Will there be any payments for participation?

You will receive no payments for participating in this trial.

Costs – Will taking part in this study cost anything?

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as supportive care, clinic visits and exams, CT scans and MRIs, radiation and chemotherapy treatment. It is important to understand that some insurance companies do not cover some costs (for example, approved drugs used in a way different from the package instructions). If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

The sponsor will provide the study drug at no cost during this study.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

How will my information and/or specimen & tissue samples be used?
With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies.

By agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators and commercial companies for future research studies and/or analysis without additional consent from you. Your samples may be stored for up to 25 years. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your research samples may be used for future research studies including genetic analyses to identify the genetic characteristics and markers of both your tumor and normal tissue. These samples may also be used to characterize the molecular and cellular properties of your immune response to the study treatment.

There will be no direct benefit to you from allowing your data to be collected kept and used for future research. However, the data collected and generated will contribute to the advancement of science and understanding of health and disease. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include: your medical history and demographics, information that is created or collected during your participation in the study including medical and treatment history, information you give us during your participation in the study such as during interviews or from questionnaires, results of blood tests; demographic information like your age, marital status, the type of work you do and the years of education you have completed.

We will get this information by you, your doctor(s), and/or looking at your chart from the University of Texas Southwestern and/or Parkland Health and Hospital System.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- Apexigen America, Inc. is helping fund the study and providing the drug. They will receive written reports about your participation in the research. They may look at your de-identified health information to assure the quality of the information used in the research.
- The company, Apexigen America, Inc., makes the study drug.
- The following collaborators at other institution that are involved with the study: Adel Kardosh, MD and his team for Division of Hematology and Oncology at Oregon Health & Science University
- The Simmons Comprehensive Cancer Center Data Safety Monitoring Board: the committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason.
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Research offices at the University of Texas Southwestern Medical Center, Parkland Health and Hospital System.
- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group 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 when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of the University of Texas Southwestern Medical Center and Parkland Health and Hospital System for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties, but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to:

Todd Aguilera, MD, PhD
Department of Radiation Oncology
UT Southwestern Medical Center
2280 Inwood Rd
Dallas, TX 75390
Tel: 214/645-8525

If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

How long will your PHI be used?
By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends, and all required study monitoring is over.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:

Dr. Todd Aguilera, MD, PhD can be reached at 214-645-8525 during regular business hours and at 214-645-8525 after hours and on weekends and holidays.

If primary is not available, contact

The Radiation Oncology Clinical Research Office at 214-645-7322.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at 214-648-3060.

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

Printed Name of Participant	Signature of Participant	Date	Time AM PM
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time AM PM

Witness / Interpreter Signature Section

Interpreter/witness (Interpreter signature required per hospital policies when physically present.)

I attest that I have interpreted the information in this consent form and it was explained to, and apparently understood by the subject or the subject's legal authorized representative, and that informed consent was freely given by the subject or the subject's legally authorized representative as indicated by their signature on the associated **short form**.

Printed Name of Interpreter	Signature of Interpreter	Date	Time AM PM

Witness Signature (required when interpreter is not physically present-e.g., Language Line is used):

By signing below:

I attest that the information in the consent form was accurately explained to, and apparently understood by the subject or the subject's legal authorized representative, and that informed consent was freely given by the subject or the subject's legally authorized representative as indicated by their signature on the associated **short form**.

Printed Name of witness	Signature of witness	Date	Time AM PM

Blind or Illiterate Signature Section *At the time of consent, also complete this section if consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English (e.g., blind, physically unable to write, etc.)*

Declaration of witness:

By signing below, I confirm I was present for the entire consent process. The method used for communication (e.g., verbal, written, etc.) with the subject was: _____ .

The specific means (e.g., verbal, written, etc.) by which the subject communicated agreement to participate was: _____.

Printed Name of Witness	Signature of Witness	Date	Time AM PM