The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	A phase II, multi-cohort trial of combination nivolumab and temozolomide in recurrent/refractory small-cell lung cancer and advanced neuroendocrine tumors.
Principal Investigator:	Dwight Owen, MD, MS A450B Starling Loving Hall 320 West 10th Avenue Columbus, Ohio 43210, United States
Study-Related Phone Numbers:	614-685-2039 (office) 614-293-8000 (24 hours)
Sponsor:	The Ohio State University North American Neuroendocrine Tumor Society
Support:	Bristol-Myers Squibb Research and Development and Ono Pharmaceutical Co., Ltd

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

The purpose of this study is to evaluate the combination of nivolumab and temozolomide in treating patients with extensive stage small cell lung cancer and other neuroendocrine malignancies. Approximately 85 participants will take part in this study at Ohio State. Taking part in this research study may or may not make your cancer better. However, there is some evidence that your type of cancer might respond to the study drugs, nivolumab and temozolomide. If you are being treated for small cell lung cancer: instead of taking part in this study, you may be treated with other second line FDA-approved treatments such as topotecan. Topotecan is a form of chemotherapy that has been shown to shrink tumors in about a quarter (24%) of patients with small cell lung cancer. It is FDA approved for the treatment of small cell lung cancers in patients with chemotherapy-sensitive disease after failure of first-line chemotherapy.

If you are being treated for neuroendocrine tumor (NET): instead of taking part in this study, there are several FDA-approved therapies that you may receive as part of your treatment. These include (DOTATATE (Lutathera) in patients with gastroenteropancreatic NET, everolimus and sunitinib for patients with advanced progressive pancreatic neuroendocrine tumors; everolimus for lung or gastrointestinal NET. Patients with Grade 3 NET are usually treated according to guidelines for small cell lung cancer with platinum-based combination as their first treatment option.

Serious toxicities associated with nivolumab include pneumonitis (an inflammation of the lungs that causes shortness of breath), colitis (an inflammation of the bowel that causes abdominal pain and diarrhea) and hepatitis (an inflammation of the liver that can lead to liver injury). These risks are detailed later in this document. Serious toxicities associated with temozolomide include low blood counts which may lead to serious infection, rash which may be serious, serious allergic reactions, and cancers of the bone marrow.

1. Why is this study being done?

We are asking you to take part in this research study because you have been diagnosed with a type of cancer called either small cell lung cancer or neuroendocrine carcinoma, and your doctor believes that the combination of the study drugs nivolumab and temozolomide, might be useful in treating your cancer. Your doctor and researchers also want to find out if the combination of these two study drugs, nivolumab and temozolomide is safe and tolerable.

Nivolumab (Opdivo®) is a type of prescription drug that works with your immune system cells to fight cancer. Nivolumab is used to treat several different types of cancer, including types of lung cancer. Temozolomide (Temodar®) is a chemotherapy drug designed to combat cancer cells directly and is used to treat other types of cancer, such as small cell lung cancer and brain cancers. However, the use of these drugs in combination is investigational. Investigational means that it is not approved by the U.S. Food and Drug Administration (FDA).

2. How many people will take part in this study?

Approximately 85 participants will take part in this study at Ohio State.

3. What will happen if I take part in this study?

The study team will explain the research study and answer any questions you have about the study. If you want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins. Many of the procedures that will be performed during the study, including routine blood tests, tumor evaluations (radiology scans), physical examinations, heart tests (electrocardiogram), vital signs (blood pressure, heart rate, breathing rate, and temperature) and measurement of height and weight, would normally be done as part of your standard of care regardless of study participation. However, some of these may be done more frequently as a result of your participation in this study. Administration of the study drug combination, tissue and some blood sample collection and analysis are solely for research purposes. Tests and procedures that are done more often than your regular medical care because of your study participation and that are solely for research purposes will be identified below. The study staff will inform you of the types of tests and procedures you have to undergo during the study.

During the study you must:
• Follow the instructions you are given.
• Come to the study center for your visits with the study doctor.
• Tell the study doctor or study staff about any changes in your health and/or medications you are taking.
• Tell the study doctor or study staff if you want to stop being in the study at any time.

Study visits listed below may be done via Telehealth (phone call, email, video, etc.) at the discretion of the investigator to minimize exposure to healthcare settings during pandemics or national, state, or University-wide states of emergency.

If this occurs, you may still be required to be assessed in clinic by the study team, or by a local physician, at the discretion of your study doctor. This is to ensure your safety.

Before the study/Screening Phase:

- You will review this informed consent and will discuss the study with your doctor, his/her research staff and your family.
- You will sign this form prior to any study procedures.
- Your doctor and his/her research staff will review your medical chart to confirm that you are eligible for this study.
- Obtain a tissue sample from your previous biopsy or surgery

- **Treatment Phase:** You will receive the investigational drug combination of nivolumab and temozolomide.
    - Nivolumab will be given to you intravenously (infusion by IV) at Ohio State, once every four weeks.
    - Temozolomide will be given to you as capsules. Temozolomide is taken orally with a full glass (8 ounces or one cup) of water on an empty stomach, no food two hours before or one after dosing. Because temozolomide can sometimes cause an upset stomach, your study doctors will give you an anti-nausea medication (ondansetron) to take 30 to 60 minutes before you take the temozolomide. You will record your dosing with temozolomide in a medication diary every day that you take the medication.
    - Temozolomide is commercially supplied and will be billed through your insurance. Depending on what pharmacy your insurance authorizes, temozolomide will either be delivered to your home or you will pick it up from a specialty pharmacy. You should not take temozolomide until after you see your study doctor on Day 1 of each cycle and are instructed to start dosing. Please contact your study doctor if you have questions about when to take temozolomide.
    - Please bring your medication diary with you to your clinic appointments and give it to your study doctor when you see him/her at your next appointment. You will take the directed dose by mouth (swallow capsule), every day for 5 days in a row out of 28 days. Therefore there will be 23 days where you do not take any capsules before starting another round of treatment.
- Again, your doctor and his/her research staff will review your medical chart and assess your health.
    - General lab work, physical exams, vital signs, electrocardiograms
        - Electrocardiograms or ECG, is a test that records the electrical activity of the heart. Risk associated with this procedure are outlined below.
- Complete Pill Diary
    - You will receive a patient pill diary for you to record all the dates and times you take the temozolomide pill. The study team will go over the diary with you and will ask you to bring the completed diary back to the study site for review at each visit.
- Adverse Events Monitoring
    - You will be asked if any changes to your health have happened since you started the study or since your last visit. Your study doctor and researchers want to see if you have experienced any side effects that might be related to the study. If you feel unwell or experience side effects, they will be recorded.

- Tumor imaging/scans will be done to determine if your cancer is responding to the treatment.
- The FDA recommends checking a routine blood test 3 weeks after the beginning of each treatment cycle (ie day 22 of each cycle) for all patients treated with temozolomide so that your doctor can monitor your blood counts during treatment.
- Additional blood will be collected for research purposes only and will be done to perform biomarker testing. Blood will be collected to assess the immune composition of your blood, how it is affected by treatment, and whether changes in tumor DNA can be detected at baseline or during treatment. These tests may be "batched" so that they will be performed once a number of samples are available.
- A sample of a previously obtained tumor tissue (from prior surgery or biopsy) will be studied to learn about factors that may make you more or less likely to respond to the study treatment.

Post-Treatment/Follow-up Phase:

- A mandatory safety follow-up visit will be conducted approximately 30 days after your last dose of study drugs or before you start a new anti-cancer treatment (whichever comes first).
    - Again the study doctor or research staff will ask you if you have experienced any health changes or side effects.
- Other follow-up visits
    - These follow-up visits will occur about every 8 weeks after you stopped treatment. Your study doctor or research staff will ask how your general health is, your cancer status, and whether you have started any other anti-cancer treatments.
    - If your cancer comes back or gets worse while you are part of this clinical trial, or if you decide to start a new anti-cancer treatment you will be contacted by telephone about every 12 weeks by your study doctor or research staff to ask how you are doing.

4. How long will I be in the study?

The duration of your participation in this study will depend on your ability to safely tolerate the treatment, how your cancer responds (if at all), and on you and/or your doctor's decision to continue study treatment. Participants will continue to be treated as long as their cancer hasn't gotten worse, they have unacceptable side effects, the participant cannot follow the rules of the trial, or a study doctor feels the trial is not in the participant's best interest. Participation in this trial will include time you are actively being treated by a study doctor and part of the time you will be in follow-up.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are

otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

Temozolomide Side Effects:
Temozolomide, also referred to as Temodar®, is approved worldwide including in Europe and the US. The following side effects have been reported with use of temozolomide, this information is also available in the package insert:

Risks and side effects related to the temozolomide include:

COMMON, SOME MAY BE SERIOUS

Out of 100 people receiving Temozolomide, more than 20 and up to 100 may have:

- Constipation, nausea, vomiting, diarrhea
- Dizziness
- Muscle weakness, paralysis, difficulty walking
- Trouble with memory, confusion
- Tiredness
- Difficulty sleeping
- Hair loss

OCCASIONAL, SOME MAY BE SERIOUS

Out of 100 people receiving Temozolomide, from 4 to 20 may have:

- Headache, seizure
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness
- Bruising, bleeding
- Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require blood transfusions

RARE AND SERIOUS

Out of 100 people receiving Temozolomide, 3 or fewer may have:

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Cancer of bone marrow caused by chemotherapy
- Rash
- Severe skin rash with blisters and can involve inside of mouth and other parts of the body
- Liver damage which may cause yellowing of eyes and skin, swelling and may result

in liver failure.
- Hallucinations

Nivolumab Side Effects:

Possible Side Effects of Nivolumab
Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects that you experience.

The most common (occurring in more than 10% of people) side effects of nivolumab are:

- Fatigue
- Skin reactions: including rash, itching, hives, redness, and dry skin.
- Diarrhea
- Nausea
- Abdominal pain
- Decreased appetite
- Low red blood cells
- Fever
- Joint pain or stiffness

Less common (occurring in less than 10% of people) side effects of nivolumab include:

- Bowel inflammation
- Liver function blood test abnormalities
- Loss of color (pigment) from areas of skin
- Dry mouth
- Vomiting
- Weight loss
- Thyroid gland abnormalities
- Blood chemistry abnormalities, including low blood phosphate, magnesium, and potassium levels. If severe, these could contribute to fatigue, muscle weakness, muscle aches, problems with the electrical system of the heart, seizures, and numbness or tingling.
- High blood uric acid level (may lead to gout or kidney stones)
- Lung inflammation (pneumonitis - see details below)
- Cough
- Dizziness
- Headache
- Low white blood cells (may lead to infection)
- Chills

- Muscle soreness, weakness, stiffness spasms or paralysis
- Pain in arms or legs
- Tingling, burning, or numbness in hands and feet
- Shortness of breath
- Abnormal taste
- Flushing
- High or low blood pressure
- Allergic reaction during or between study drug infusions. Symptoms of an allergic reaction include, rash, trouble breathing, wheezing, dizziness or lightheadedness, swelling, fast pulse, sweating, and could be life-threatening.
- Increased sensitivity of skin to sunlight
- Constipation
- Difficulty swallowing
- Heartburn
- Low blood platelets (may increase risk of bleeding)

Rare (occurring in less than 1% of people) but potentially serious side effects of nivolumab include:

- Low blood oxygen level
- Acute lung injury or failure
- Collection of fluid around the lungs
- Inflammation of the appendix
- Increase in inflammatory blood proteins (e.g., lipase)
- Adrenal gland abnormalities
- Pituitary gland inflammation
- Changes in vision (including decreased or blurry vision), inflammation of the eye, or bleeding into the eye
- Liver inflammation
- Acute kidney injury or failure
- Abnormal blood cell production
- Inflammation of the mouth and lining of the digestive tract
- Swelling of the face, arms, or legs
- Inflammation of the pancreas
- Back pain
- Autoimmune disorders, including Guillain-Barre syndrome (associated with progressive muscle weakness or paralysis)
- Chest discomfort
- Heart palpitations
- Inflammation of the heart or its lining
- Collection of fluid around the heart
- Increased blood sugar
- Dehydration
- Infections: including sepsis, lung infections, and skin infections.
- Decreased movement of the intestines

- Disorientation
- Swelling of the optic disc (an area of nerves in the eye)
- Inflammation of the optic (eye) nerve
- Inflammation or loss of the lining of the brain and spinal cord
- Drug reaction with rash, blood cell abnormalities, enlarged lymph nodes, and internal organ involvement (including liver, kidney, and lung); known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles. One death in a patient who received nivolumab combined with ipilimumab was considered due to myasthenia gravis and severe infection (sepsis).
- Abnormal brain function due to brain inflammation (encephalitis), potentially life-threatening or fatal.
- A potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn, has occurred in patients who received nivolumab (Toxic epidermal necrolysis).
- Muscle fiber is damaged and released into the blood stream which could damage your kidney (Rhabdomyolysis) and chronic muscle inflammation with muscle weakness (polymyositis) has been reported in one patient.

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.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest X-rays and/or CT scans.

Please inform your study doctor or nurse <u>AT ONCE</u> if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example, any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to

your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest X-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

Risks associated with study procedures:

- **IV Line (Nivolumab Infusion):** may cause discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely, infection, nausea, and lightheadedness.
- **Blood Draw:** Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.
- **Electrocardiograms (ECGs):** To perform the test, electrodes, i.e., stickers with wires attached, will be placed on your skin to record your heart's activity. No pain or other side effects are expected to be associated with these tests, but you may feel some discomfort, similar to pulling off an adhesive bandage, when the technician removes the electrodes after the procedure.
- **CT Scans:** CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause flushing, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.
- **MRI Scan:** During the MRI, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI

staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent. The magnetic field used in MRI scanning may harm people who have metal in their bodies (pacemakers, neurostimulators, certain clips, or staples from surgery). It may cause problems with devices, such as pacemakers. If you have metal in your body or a pacemaker, you should not have an MRI.

Dr. David Carbone, a researcher helping to perform this study, is a paid consultant for Bristol-Myers Squibb, the manufacturer of the study drug being tested. A conflict of interest committee at Ohio State has reviewed this information and determined that Dr. David Carbone's involvement presents no additional significant risk to the study's participants. Any questions about this information can be answered by Dr. Dwight Owen at 614-685-2039 or 614-293-8000 (24 hours).

Reproduction Risks:

It is not known if nivolumab affects an unborn or nursing baby; however, other immunotherapy drugs can cause harm to an unborn baby. If you are pregnant, trying to become pregnant or breast-feeding, you should not be in the study.

If you are able to have a baby, you must remain abstinent or use a reliable birth control method during the study and for a period of 5 months after your last dose of study drug. The following birth control methods are allowed during the study:

- Hormonal contraceptive: oral contraceptive pill (estrogen/progestin pill or progestin-only pill), contraceptive patch, vaginal contraceptive ring, or contraceptive injection
- Intrauterine hormone-releasing system (IUS)
- Intrauterine device (IUD)
- Bilateral tubal occlusion
- Vasectomized partner

If you become pregnant during the study or within 5 months after last treatment, you must notify the study doctor right away. The study drug will be stopped and your pregnancy will be monitored for outcome.

Women participating in this trial are to not get pregnant or breast feed or donate eggs during the trial and for 5 months after last treatment dose.

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Unknown/Unexpected Risks and Discomforts:

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of these medications, including severe or life-threatening allergic reactions, interactions between study medications or interactions with another medication. You will be informed in a timely manner, both verbally and in writing

of any new information, findings, or changes to the way the research will be done that might influence your willingness to continue your participation in this study.

Blood samples (Mandatory)

You will be asked to give a small volume blood sample at seven times during this study at the time of your routine blood tests (so as not to have an additional blood draw just for this sample). This blood sample is mandatory and would require now more than about 4 tablespoons (60ml) of blood at any one time. The total volume of blood collected over the entire study will be about 300 ml (20 tablespoons, or 1.25 cups). This is in addition to the routine blood testing you will have performed on day 1 and day 22 of each cycle which is standard practice to monitor your blood counts during treatment with temozolomide. See below for a summary of blood collection timing:

	Screening	Cycle 1 Day1	Cycle 1 Day15	Cycle 2 Day1	Cycle 3 Day1	Cycle 5 Day1	End of study
Nivolumab		X	X	X	X	X	
Temozolomide		X	X	X	X	X	
Research blood	X	X	X	X	X	X	X

Some of your blood samples will be used to help understand how your cancer responds to treatment; the results of these tests would not be given to you or your doctor and will not be used in planning your care. These tests are for research purposes only and you will not have to pay for them. Some of your blood will be sent to NantHealth to perform LiquidGenomics ® testing. Some of your blood will be sent to Guardant Health to perform additional testing. Some of the research will study genes in your blood. Genes carry information about features that are found in you and in people who are related to you. These tests may be "batched" so that they will be performed once a number of samples are available, and no additional testing will be performed other than what is stated here. Research using your specimens may include mapping your DNA (whole genome sequencing). This information could identify you. Ask the study team if you have questions.

Tissue Samples (Mandatory)

Tumor tissue sample and the microscope slides that are made from the tissue from a previous biopsy or surgery will be retrieved and analyzed as part of this study at no cost to you. Additional tumor tissue may be requested from your physician for the research. This would not involve additional surgery but would be obtained from the tissue taken at the time of your prior surgery/biopsy.

7. What benefits can I expect from being in the study?

Taking part in this research study may or may not make your cancer better. However, there is some evidence that your type of cancer might respond to the study drugs, nivolumab and temozolomide. How any given tumor responds to this treatment can be different from on patient to another. Your tumor may get smaller however may still be

present. There is the possibility that your tumor may completely go away. There is also the possibility that your tumor might stop growing but then after time begin to grow again.

Information from this study may help doctors better understand the type of cancer you have (refractory advanced thymic carcinoma) and help to better treat cancer patients in the future.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled. Depending on the cancer that you are being treated for, there are several additional FDA-approved treatments that may be available for you that your treating physician should discuss with you.
If you are being treated for small cell lung cancer: instead of taking part in this study, you may be treated with other second line FDA-approved treatments such as topotecan. Topotecan is a form of chemotherapy that has been shown to shrink tumors in about a quarter (24%) of patients with small cell lung cancer. It is FDA approved for the treatment of small cell lung cancers in patients with chemotherapy-sensitive disease after failure of first-line chemotherapy.

If you are being treated for neuroendocrine tumor (NET): instead of taking part in this study, there are several FDA-approved therapies that you may receive as part of your treatment. These include (DOTATATE (Lutathera) in patients with gastroenteropancreatic NET, everolimus and sunitinib for patients with advanced progressive pancreatic neuroendocrine tumors; everolimus for lung or gastrointestinal NET. Patients with Grade 3 NET are usually treated according to guidelines for small cell lung cancer with platinum-based combination as their first treatment option.

9. What are the costs of taking part in this study?

Nivolumab will be provided at no cost to you or your insurance company. Temozolomide, which is a recommended treatment for your cancer, will be billed through your insurance company as any standard treatment would be. The costs of research blood tests will also be covered by the study. Your study doctor or coordinator can tell you specifically which additional costs are covered by the study

Most of the care during this study is considered routine for your disease because you would receive it even if you were not participating in a clinical trial. This includes doctor’s visits, lab testing, study drug infusions, CT scans, and electrocardiograms. This may also include services and medications to treat side effects or complications. These services will be billed to you and your insurance in the usual manner. You will be responsible for your deductible, coinsurance and copayments as required by your plan.

If you are a Medicare Advantage Plan participant (HMO or PPO), original Medicare is billed first for routine, study-related services while you participate in an approved trial.

Your Advantage Plan is billed second for their share of your costs. You may or may not have additional out of pocket costs after Medicare or your Advantage Plan pays. Additional information can be obtained from your Advantage Plan and online at:

https://www.medicare.gov/Pubs/pdf/02226-Medicare-and-Clinical-Research-Studies.pdf

Most government and private insurance plans cover routine costs when you participate in an approved clinical trial. Some may limit what they pay or will not pay at all. Before participating in this study, we recommend that you ask your insurance company if there are any limitations or restrictions to your particular plan.

10. Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

11. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

13. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, it/they may be used or shared with only the other researchers listed below without your additional informed consent.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors;
- Guardant Health (the company evaluating blood samples)
- Bristol-Myers Squibb, the company that is providing nivolumab; and
- Your insurance company (if charges are billed to insurance).

If we find information that significantly impacts your health, we **will not** share it with you, as research tests will only be performed after the study is completed.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

14. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;

- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  Physical exams
  Laboratory, x-ray, and other test results
  Diaries and questionnaires
- Records about any study drug you received.

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician's office record;
- Others: BMS (provider of nivolumab); NantHealth (research blood testing)

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.
- Bristol-Myers Squibb, the company that is providing nivolumab
- NantHealth, the company that is performing blood-based research testing as part of this trial

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers or by calling the researchers. Contact information is listed on the first page of this document.

If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

15. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact the study doctor, Dwight Owen MD at 614-685-2039 or 614-293-8000 (24 hours).

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact:

HIPAA Privacy Manager
The Ohio State University Medical Center

600 Ackerman Road, Suite E2140
Columbus, OH 43202
Phone number: 614-293-4477

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of subject	**Signature of subject**
	_____ **AM/PM**
	Date and time

Investigator/Research Staff

I have explained the research to the participant before requesting the signature above. There are no blanks in this document. A copy of this form has been given to the participant.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	_____ **AM/PM**
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	_____ **AM/PM**
	Date and time
Printed name of witness	**Signature of witness**
	_____ **AM/PM**
	Date and time