SUMMARY OF CHANGES – Consent

NCI Protocol #: 10347
Local Protocol #: 202105074
Protocol Version Date: July 29, 2025

Protocol Title: A phase I study with an expansion cohort of duvelisib and nivolumab in mycosis fungoides (MF) and Sézary syndrome (SS)

Informed Consent Version Date: July 29, 2025

Response to a Request for Rapid Amendment Dated 07/14/25

#	Section	Comments
1.	Header	Updated version date

2	Possible Side Effects of Nivolumab	The terminology for CTEP's suggested lay terms may change periodically. The condensed risk profile represents CAEPR risks in lay terms in a "patient-friendly" condensed form. The condensed risk profile is provided as a guide to facilitate the inclusion of all risks listed in the current CAEPR. It should be used as written unless there is a compelling reason to add new language or reformat the list. If changes are made, please state, "The condensed risk profile has been modified" in the cover memo and specify the reasons in the Summary of Changes.
		• Added New Risk:
		  • Rare: Rejection of organ transplant; Low grade skin tumor that is skin-colored or red which may cause itching
		• Provided Further Clarification:
		  • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage) and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased (under Rare). is now reported as Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage) and can lead to death. If you are considering an allogeneic stem cell transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased (under Rare).
		  • A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss (under Rare) is now listed under the section "Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:" (under Rare)

Research Study Informed Consent Document

Study Title for Participants: Nivolumab and duvelisib for advanced mycosis fungoides and Sézary syndrome

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10347, A phase I study with an expansion cohort of duvelisib and nivolumab in mycosis fungoides (MF) and Sézary syndrome (SS)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have advanced mycosis fungoides or Sézary syndrome that has not responded to at least one type of treatment.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

What is the highest dose of duvelisib that can be given in combination with nivolumab with tolerable side effects in advanced mycosis fungoides and Sézary syndrome?

In addition, we are doing this study to answer the question: Does combining duvelisib and nivolumab improve how well tumors respond compared to each of these medications given individually?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your advanced mycosis fungoides or Sézary syndrome. The usual approach is defined as care most people get for mycosis fungoides and Sézary syndrome.

What is the usual approach to my mycosis fungoides or Sézary syndrome?

The usual approach for patients who are not in a study is treatment with chemotherapy drugs, antibody drugs, drugs that change the way genes are expressed in the cancer cells, or other medicines that slow the growth of cancer cells. Many of these drugs are approved by the FDA for the treatment of mycosis fungoides and Sézary syndrome. In very selected patients, a donor stem cell transplant may be used. These medicines are sometimes combined with radiation to sites that are causing the most pain or other symptoms. These treatments shrink tumors and improve disease-related symptoms like pain and itching. They do not cure the disease and are usually given for as long as they control the cancer without causing too many side effects. Most of these treatments work well only for a fraction of patients. They often work for months, but eventually stop working. Patients then move on to another of these chemotherapy drugs or similar medicines.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get duvelisib and nivolumab while you and your doctor feel that you are having better disease control and minimal side effects from the treatment. You will continue on this therapy until your disease gets worse or the side effects become too severe.

You will be asked to return to the clinic every week for the first three weeks and then every four weeks while getting the treatment. If you come off treatment for any reason, you will no longer have to come to clinic routinely for study purposes. However, research staff will still follow up with you every 6 months through phone calls to monitor your long-term clinical course for two years following completion of the study.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Tiredness
- Nausea or vomiting
- Diarrhea
- Rash
- Headaches
- Low white blood cell count
- Abnormal liver laboratory tests

There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence in human tumors that this treatment can shrink or stabilize cancer for longer than the usual approach, but we do not know if this will happen in people. It is unlikely that this treatment will help you live longer. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.

- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The primary purpose of this study is to test the safety of a combination of drugs called duvelisib and nivolumab. This study tests different doses of duvelisib in combination with nivolumab to see which dose is safer for people. Both duvelisib and nivolumab are FDA approved for other types of cancer but are considered investigational for the treatment of mycosis fungoides and Sézary syndrome.

A second purpose of this study is to see if combining duvelisib and nivolumab can improve the anti-tumor effect compared to each of these medications given individually. This study will also determine if combining these two drugs increases the number and/or severity of side effects.

There will be up to 33 people taking part in this study.

What are the study groups?

There are two parts in this study, a dose escalation part and a dose expansion part. Your doctor will tell you which part you are in.

In the dose escalation part of this study, different people will get different doses of the study drug duvelisib in combination with the study drug nivolumab.

The first three people taking part in this study will get the starting dose. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. The study doctor will watch each group carefully as they increase the dose. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, the dose escalation is stopped.

In the dose expansion part of this study, the highest dose with manageable side effects will be given to nine more people. This will help study doctors better understand the side effects that may happen with this drug.

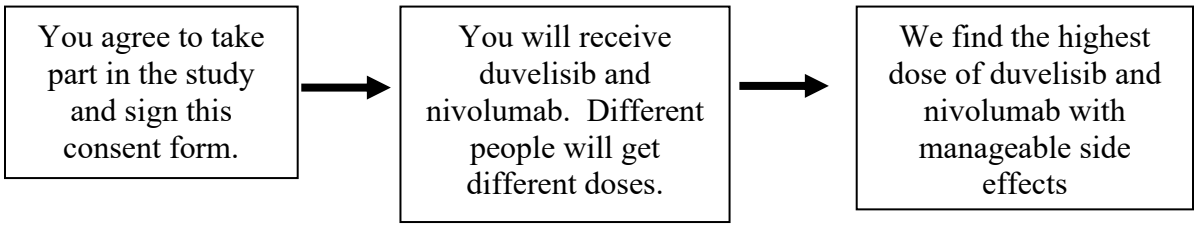
Treatment schedule: You will get duvelisib by mouth once or twice per day either days 1 through 14 or days 1 through 28 of each cycle. Each cycle lasts 28 days. You will get nivolumab through a vein in your arm (or the port that your doctor has placed under your skin to deliver medications into a vein if you have one) on the first day of each cycle. This study will

continue until your cancer progresses or until the side effects become too severe. See the study calendar for more information.

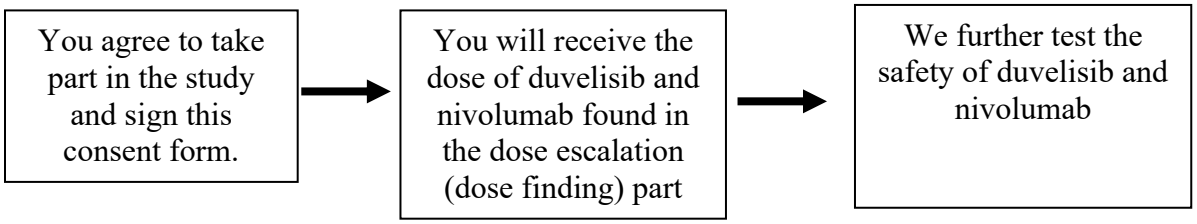
You will not be able to get additional doses of the drugs. These drugs are not approved by the FDA for treatment of your disease.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.

Schema:
Dose Escalation (Dose Finding)



Dose Expansion (where the established dose is further tested)



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Physical exams done before you begin the study, weekly during Cycle 1, and on Day 1 of each cycle after that.

- Blood counts done before you begin the study, weekly during Cycle 1, and on Day 1 of each cycle after that.
- Pregnancy test for women of childbearing potential done before you begin the study.
- Electrocardiogram (EKG) before you begin the study.
- Thyroid testing done before you begin the study and before Cycle 3, 5, and every three cycles thereafter.
- Blood tests to check for certain infections before starting on the study. Patients whose initial labs suggest that they are at higher risk for development of these infections while getting study medications will then have this bloodwork repeated approximately every 3 cycles while getting the study treatments.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

You will need to have biopsies for the study. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. The first biopsy will be done before you begin the study drug. For most patients, this will be a "punch" biopsy of the skin done in the office. For optional studies, if a biopsy is not possible or cannot be done safely before you begin the study drug, then your study doctor, with your consent, will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer. If a tumor tissue sample cannot be obtained by biopsy or by using left over tissue, your study doctor will let you know if you are still able to participate in the study. Additional biopsies will be collected on Day 1 of Cycle 2, if you have a "flare" (or worsening of your rash), and after you complete the treatment. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsies at the hospital or clinic where the biopsy is done.

Blood samples will also be taken for the study. The first blood sample will be collected before you begin the study drug. Additional blood samples will be collected on Day 1 of Cycle 2, if you have a flare, and after you complete the treatment.

Urine samples will also be taken for the study. The first urine sample will be collected before you begin the study drug. Additional urine samples will be collected on Day 1 of Cycle 2, if you have a flare, and after you complete the treatment.

Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA that may occur during treatment. You and your study doctor will not get any results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

A patient study calendar is attached at the end of this document. It shows how often these procedures will be done.

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

General Risks

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 7 months after you have completed the study.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for genetic changes that may predict your response to the treatment. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

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 test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.

2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

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

The combination of both medicines can increase the risk of increased liver enzymes. Some patients may need to discontinue study medication, be placed on steroids, or receive other immunosuppressive medications to treat the elevated liver enzymes.

Possible Side Effects of Duvelisib
(Table Version Date: July 10, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving duvelisib (VS-0145, IPI-145), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Pain • Diarrhea, nausea • Tiredness, fever • Infection, especially when white blood cell count is low • Cough • Rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving duvelisib (VS-0145, IPI-145), from 4 to 20 may have:

- Constipation, vomiting
- Sores in the bowels
- Swelling of the body
- Severe blood Infection
- Cold symptoms such as stuffy nose, sneezing, sore throat
- Bruising, bleeding
- Loss of appetite, weight loss
- Headache
- Kidney damage which may require dialysis
- Shortness of breath
- Damage to the lungs which may cause shortness of breath
- Dry skin

RARE, AND SERIOUS
In 100 people receiving duvelisib (VS-0145, IPI-145), 3 or fewer may have:

- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Nivolumab
(Table Version Date: May 14, 2025)

Special precautions

Side effects of nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, more than 20 and up to 100 may have:

- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, from 4 to 20 may have:

- Anemia which may require blood transfusion
- Swelling and redness of the eye
- Pain
- Diarrhea, nausea
- Dry mouth
- Fever
- Swelling and redness at the site of the medication injection
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Bruising, bleeding
- Loss of appetite
- Pain or swelling of the joints

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Lung problems (pneumonitis and pleural effusion). Symptoms may include: New or worsening cough, chest pain, shortness of breath.
- Skin: Itching; rash, blisters including inside the mouth; loss of skin pigment

RARE, AND SERIOUS

In 100 people receiving nivolumab, 3 or fewer may have:

- Swelling of arms and legs which may cause a feeling of heaviness and tightness
- Dry eye
- Sores in the mouth which may cause difficulty swallowing
- Swelling of the bowels
- Rejection of organ transplant
- Low grade skin tumor that is skin-colored or red which may cause itching

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness

- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss.
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage) and can lead to death. If you are considering an allogeneic stem cell transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck, confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome).
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: Numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: Decrease in the amount of urine, blood in your urine, ankle swelling.

Additional Drug Risks

The study drug could interact with other drugs. It will be important to discuss any medications or herbal supplements (including but not limited to St. John's Wort) with your doctor and the study team. You will need to avoid eating grapefruit or grapefruit-containing foods while on the study medications. Your study doctor will give you a patient clinical trial wallet card that lists the medications you are taking. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.

- Write down in your medication diary when you take the study drug at home and bring this medication diary and your blister cards of duvelisib capsules when you return for each appointment.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 7 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the duvelisib and nivolumab ready and giving them to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The biopsy and blood collections for predicting your response to treatment and identifying signs that you are becoming resistant to treatment, at the beginning of the study, on Day 1 of Cycle 2, if you have a flare, and after you complete the treatment
- The blood collections for research, before you begin the study, on Day 1 of Cycle 2, if you have a flare, and after you complete the treatment
- The urine collections for research, before you begin the study, on Day 1 of Cycle 2, if you have a flare, and after you complete the treatment.

You or your insurance provider will not have to pay for the duvelisib or nivolumab while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study agents now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this

data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading this optional study hope the results will help other people with

cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the following study.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect a skin biopsy for research on predicting your response to treatment and identifying signs that you are becoming resistant to treatment. This optional biopsy will be collected before you begin the study, on Day 1 of Cycle 2, if you experience a flare, and after you complete the study treatment.

Unknown future studies

If you choose to take part in this optional study, any of your skin biopsies or blood samples left over from the genomic sequencing and antibody staining will be stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio, and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood and/or tumor samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. Additional samples of tissue will be collected during the skin biopsies required for this study. The biopsy collection will be performed before you begin the study, on Day 1 of Cycle 2, if you experience a flare, and after you complete study treatment.
2. Your leftover samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to a skin biopsy are pain, local swelling, bleeding, infection, and s small scar at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection and significant bleeding can occur..
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number; your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the biopsy and biobanking of your specimen(s). You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I need my tissue or blood samples to be returned?

Tumor tissue or blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary

events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue or blood samples and genetic material (DNA and RNA) that is no longer in the biobank or that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory study described above.

YES NO

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

Cycle # (28-day cycles)	Before you receive study treatment	Cycle 1				Cycle 2				Cycle 3+				If you have a "Skin flare" (worsening of your rash)	After you complete study treatment
		Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4		
Nivolumab		A				A				A					
Duvelisib (28 day regimen)		B----------B				B----------B				B----------B					
Duvelisib (14 day regimen)		B-------B				B-------B				B-------B					
Pre-study procedures including informed consent, demographics, medical history, and an assessment of how you perform everyday tasks and activities	X														
Review of other medications you are taking by the study team	X	X----------X													
Physical exam including vital signs	X	X	X	X	X	Day 1				Day 1					X
Blood draws for complete blood count and general health status	X	X	X	X	X	Day 1				Day 1					X
Thyroid Tests	X	X								X[a]					X
EKG	X														
Side effects evaluation		X----------X													X
Tumor Measurements	X									X[a]					X
Pregnancy test (for women of childbearing potential only)	X														
Skin biopsies for research purposes	X[c]					Day 1								X	X

Cycle # (28-day cycles)	Before you receive study treatment	Cycle 1				Cycle 2				Cycle 3+				If you have a "Skin flare" (worsening of your rash)	After you complete study treatment
		Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4		
Blood collection for research purposes	X[c]					Day 1								X	X
Urine collection for research purposes	X[c]					Day 1								X	X
Phone calls to check on your health and status of your cancer															X[b]

A: Nivolumab: dose as assigned; performed on Day 1 of each cycle
B: Duvelisib: dose as assigned once or twice a day, either on days 1 through 14 or days 1 through 28.
a: Performed before starting Cycle 3, before starting Cycle 5, and every 3 cycles thereafter.
b: Performed every 6 months for two years from the time you complete or come off the study treatment.
c: These tests may be done on Cycle 1 Day 1 before treatment (except urine collection, which may occur at any point before or on Cycle 1 Day 1).