

CONSENT FOR CANCER RESEARCH

Project Title: CASE 3516: Phase II Evaluation of Nivolumab, an Immune Checkpoint Inhibitor alone or in combination with Oral Decitabine/Tetrahydrouridine as Second Line Therapy for Non-Small Cell Lung Cancer

Sponsor: Yogen Sauntharajah, MD, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195

Principal Investigator(s): Dr. Nathan Pennell

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC) and the National Institutes of Health (NIH).

Conflict of Interest Disclosure

Dr. Yogen Sauntharajah, the sponsor of this study and a Cleveland Clinic physician, is an inventor of the drug combination used in this study. In the future, he may receive royalties for sales of that product. He may benefit financially if this research is successful. These financial interests are being managed and are within permissible limits established by the local institutional Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask your study doctor or call the Cleveland Clinic Institutional Review Board at (216) 444-2924.

What is the usual approach to my Non-Small Cell Lung Cancer (NSCLC)?

Current treatment options for non-small cell lung cancer that has worsened after initial platinum based chemotherapy include second-line treatment with immunotherapy drugs like Nivolumab.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer. For example: comfort/palliative care

Why is this study being done?

The purpose of this study is to assess whether treatment with the study drug tetrahydrouridine-decitabine (THU-Dec) in combination with nivolumab is more effective than treatment with nivolumab alone in patients with NSCLC.

Decitabine is an investigational (experimental) drug that works by depleting DNA methyltransferase 1 (DNMT1). DNMT1 is an enzyme, or protein that causes chemical changes, often increased in cancer. Blocking DNMT1 has been shown to reduce tumor formation. Decitabine is experimental in this study because it is not approved by the Food and Drug

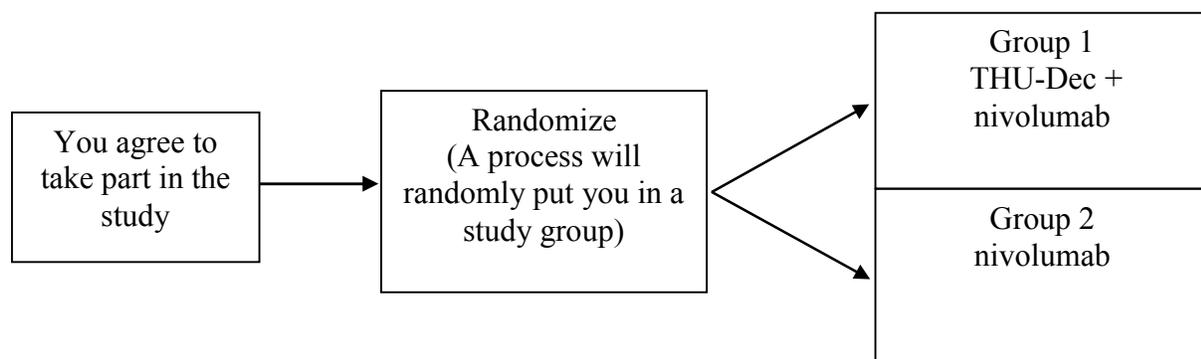
Administration (FDA) for patients with NSCLC. Decitabine is approved by the FDA for treating patients with a blood disease called myelodysplastic syndrome (MDS, a condition where the bone marrow does not make blood cells normally).

THU is an investigational (experimental) drug that works by blocking an enzyme that breaks down decitabine. So, THU will increase the time cells in your body are exposed to decitabine. THU is experimental because it is also not approved by the FDA, although it has been extensively used in clinical trials, including several cancer trials.

What are the study groups?

This study has two study groups. Group 1 will receive THU-Dec in combination with nivolumab and Group 2 will receive nivolumab alone.

A process (called randomization) will be used to assign you, by chance (like pulling your name out of a hat), to one of the study groups. Neither you nor your doctor can choose which group you are in. This is done by chance because no one knows if one study group is better or worse than the other.



How long will I be in this study?

You will receive the nivolumab with or without THU-Dec until your disease progresses or the study stops. After you finish treatment, your doctor will continue to watch you for side effects and follow your condition every 12 weeks. The study doctor may review your medical records, or contact you or your medical provider; you do not have to come to the clinic every 12 weeks.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there may be some extra procedures that you will need to have if you take part in this study.

Immunebiomarker tests determine if your body's immune system is mounting a response to the study drug. At Cycle 1 Day 1, Cycle 2 Day 15, Cycle 4 Day 15, Cycle 6 Day 15, Cycle 8 Day 15, and the first day of every cycle after Cycle 9 about 60 mL (approximately 4 tablespoons) of blood will be drawn for research purposes. At screening, Cycle 3 Day 1, Cycle 5 Day 1, and Cycle 7 Day 1, 32 mL (approximately 2 tablespoons) of blood will be drawn for research purposes. About 92 mL (approximately 6 tablespoons) of blood will be drawn at the end of treatment.

Research biopsies

Tumor biopsies will be done prior to study enrollment to check for a protein called PD-L1 (this is considered standard of care) however an additional research biopsy will be performed during Cycle 2 to help understand the effects of the drug on the tumor and the interaction with the immune system and to identify factors in the tumor that might influence tumors response or resistance to the drug. A tumor biopsy is the removal of a small piece of tumor using a needle biopsy typically using an ultrasound or a CT or a bronchoscope approach.

An optional biopsy at the time of cancer progression may be requested; the purpose of this is to determine reasons why the treatment is not working. You will be given more information about this optional biopsy and an opportunity to indicate your preference for participation at the end of this consent form.

Before you begin the study:

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there may be some extra exams and procedures that you will need to have if you take part in this study

Screening

Exams and tests will be used to determine your ability to participate in this study, after you sign this informed consent form. All evaluations must be completed within 4 weeks before the first dose of study treatment.

- Informed Consent (signing this form)
- ECOG Performance Status (this describes how well you are functioning in your daily activities)
- Height and Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Medical History
- Complete physical examination
- If you are a female who could become pregnant you will have a blood pregnancy test.
- Blood samples will be collected for safety and diagnostic tests.
- Tissue samples will be collected from a tumor biopsy
- CT scan of the chest, abdomen, and pelvis to measure the disease in your body. Magnetic Resonance Imaging (MRI) is also acceptable.

During the study the following will be additional research procedures:

If these tests show that you are eligible and you agree to participate in the study, you will come to the clinic for procedures described in the schedule of study visits and assessments listed below:

Treatment Period

- Treatment cycles are 28 days long. If you are randomized to Group 1 (THU-Dec + nivolumab), you will be asked to take your study medication two days in a row each week. On treatment dosing days, you should take your required number of THU oral capsules with or without food (as you wish). Then 60 minutes later, you should take your required number of Decitabine oral capsules with or without food (as you wish). A member of your study team will provide you with a diary to keep track of the days you

take your study medication. Please bring this diary with you to all scheduled appointments.

Cycle 1 Day 1

- ECOG Performance Status
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Directed physical examination
- Blood samples will be collected for safety and diagnostic tests.
- We will ask you about any side effects you may be having.
- Start treatment

Odd Cycles (1, 3, 5, etc) Day 15

- ECOG Performance Status
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Directed physical examination
- Blood samples will be collected for safety and diagnostic tests.
- We will ask you about any side effects you may be having.
- Continue treatment

Cycle 2 Day 1

- ECOG Performance Status
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Directed physical examination
- Blood samples will be collected for safety and diagnostic tests.
- Collection of tissue samples from a biopsy.
- We will ask you about any side effects you may be having.
- Continue treatment

Even Cycles (2, 4, 6, etc) Day 15

- ECOG Performance Status
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Directed physical examination
- Blood samples will be collected for safety and diagnostic tests.
- Blood samples will be collected for research purposes
- We will ask you about any side effects you may be having.
- Continue treatment

Odd Cycles (3, 5, 7, etc) Day 1

- ECOG Performance Status
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature
- Directed physical examination

- Blood samples will be collected for safety and diagnostic tests.
- Blood samples will be drawn for research purposes
- CT scan of the chest, abdomen, and pelvis to measure the disease in your body Magnetic Resonance Imaging (MRI) is also acceptable
- We will ask you about any side effects you may be having.
- Continue treatment

If your disease worsens or you no longer tolerate treatment, your treatment will be discontinued. If your disease progresses while you are on this study, you will be asked to have the following assessments

- Blood samples will be collected for research purposes
- Directed physical examination

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- The study drug may not be better, and could possibly be worse, than the usual approach for your cancer.

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

The possible side effects of decitabine listed below.

COMMON, SOME MAY BE SERIOUS
In 100 people receiving decitabine, more than 20 and up to 100 may have:
<ul style="list-style-type: none">▪ Slight decrease in the number of white cells (blood cells that fight infection)▪ Slight increase in the number of platelets (blood cells that form blood clots)▪ Testicular toxicity. Studies in animals suggest an effect on sperm counts even with low doses of decitabine. This toxicity appears reversible.

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving decitabine, from 4 to 20 may have:
<ul style="list-style-type: none">▪ Moderate decrease in the number of white cells (blood cells that fight infection)▪ Moderate decrease in the number of platelets (blood cells that help blood to clot)▪ Nausea▪ Changes in bowel habits (diarrhea or constipation)

RARE, SOME MAY BE SERIOUS
In 100 people receiving decitabine, 3 or fewer may have:
<ul style="list-style-type: none">▪ Infection. We will monitor your blood counts to avoid too low white cell counts; however, it is possible that an infection could result from a decreased white cell count.▪ Blood clots. We anticipate that your platelet count will increase with treatment. Platelets normally form blood clots when there is injury to prevent excessive bleeding. We do not think that this elevated platelet count will cause a blood clot inside your body, but this is a possibility that we cannot rule out.▪ DNA alteration. In test tubes, decitabine, like other chemotherapy drugs, sometimes alters the DNA (genetic roadmap) of cells. In theory, these changes have the rare possibility of leading to cancer.▪ Allergic reaction. Some people have allergic reactions to decitabine. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:<ul style="list-style-type: none">○ a rash○ hives○ having a hard time breathing○ wheezing when you breathe○ a sudden drop in blood pressure (making you feel dizzy or lightheaded)○ swelling around the face, mouth, lips, tongue, throat, or eyes○ a fast pulse○ sweating

Possible side effects of tetrahydrouridine

There have been no risks or side effects identified with tetrahydrouridine by itself. It has been used in other clinical studies in combination with other anti-cancer drugs, and no specific risks of tetrahydrouridine have been identified.

When tetrahydrouridine is taken together with other drugs, the risks resemble having more of the other drug it is being given with. In other words, the risks from taking tetrahydrouridine together with decitabine are the risks that would be expected from taking a higher amount of decitabine.

Possible side effects of nivolumab, which is the usual approach for this type of cancer:

VERY COMMON, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, more than 10 may have:
<ul style="list-style-type: none">▪ Fatigue▪ Rash

COMMON, AND SERIOUS

In 100 people receiving nivolumab, more than 1 and up to 10 may have:

- Abdominal pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- ALT increased: lab test result associated with abnormal liver function
- Amylase increased: lab test result associated with pancreas inflammation
- AST increased: lab test result associated with abnormal liver function
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased appetite
- Diarrhea
- Dry mouth
- Dry skin
- Fever
- Headache
- Lipase increased: lab test result associated with pancreas inflammation
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Itching
- Joint pain or stiffness
- Loss of color (pigment) from areas of skin
- Lung inflammation (pneumonitis - see details below)
- Musculoskeletal pain
- Nausea
- Shortness of breath
- Swelling, including face, arms, and legs
- Thyroid gland function decreased
- Thyroid gland function increased
- Thyroid stimulating hormone increased: lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Vomiting

UNCOMMON, AND SERIOUS

As few as 1 in 1000 people to as many as 1 in 100 people receiving nivolumab may have:

- Adrenal gland function decreased
- Allergic reaction
- Bilirubin (liver function blood test) increased
- Bronchitis
- Cranial nerve disorder
- Diabetes
- Dizziness
- Dry eye
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Increased blood sugar
- Inflammation of the eye
- Inflammation of the heart
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Liver inflammation
- Low blood pressure
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Redness
- Renal failure
- Respiratory failure
- Sodium levels in blood low
- Upper respiratory tract infection
- Vertigo
- Vision blurred

RARE, AND SERIOUS

As few as 1 in 10,000 people to as many as 1 in 1000 people receiving nivolumab may have:

- Anaphylactic reaction (severe allergic reaction)
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids and diabetic coma
- Erythema multiforme: skin inflammatory reaction
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of blood vessels
- Inflammation of the brain, potentially life-threatening or fatal
- Lung infiltrates, associated with infection or inflammation
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.

Lung Inflammation (pneumonitis): It is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported infrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.

Potential Risk or Discomfort from Research Procedures

Blood Draws

The insertion of the needle to draw blood is painful; however, the discomfort is usually brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Biopsies

Risks associated with biopsies include pain, redness, swelling, low blood pressure, excessive bleeding, bruising, or draining at the needle site, abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site. Two to 3% of patients require hospitalization after a tumor biopsy. Rarely, an infection can occur. Your doctor will determine the safest way of the biopsy. The procedure will be done using local anesthesia or sedation to minimize discomfort from the biopsy. The specific risks of the biopsy depend on the location and the type of biopsy and will be discussed by the physician performing the procedure.

Risks specifically associated with lung biopsy are pneumothorax (collapse of lung), air embolus (air in a blood vessel), hemopericardium (blood around the heart), and lung torsion (twisting that interrupts the blood supply to the lung). Sometimes you might cough up blood.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks:

THU-Dec

You should not get pregnant, breastfeed, or father a baby while in this study. The THU-Dec used in this study could be very damaging to an unborn baby. Decitabine caused harmful effects to offspring of exposed pregnant animals, although, the effects of decitabine to human mothers and their babies during pregnancy or breast feeding have not been formally studied. Since decitabine may affect the behavior of DNA in actively dividing cells, including the developing fetus, birth-control is necessary for the participants in this study and their partners. Taking decitabine may also involve unknown risks to a man or woman's ability to father a child or to become pregnant in the future.

Female Participants

Participating in this research may involve risks to pregnant women and/ or an unborn baby which are currently unforeseeable. To protect against possible side effects of the study drug, if you are pregnant or nursing a child you may not take part in this study. If you think that you have become pregnant during the study, you must tell the doctor immediately. If you become pregnant, your participation will be stopped.

If you are a female and you have child bearing potential, then you must agree to take important actions to avoid pregnancy during the study, from the time of agreeing to participate in this study by signing this informed consent form and during the duration of the study.

These actions are either:

- Not having heterosexual sexual contact beginning at the screening visit and continuing until 4 weeks after the last dose of decitabine/THU OR

- Using TWO (2) methods of birth control beginning at the screening visit and continuing until 4 weeks after the last dose of decitabine/THU:
 - One birth control method must be highly effective, such as an Intrauterine Device (IUD), birth control pills, depo-provera (medroxyprogesterone acetate) injections, or tying of the fallopian tubes.
 - The other additional effective birth control method can be use of a diaphragm or a condom by the male partner.

These steps must be taken even if you have a history of infertility, unless you have had a hysterectomy or have not had periods for at least 24 months.

Male Participants

Because decitabine has unknown effects to semen, you must agree to use a latex condom when engaging in any sexual contact with a woman of child-bearing age even if you have had a successful vasectomy.

Nivolumab

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments. Females should not breastfeed while receiving nivolumab and up to 5 months from the last dose of nivolumab. You must use an adequate method to avoid pregnancy for the duration of this study and for up to 5 months after the last dose of study drug. Male subjects who are sexually active with a woman of child bearing potential should also use an adequate method of birth control to avoid pregnancy of their partner for up to 7 months after the last dose of nivolumab. You should immediately contact your study doctor if there is a change in your method to avoid pregnancy or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

If you become pregnant, your participation will be stopped.

There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

The use of nivolumab in pregnant women has not been formally studied in clinical studies. One case has been identified of a nivolumab treated male patient with a female partner who became pregnant. The pregnancy was uneventful and at birth, the infant was slightly underweight.

In case of a pregnancy, your pregnancy and its outcome will be reported to the investigator/Sponsor and to Bristol-Myers Squibb.

You are asked to inform your study doctor if your partner becomes pregnant while you are enrolled in this clinical trial, and you and your partner will be asked to provide information about the pregnancy outcome.

What possible benefits can I expect from taking part in this study?

We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your cancer, which may give you relief from some symptoms, improve your quality of life or prolong your survival. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with NSCLC.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?

Your involvement in this research study is voluntary and you will not be paid for your participation.

The study agent, THU-Dec, will be provided free of charge by the study sponsor while you are participating in this study. Neither you nor your insurance provider will be responsible for the costs of any research-only tests or procedures. The blood work for research purposes will not be charged to you. It will be paid for by the research study. Neither you nor your health care plan/insurance carrier will be billed for the collection of the tissue that will be used for this study. Nivolumab will be supplied by Bristol Myers-Squibb for this study at no cost to you.

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study (i.e., medical history, review of medications, physical exams, performance status, routine blood tests, pregnancy test, x-rays and/or scans for tumor measurement). Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://www.cancer.gov/clinicaltrials/learningabout>.

What happens if I am injured or hurt because I took part in this study?

If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

If injury occurs as a result of your involvement in this research, medical treatment is available from Cleveland Clinic or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924.

Optional Biopsy at Disease Progression

If you choose to take part in this study and your disease progresses, you will be asked to have an additional, optional biopsy. This biopsy will be done to look at the progressing cancer tumor tissue more closely. Researchers hope this kind of *procedure* might one day be used to identify which patients are best suited for which cancer treatments by learning more about what happens to growing tumors after treatment with nivolumab with or without THU-Dec. The use of this tissue is still being tested and researchers do not know how accurate or useful it is.

The results of the biopsy would only be used for research and not to guide your medical care.

I agree to allow the biopsy at disease progression.

Yes _____ No _____ Initials _____

HIPAA AUTHORIZATION

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Nathan Pennell, MD, PhD and the research study staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition..

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record. In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Dr. Yogen Sauntharajah, study monitors and representatives
- Dr. Yogen Sauntharajah's collaborators and licensees
- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards
- Bristol Myers-Squibb

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Nathan Pennell, MD, PhD
Case Comprehensive Cancer Center
Cleveland Clinic
9500 Euclid Ave.
Cleveland, OH 44195

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Voluntary Participation

Your participation in this research study is voluntary. Choosing not to participate will not alter

your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Questions about the Research

If you have any questions, you can ask the Principal Investigator and/or research staff at (216) 444-8665.

Emergency or after-hours contact information

If you are a Cleveland Clinic patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

Where Can I Get More Information?

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, if applicable, 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.

Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

Signature of Participant

Date

Printed Name of Participant

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

Signature of Person Obtaining Consent

Date

Printed Name of Person Obtaining Consent