Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH:
A Phase IB/II study of ALT-803 in Combination with Nivolumab in Advanced Non-Small Cell Lung Cancer (NCSLC)

MUSC CTO 102323
MUSC PI: John Wrangle, MD

A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand.

The study drugs being looked at for this study are ALT-803 in combination with an approved drug called nivolumab. ALT-803 is made up of a type of substance normally found in our cells, called interleukin-15 (IL-15). It is made by certain white blood cells that help to fight infection and to kill cancer cells. This drug has been tested in animals and in a limited number of in people. The use of this substance in patients with non-small cell lung cancer (NSCLC) has not been approved by the United States Food and Drug Administration (FDA). It is experimental, but the FDA has given its permission for ALT-803 to be tested in this research study.

Nivolumab is approved by the FDA for your type of cancer. Combination therapies with nivolumab are commonly used to treat NSCLC. You are being asked to participate in this study because you have been diagnosed with NSCLC.

This study is divided into two phases. The Phase I portion has been completed and the best dose of ALT-803 and nivolumab has been determined. Now, researchers are accepting new patients for the Phase II portion. You are being asked to participate in the Phase II portion of this study. The goal of the Phase II portion of the study is to continue studying the safety and effectiveness of ALT-803 and nivolumab in NSCLC.

The study is sponsored by the Medical University of South Carolina (MUSC). The investigator in charge of this study is Dr. John Wrangle. Altor Bioscience Corporation (Altor) is supplying the drug ALT-803. Altor is also providing payments to MUSC and Dr. Wrangle to support activities that are required to conduct and manage the study. Dr. Wrangle also receives financial support from Altor to conduct other research projects. No one on the research team will receive a direct payment or an increase in salary for conducting the study.

Up to 70 people will be enrolled in the Phase II part of this study. MUSC will enroll about 21 participants.

B. PROCEDURES

If you agree to be in this study, the following will happen:

Before You Begin the Study:
You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to the study doctor.

- History and physical exam. Your doctor will also review any medications you are taking.
- Vital signs (heart rate, breathing rate, and blood pressure), weight
- Blood tests to look at blood cell counts (numbers of each type of blood cells), chemistries (elements and minerals in your blood), thyroid function and pancreatic function. You will also have a hepatitis B and C screening (if not done in the last two years). The amount of blood taken at this blood draw is about 20ml or 4 teaspoons.
- Serum pregnancy test for women who may be able to have children (about 5 mL or 1 teaspoon of blood)
- Electrocardiogram (EKG) to look at the electrical activity of your heart
- If you are a woman of childbearing potential or a man capable of fathering a child before, during, and/or after participation, use of an acceptable form of birth control is required. Examples of acceptable methods of birth control for participants involved in the study includes: birth control pills, patch, IUD, condom, sponge, diaphragm with spermicide, or avoiding sexual activity that could cause you or your partner to become pregnant.
- Radiographic scans using Computed Tomography (CT) scan (a series of images taken with x-rays), magnetic resonance imaging (MRI) or positron emission tomography (PET) scan of the chest, pelvis and abdomen. These scans will give a detailed picture of the areas of the body taken from different angles. The procedure for this is described below.

  A CT scan is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the patient table (usually on your back) inside of the CT machine. You should get comfortable because it is very important not to move during certain parts of the test.

  CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the technologist or from the machine about your breathing. Before or during the study, you may be given an injection of a

contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist. If your study doctor finds that you do not meet the specific eligibility requirements to be in this study, you will not be able to participate. You will continue to see your regular doctor who will discuss with you additional options for your disease.

MRI uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise.

A PET Scan is a diagnostic tool used to detect cancer and find out the cancer's stage (a way of describing where the cancer is located, if or where it has spread, and whether it is affecting the functions of other organs in the body).

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will be registered to the study and will begin study participation.

During the Study:

The study is divided into intervals called cycles. These cycles are made up of 6 weeks or 42 days. During the first 4 cycles, you will be given nivolumab and ALT-803. After the end of cycle 4, you will be given nivolumab only. The table below describes these drugs that will be given during the study.

Please also review the section of this consent called the "Required Correlative Research." In addition to the procedures above, additional blood draws will be required as outlined in that section.

Drug Name	How much?	How is it given?	How often?
Nivolumab	You will receive 240 mg	Nivolumab will be given by a needle in the vein (called *i*ntravenously, or IV) over about 30 minutes.	Every two weeks while you are on study.
ALT-803	You will receive 20mcg	ALT-803 will be injected under your skin or subcutaneously after nivolumab has been given.	For Cycles 1-4, you will get ALT-803 on the first day of each week during Weeks 1-5 of each cycle. You will not get ALT-803 on Week 6.

Cycle 1 (Nivolumab and ALT-803)

Day 1

- After ALT-803 is given you will be asked to stay at MUSC for up to 2 hours.

Day 1 of each week of Weeks 1-5:

- Physical exam. Your doctor will also review any medications you are taking and any side effects you may be feeling.
- At the beginning of each week, you will be given a diary to record any side effects you may be experiencing. You will be asked to bring this diary back at the beginning of the next week.
- Vital signs and weight
- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.
    - On day 1 of week 4, you will also have a blood test to look at your thyroid and pancreatic function (about 5mL or 1 teaspoon of blood)

Day 4 of week 1only:

- Blood test to look at your blood counts (2mL or about half a teaspoon)

End of cycle 1:

CT, MRI or PET scan of the chest, pelvis and abdomen

Cycle 2 (Nivolumab and ALT-803)

Day 1 of Weeks 1, 3, and 5:

- Physical exam. Your doctor will also review any medications you are taking and any side effects you may be feeling.
- At the beginning of each week, you will be given a diary to record any side effects you may be experiencing. You will be asked to bring this diary back at the beginning of the next week.
- Vital signs and weight
- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.

Day 4 of week 1only:

- Blood test to look at your blood counts (2mL or about half a teaspoon)

Day 1 of week 2 and week 4:

- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.
    - On day 1 of week 4, you will also have a blood test to look at your thyroid and pancreatic function (about 5mL or 1 teaspoon of blood)
- Side effect diary review

End of cycle 2:
CT, MRI or PET scan of the chest, pelvis and abdomen

Cycle 3-4 (Nivolumab and ALT-803)
Day 1 of Week 1:

- Physical exam. Your doctor will also review any medications you are taking and any side effects you may be feeling.
- Side effect diary review
- Vital signs and weight
- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.

Day 1 of weeks 2-5:

- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.
    - On day 1 of week 4, you will also have a blood test to look at your thyroid and pancreatic function (about 5mL or 1 teaspoon of blood)
- Side effect diary review

End of cycle 3 and cycle 4:
CT, MRI or PET scan of the chest, pelvis and abdomen

Each Additional Cycle (Nivolumab Only)
Starting with Cycle 5, you will receive nivolumab only every other week and you will have the following tests or assessments:

Week 1 Day 1:

- Physical exam. Your doctor will also review any medications you are taking and any side effects you may be feeling.
- Blood tests to look at blood cell counts, chemistries, thyroid function and pancreatic function. The amount of blood taken at this blood draw is about 15ml or 3 teaspoons.

Cycle 5 Week 5 Day 1 only

- Blood test to look at your blood counts (2mL or about half a teaspoon)

Every 6 weeks:
CT, MRI or PET scan of the chest, pelvis and abdomen

End of Study Visit
After you finish the study or if you discontinue the study early, you will be asked to return for an end of study visit and will have the following tests or procedures:

- Physical exam. Your doctor will also review any medications you are taking and any

side effects you may be feeling.
- Vital signs and weight
- Blood tests to look at blood cell counts and chemistries. The amount of blood taken at this blood draw is about 15mL or 3 teaspoons.
    - On day 1 of week 4, you will also have a blood test to look at your thyroid and pancreatic function (5mL or 1 teaspoon of blood)
- CT, MRI of PET scan of the chest, pelvis and abdomen

After the Study:
After you complete the end of study visit, you will enter a follow up period. The study team will follow your care by clinic visit, review of medical record and/or telephone call every 3 months during years 1 and 2 and every 6 months during year 3.

Withdrawal
Taking part in this study is voluntary. You do not have to be in this research study. You can agree to be in the study now and change your mind later. You may discontinue your study participation at any time. Your decision will not affect your regular care. It will not affect your getting all the care, medicine, and equipment you should be getting.

The study doctor, Altor or the FDA can take you out of the study at any time with or without your agreement. These decisions will be made if:

- It is in your best medical interests to stop your participation
- You do not follow instructions
- The study is canceled.

The doctor will explain the reasons for doing so and will help arrange for your continued care by your own doctor, if needed. If you leave the study for any reason you will be asked to have the procedures completed for the final visit.

If you cancel your permission after you have started in the study, the study staff and the study doctor will stop collecting your health information. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the study results. If you start the study and then cancel your permission, you will not be able to continue to participate in the study or receive any drug as part of the study. This is because the study staff and/or the Study doctor would not be able to collect the information needed to evaluate the study drug.

Required Correlative Research

Tumor Tissue Analysis

Researchers will look at the leftover tumor tissue (tissue not used for your diagnosis) from your original biopsy or surgery to do tissue analysis which may include genetic research. This genetic research will look at the DNA and other characteristics of your tumor. Your genes are made up of DNA. DNA is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. Researchers will look at changes to your DNA due to the tumor and other molecular features that may be in your tumor. This will help them see if there is a difference in how your tumor responds based on these features of your tumor. Research to identify genes that cause or contribute to a disease or trait is an increasingly important way to try to understand the role of genes in human disease.

Your study doctor may also ask you to participate in an additional tumor tissue collection study. If you are asked to participate in this tissue collection, you will be asked to sign a separate informed consent.

Blood Collection

One of the goals of the study is to look at how the combination of ALT-803 and nivolumab affect your cells in your body. To study this, researchers will look at blood collected at different timepoints during your study participation. These blood samples will show researchers how your cells and body absorb, process, and respond to the study drug. When these draws will take place and the amount of blood collected are described in this section. The amount of blood collected is in addition to the blood collected for the regular study blood tests.

When the research blood draw will happen	Amount of research blood collected
Cycle 1 Week 1 Day 1	7 teaspoons
Cycle 1 Week 1 Day 4	7 teaspoons
Cycle 1 Week 2 Day 1	7 teaspoons
Cycle 1 Week 3 Day 1	7 teaspoons
Cycle 1 Week 5 Day 1	1 teaspoon
Cycle 2 Week 1 Day 1	7 teaspoons
Cycle 2 Week 1 Day 4	7 teaspoons
Cycle 2 Week 3 Day 1	1 teaspoon
Cycle 3 Week 1 Day 1	7 teaspoons
Cycle 3 Week 2 Day 1	1 teaspoon

When the research blood draw will happen	Amount of research blood collected
Cycle 4 Week 1 Day 1	1 teaspoon
Cycle 5 Week 1 Day 1	7 teaspoons
End of Study	7 teaspoons

C. DURATION

It is estimated that the study visits will take 1-3 hours, depending on the clinic schedules. After your first dose, you will be asked to stay at MUSC for up to 2 hours after ALT-803 is given so that we can carefully monitor your body's functions and closely watch for potential side effects of the study drug on your body. You may be asked by the study doctor to stay longer than 2 hours if he or she thinks it is necessary.

You will come to clinic about once every week for the first 4 cycles (24 weeks) of the study. After the 4th cycle, you will come to clinic every two weeks for the rest of your time on study.

Your participation on study will likely last for at least 6 cycles (36 weeks). However, you may continue on the study as long as your doctor feels you are benefiting from the therapy and your cancer is not getting worse. You can stop participating in the study at any time for any reason.

D. RISKS AND DISCOMFORTS

While on this study, you are at risk for the side effects listed below. Not everyone will get these side effects. You may have none or several. Most people do not experience all of the side effects listed. A side effect may get worse through while on the study drug, or more side effects may develop as the longer you stay on study. This depends on your general health and the amount of the study drug you receive (the dose).

Many side effects are inconvenient but not damaging to your health. They are almost always reversible and usually go away shortly after study drug is complete. <u>However, some side effects are serious medical conditions that may cause your death or cause your condition to deteriorate.</u> The study doctor will closely monitor and treat/prevent the side effects you might have through the study period. Other drugs and procedures may be given to make side effects less serious and less uncomfortable.

After the study drug is given, you will be asked to stay at MUSC for up to 2 hours. This will allow the study doctor or study staff to carefully monitor your body's functions and to watch you closely for any side effects. If any severe side effects occur you may be admitted to the hospital for observation and/or treatment at the study doctor's discretion. If severe side effects occur, or if your condition deteriorates while you are on this study, your participation may be discontinued at the study doctor's discretion without your consent. You should discuss this with your cancer doctor, the study doctor and/or the study staff.

There may also be other side effects that we cannot predict. While on the study, we want you to talk to the study doctor or study staff about all your side effects so that they can help you manage them.

ALT-803

The study drug ALT-803 can cause many side effects which may be similar to the side effects of Proleukin® (IL-2). The side effects of Proleukin are reported below.

Most likely (greater than 10%):

- Weight gain: weight gain may occur which could be as much as 20 pounds of fluid over the course of receiving the study drug. This weight gain results in swelling in the arms and legs. This swelling can be treated with a medicine called a diuretic, which will cause you to have increased urination to remove the excess fluid.
- Shortness of breath: ALT-803 can cause fluid to collect in the lungs, which can cause shortness of breath. Shortness of breath is common and you may require oxygen during some portion of your study participation. Some subjects who have received ALT-803 have rarely required intubation (the insertion of a tube into the air passage) and the temporary aid of a breathing machine to assist breathing. Your lung function will be monitored while you are on this study.
- Anemia (a drop in the number of red blood cells made by your bone marrow): Anemia can cause you to feel tired; you may feel tired after you have stopped ALT-803, but most people find that their energy levels are back to normal from 6 months to a year after stopping this study drug. Blood transfusions may be used to correct the anemia, which can produce allergic reactions.
- Hypotension (drop in your blood pressure): you may be given fluids before, during and after receiving ALT-803 to help prevent this from occurring. This may also require the use of medicines called pressors to raise your blood pressure to a safe level. If the use of fluids cannot keep your blood pressure at a safe level at the time of the next scheduled injection of ALT-803, that injection will be skipped. If the symptom persists for more than 24 hours, you may not continue to receive the study drug ALT-803. In previous studies with a similar drug, called IL-2, this side-effect of low blood pressure was temporary and returned to normal after the drug was stopped. The drop in blood pressure may cause breathing difficulties, weight gain and swelling in your ankles, legs and face (edema) and/or a drop in the amount of urine you make. Very rarely there may be a need for hemodialysis, in which a machine substitutes for the kidneys because of decreased kidney function. On rare occasions swelling or decreased blood supply to the bowel occurs, which may result in bowel death or rupture.
- Flu-like symptoms: you may experience fever, chills, shaking, headache, stiffness, aching muscles and joints. These symptoms usually get better as your course of ALT-803 continues. The symptoms usually begin 2 - 4 hours after your injection and last for

about 12 hours. Rarely, some people have experienced high fevers. The fevers and flu-like symptoms can be controlled with acetaminophen and indomethacin, which are medicines given by mouth. You may also develop nausea, diarrhea, skin rash with itching, nasal congestion, and abnormalities in kidney and liver function. The fever, chills, shaking, nausea, diarrhea, and itching may be controlled with medicines given before, during and after receiving ALT-803.

- Increased risk of infection: this is due to a temporary drop in the number of white blood cells produced by the bone marrow. Having a low white blood count means that you are less able to fight infections. You may have headaches, aching muscles, cough, sore throat, pain passing urine or feel cold and have chills. During the study you will require a catheter or tube placed into a large vein in your chest or arm. In previous studies, there has been a 1 in 4 chance that infection will develop at that site, which would require removal of the catheter and treatment with antibiotics. Such infections can cause additional side effects leading to prolonged hospitalization, and at least 2 cases with IL-2 have been fatal. The use of antibiotics in all people receiving IL-2 has reduced the chance of infection to about 1 in 20. You will receive antibiotics if you have a fever.

  Infections can sometimes be life-threatening. You should urgently contact your study doctor if you think you have an infection.

- Bruising: this is due to a drop in the number of blood clotting platelet cells produced by your bone marrow. You may have lots of tiny red spots or bruises on your arms or legs.
- Nosebleeds, bleeding gums: if that happens you may receive a platelet transfusion.
- Skin rash, peeling skin, small blisters: you may have red, dry and itchy skin. Your skin may peel or you may have small blisters.
- Weakness, headache, dizziness
- Vomiting, nausea, loss of appetite
- Lowered levels of electrolytes (magnesium, potassium, phosphate, sodium and calcium) in your blood: these levels will be monitored by the study doctor and replacement drugs will be given if necessary.

Less likely (3-10% of subjects):

- Heart attack: some subjects have developed heart attacks during or shortly after receiving IL-2, a drug similar to ALT-803. In at least one case the heart attack was fatal with IL-2. The heart troubles are felt to be related to the added stress placed on the heart during the IL-2. Therefore, if you have any history of heart problems, be sure to tell your study doctor. Your heart function will be monitored during this study.
- Heart problems: sometimes the study drug ALT-803 can affect the way your heart works, causing low blood pressure, dizziness, chest pain or changes in heart rhythm (heart beat). These are quite uncommon and nearly always get better when ALT-803 has

stopped. If the abnormal heart rhythms continue, you will be treated with anti-arrhythmia medicines. You should tell your study doctor if you have had heart problems before or if you have any of these side effects.

- Pain and redness in the injection area.
- Altered blood tests: the study drug ALT-803 can raise the amount of chemicals called bilirubin and creatinine in your blood. Your study doctor will take regular blood tests to monitor this.
- Cough and shortness of breath
- Mouth sores.
- Confusion, depression and extreme sleepiness: this is more common in older people or those who have had depression before. Tell your study doctor if you have these symptoms.

Rarely (less than 3%):

- Allergic reaction
- Hair thinning

Nivolumab

Most Common (greater than or equal to 10% of subjects)

- Fatigue (50%)
- Lack of energy or feeling of physical weakness (19%)
- Buildup of fluids in the body (edema) (17%)
- Fever (17%)
- Chest discomfort and non-cardiac chest pain (13%)
- General pain (10%)
- Shortness of breath (38%)
- Cough (32%)
- Musculoskeletal pain (36%)
- Joint pain (13%)
- Decreased appetite (35%)
- Nausea (29%)
- Constipation (24%)
- Vomiting (19%)
- Diarrhea (18%)
- Abdominal pain (16%)
- Rash (16%)
- Itching skin (16)
- Weight loss (11%)
- Lung infection, including pneumonia (10%)

- Changes in blood chemistries, including liver functions (38%)
- Changes in blood counts (47%)

Less common (less than 10% of subjects)

- painful swelling and sores inside the mouth (stomatitis)
- Feeling of weakness, numbness and pain in the hands and feet (peripheral neuropathy)
- Bronchitis
- Upper respiratory tract infection
- Inflammation of the tissue in the lung (pneumonitis)
- Inflammatory reaction in the colon (colitis)
- Renal dysfunction caused by the kidneys not being able to remove waste and balance the fluids in the body.
- Changes in thyroid function
- Adrenal insufficiency which is a disorder caused by the adrenal glands not being able to produce enough hormones
- Inflammation of the middle layer of the eye (uveitis)
- Inflammation of the pancreas (pancreatitis)
- Weakness or partial loss of movement in the facial nerve
- A disease of the nervous system that can cause changes in sensation, movement, and cognition called demyelination
- Changes in functioning of the muscles, nerves or center that produces movement (motor dysfunction)
- Inflammation of the blood vessels that causes changes in the vessel walls.

Risks/Side Effects from Insertion of a Peripheral/Central Venous Catheter/Port

Risks associated with venous catheters are not likely but may occur. These risks include infection and bleeding. Rarely, perforation of the lung may occur during the insertion of the catheter. The risks associated with this procedure will be reviewed in detail with you by the individual who places the catheter.

Reproductive Risks

The study drug ALT-803 may pass the placenta and be secreted in milk, and may be harmful to fetal and infant development. Therefore, breast-feeding and pregnant women are not allowed to take part in the study. If you are pregnant or become pregnant, there may be risks to the embryo or fetus that are unknown at this time. If you are a woman of childbearing potential, a blood pregnancy test will be done, and it must be negative before you can enter this study.

You should not nurse your baby while on this study. There have been no studies conducted assessing the effect of the study drug on fertility. If sexually active, you, either male or female, must agree to use effective contraceptive measures for the duration of the study. Ask the study doctor about counseling and more information about preventing pregnancy. If you or your partner does become pregnant during this study, you must inform your study doctor immediately.

Risks/Side Effects from Blood Draws
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely.

CT Scan
The CT scan used to measure the tumor size will expose you to some radiation. Although the radiation from each scan is within acceptable limits, these exposures add up over one's life. The amount of radiation, you will be exposed to is relatively small. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you have already had many x-rays, you should discuss this with the researchers before agreeing to be in the study.

A contrast dye may be used in order to help your organs show up in the scan. If used, the contrast dye will be injected into your vein to assist your study doctor and site staff in viewing the scan. One risk associated with contrast dyes include excessive scarring of the skin tissue, joints, eyes and internal organs. Such scarring is called nephrogenic systemic fibrosis and is particularly hazardous for patients with pre-existing kidney problems. Other risks include itching or irritation at the injection site and possible allergic reactions. Your study doctor will discuss this with you.

MRI Scan
There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from participation in this research study. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner. Please inform the study staff if you have a history of claustrophobia (extreme anxiety in close spaces). This may also be a contraindication to participation in the study.

PET Scan
During the PET scan you will be exposed to a small amount of radiation, which is injected into the blood. Risks may include allergic reaction to the radiation injection.

EKG
The EKG procedure may cause some mild discomfort during the placement and removal of the leads to and from the skin. You may also experience some local irritation, redness, or burning in the areas where the leads are attached.

Hepatitis screening
Per South Carolina law, if you test positive for Hepatitis B or C, the results of your test must be reported to the South Carolina Department of Health and Environmental Control.

Loss of confidentiality
There is a risk of loss of confidentiality since medical records will be reviewed during this study.

Unknown risks
The experimental study drug may have unknown side effects. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Recovery from the Side Effects

- You will usually be discharged from MUSC on the drug infusion days. You may be required to stay longer depending on your condition.
- You may feel very fatigued after receiving the study drug with your energy returning day by day. Any water weight gained while on study drug should come off rapidly. Your appetite is likely to be poor at first, and nausea may alternate with hunger. Expect this to be much better within a few days.
- You should feel much better overall within a week to ten days and you should be back to normal within a few weeks after you have stopped the study drug.. If you experience itching and peeling, this may be one of the last things to get better, along with gradually fading fatigue.

Genetic Research
Genetic research studies may present unique risks to human subjects and their relatives. These involve medical, psychosocial and economic risks, such as the possible loss of confidentiality (private information), loss of insurability and employability, paternity, and social stigmas. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members. Genetic research raises difficult questions about informing you and other subjects of any results, or of future results. Some people feel anxious about the possibility of having a defective gene that would place them or their children at risk. Some people want to know what is found out about them; others do not. The risks of knowing include anxiety and other psychological distress. The risks of not knowing what is found include not being aware if there is treatment for the problem being studied. But these risks can change depending on whether there is a treatment or cure for a particular disease and on how clear the results are. If there is a medical reason to seek specific information from you, your doctor will tell you this. A process called "genetic counseling" is often appropriate in such cases; you should ask your doctor or nurse about this if you have any questions.

South Carolina law mandates that your genetic information obtained from any test or from this research, be kept confidential. Our state law prohibits an insurer using this information in a discriminatory manner against your or any of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then we must take all steps to protect your identity. You will still be responsible for paying for health care, however. The Medical University of South Carolina will not be responsible for such costs, even if care is

needed for a condition revealed during research or clinical testing.

GENETIC INFORMATION NONDISCRIMINIATION ACT (GINA)

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 making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

E. BENEFITS

If you agree to take part in this study, there may or may not be direct medical benefit to you. Your participation in this study may provide important information regarding the study drug and that may lead to future clinical studies. Other patients with cancer may benefit in the future.

F. COSTS

You and/or your insurance company will be billed for the clinic visits, all standard laboratory tests (e.g. routine blood counts and blood chemistry tests) and the standard drug nivolumab. Some health plans will not pay these costs for people taking part in studies. Check with your insurance company to find out what they will pay for, as if they refuse to pay you will be held financially responsible.

The drug ALT-803 will be supplied free of charge by Altor. The following procedures are not considered standard of care and will be paid for by the study:

- Observation period after ALT-803
- EKG
- Blood samples for research purposes
- Blood tests looking at your thyroid and pancreatic function

Please ask Dr. John Wrangle if you would like to know more about which tests and studies are being done solely for research purposes.

G. PAYMENT TO PARTICIPANTS

You will not be paid for participating in this study.

H. ALTERNATIVES

Instead of being in this study, you have these options:

- Treatment with other immune-based or chemotherapy drugs.
- Treatment with other investigational drugs.
- No therapy at this time with comfort care only.
- Comfort care is not directed at curing, slowing, or reversing your disease. Comfort care is directed only at reducing symptoms, controlling pain, relieving suffering, maximizing comfort and maintaining the dignity of you and your family.

Please talk to your doctor about these and other options. Please ask any questions you may have and take as much time as you need to make your decision.

I. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

J. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

K. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

L. CLINICAL TRIALS.GOV

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.

M. SPONSOR COMMITMENT

If you become ill or get an injury or illness as a result of study medications, you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

If you have an injury or illness from the study medication or procedures required for this study, the reasonable medical expenses required to treat such injury or illness will be paid for by the study sponsor. The coverage for such injury or illness is only available if the principal investigator and study sponsor have decided that the injury/illness is directly related to the study drug or study procedures and is not the result of a pre-existing condition or the normal progression of your disease, or because you have not followed the directions of the study doctor. You should check with your insurance company about any such payments.

The Sponsor will not provide compensation for lost wages or for any other damages, expenses or losses. Signing this consent form does not change any legal rights you may have.

N. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

____**Yes, I agree to be contacted**

____**No, I do not agree to be contacted**

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, employees of the sponsor, the FDA, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event of a study related injury, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you're are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. The data collected on you to this point remains part of the study database and may not be removed. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. John Wrangle at 843-792-4271. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, you should sign below.

Signature of Person Obtaining Consent	Date	Signature of Participant	Date