THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Niraparib (PARP inhibitor) plus dostarlimab (anti-PD1) for small cell lung cancer (SCLC) and other high-grade neuroendocrine carcinomas (NEC) 2020-0412

Study Chair: Carl M. Gay, MD

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to learn if niraparib in combination with dostarlimab can be used to treat small cell lung cancer or other high-grade neuroendocrine carcinomas (NECs) in patients that have previously received therapy for the disease.

This is an investigational study. Niraparib is FDA approved and commercially available to treat ovarian, Fallopian tube, and peritoneal cancers. Dostarlimab is not FDA approved or commercially available. It is currently being used for research purposes only. Using niraparib in combination with dostarlimab to treat small cell lung cancer or other high-grade NECs is investigational. The study doctor can explain how the study drugs are designed to work.

The study drugs may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be serious or fatal. If you do not live in the Houston area, taking part in this study may require long out-of-town stays, hospitalization, and/or additional costs. Taking part in this study may delay surgery that could benefit you.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may continue receiving the study drugs for as long as the doctor thinks it is in your best interest.

Niraparib and dostarlimab will be provided at no cost to you while you are on this study. You and/or your insurance provider will be responsible for the costs of any standard of care tests, procedures, or drugs.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other chemotherapy drugs. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine testing and to check your thyroid function and for viruses like hepatitis B and C.
- Urine will be collected for routine testing.
- You will have imaging scans (MRIs, CT, or PET scans) to check the status of the disease.
- You will have a core biopsy for biomarker testing, including genetic biomarkers, and immune system tests, and the tissue collected will be used to make cell lines. Cell lines are blood or tissue cells that are grown in a laboratory or in research animals. Tissue from this biopsy will also be compared to later samples to learn how your body responds to the study drug. To perform a core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge under local anesthesia (numbing medication), which will help you feel less pain in the biopsy area.
- Leftover tissue from a previous biopsy will be collected to confirm the cancer diagnosis. If leftover tissue is not available, part of core biopsy tissue collected may be used for confirmation.
- If you can become pregnant, 7 days before the first dose of study drugs, blood (about 2 teaspoons) or urine will be collected for pregnancy testing. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 48 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Study Cycles 1-4 are each 21 days. Cycles 5 and beyond are each 42 days.

If you are found to be eligible to take part in this study, you will receive dostarlimab by vein over about 30 minutes on Day 1 of every cycle.

You will take niraparib capsules by mouth 1 time every day at about the same time with or without food and with a full glass of water (about 8 ounces). The capsule should be swallowed whole and not opened, crushed or chewed.

If you vomit or miss a dose and more than 12 hours have passed since your last dose, you should skip that dose and take the next dose at the scheduled time.

You must return any unused study drug to the clinic at the end of the study.

You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over after the follow-up visit.

Study Visits

On **Day 1 of each cycle**:

- You will have a physical exam (except Cycle 1).
- Blood (about 2 teaspoons) will be drawn for routine testing. Every 6 weeks, part of this draw will be used to check your thyroid function.

On **Days 8 of Cycles 1-2 and Day 15 of Cycle 1,** blood (about 2 teaspoons) will be drawn for routine testing.

In addition to the above, the following tests will be performed on **Day 1 of certain cycles:**

- **During Cycles 1-3**, urine will be collected for routine testing.
- **On Cycles 3, 5, and then every 6 weeks until the end of study**, you will have imaging scans to check the status of the disease.
- **Every 3 cycles (Cycles 4, 7, 10, and on)**, if you can become pregnant, part of the blood sample drawn or urine will be collected for pregnancy testing.

If you are diagnosed with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) during this study, you will have a bone marrow biopsy/aspirate to confirm you have MDS or AML. To collect a bone marrow biopsy/aspirate, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.

End of Study Visits
After your last dose of study drugs:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine testing and to check your thyroid function.
- Urine will be collected for routine testing.

Follow-Up
Within 90 days after your last dose:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine testing and to check your thyroid function.
- Urine will be collected for routine testing.
- If you can become pregnant, part of the blood or urine sample will be used for pregnancy testing.

Long-term Follow-Up
Every 6 months for 2 years, and then 1 time every year for up to 5 years after that, you will come to the clinic or the study staff will call you and ask how you are feeling and about any side effects you may be having. The phone call should last about 10-15 minutes.

Other Testing
The study staff will ask you to take part in MD Anderson research study LAB10-0442 for additional testing. The study doctor will discuss this with you, and if you agree, you will sign a separate consent document. You do not have to take part in LAB10-0442 in order to receive treatment on this study.

Other Instructions

- Tell the study doctor or the study staff about any drugs you are taking, have recently taken, or are planning to take, including herbal remedies, supplements, and drugs you take without a prescription.
- You should not be in any other study that involves an investigational drug while participating in this study. You should also not receive any anti-cancer drugs that are not given to you as part of this study.
- You should not receive a live vaccine (such as the measles, mumps, rubella, chicken pox, yellow fever, rabies vaccines) within 14 days before the first dose of study drug.
- You must not donate blood while you are in this study or for 90 days after the last dose of treatment.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form,

as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Niraparib and dostarlimab may each cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia, severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Dostarlimab Side Effects

Common (occurring in more than 20% of patients)

• nausea • diarrhea • low red blood cell count

Occasional (occurring in 3-20% of patients)

• fever • chills • skin rash • itching	• underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating)	• vomiting • abnormal liver tests (possible liver damage) • muscle pain

Rare but serious (occurring in fewer than 3% of patients)

• pituitary gland inflammation (possible headaches) • severe high blood sugar due to uncontrolled diabetes • diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure)	• inflammation of the thyroid gland (possible tenderness in the neck) • inflammation of the pancreas (possible abdominal pain) • inflammation of the intestines • liver damage (hepatitis) • destruction of red blood cells • inflammation inside the eye (possible vision problems)	• kidney inflammation (possible abnormal kidney tests [possible kidney damage], pelvic and/or abdominal pain, pain while urinating, and/or swelling of the arms/legs) • lung inflammation (possible difficulty breathing) • infusion related reactions (possible injection site redness, itching, swelling, pain, and/or heat) • allergic reaction • immune response (causing muscle weakness)

These side effects are considered rare, but serious, immune-related events when dostarlimab was used in combination with other medicines

- brain inflammation (possible paralysis and/or coma)
- inflammation of the heart muscle
- muscle inflammation
- body-wide inflammation
- immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures)

The study drug works by boosting the immune system. This may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue. These other immune-related side effects may be life-threatening or fatal.

<u>Niraparib Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue • headache • dizziness • difficulty sleeping • high blood levels of magnesium (possible abnormal muscle function and/or blood pressure)	• high blood sugar (possible diabetes) • skin rash • nausea/vomiting • constipation • decreased appetite • low blood cell counts (red, platelets, white)	• abnormal liver tests (possible liver damage) • pain • abnormal kidney blood test (possible kidney damage) • difficulty breathing • weakness • infection (such as the common cold, UTI)

Occasional (occurring in 3-20% of patients)

• irregular/fast heartbeat • high blood pressure • dizziness • anxiety • swelling (arm/leg) • low blood levels of potassium (possible weakness and/or muscle cramps) • abdominal pain	• diarrhea • mouth blisters/sores (possible difficulty swallowing) • upset stomach • weight loss • depression • nosebleed	• cough • bronchitis • painful red eyes • kidney failure

Rare but serious (occurring in fewer than 3% of patients)

• severe increase in blood pressure (possible stroke) • severe, live-threatening infection due to low white cell counts (associated with low blood pressure and possible organ failure) • a brain condition with symptoms including seizures, headache, confusion, and changes in vision • decrease in number of all types of blood cancer cells • fever with low white blood cell count

Rare but serious (Frequency Unknown)

• disorientation • hallucination (seeing or hearing things that are not there) • cognitive impairment (difficulty	• skin sensitivity to sunlight or lamps • inflammation of the lungs which can cause shortness of breath and difficulty breathing	• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

concentrating, remembering, learning new things, and/or making decisions)		

Class Effects:

Class effects are potential risks that are associated with a particular group of drugs. Niraparib belongs to the group known as poly (ADP-ribose) polymerase inhibitors (PARP) inhibitors. These class effects are potential risks for the group of drugs, but **have not yet been identified as side effects for niraparib**.

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukaemia (AML):

- **PARP inhibitors may cause blood cancers known as myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML).**
- MDS/AML, including cases with a fatal outcome with PARP inhibitors have been reported in a small number of patients who took niraparib or placebo (ie, sugar pill).
- Your doctor may want to test your bone marrow for these problems.

Secondary Primary Malignancy:

- **PARP inhibitors may also cause a new primary cancer** (that is, a cancer other than the one for which you have been treated). In 2 studies comparing niraparib to placebo (sugar pill), new primary cancers were observed in a small number of patients who took niraparib was similar to those in patients who took placebo.

Niraparib may have adverse effects on an unborn baby. Wash your hands after handling the study drug. If a caregiver is giving the study drug to you, he or she should wear disposable gloves. Notify your study doctor if it appears that the study drug is damaged or defective in any way.

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

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.

Having **bone marrow biopsies/aspirations** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the

biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Rarely (in fewer than 3% of patients), major bleeding may occur.

Occasionally (in 8-12% of patients), if you have a lung biopsy, you may have a collapsed lung and need to have a chest tube surgically placed. In 15-20% of patients, a collapsed lung that does not require placement of a chest tube may occur.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you are female, you must agree to use 2 highly effective birth control methods starting from the time you sign this consent, during the study, and for 180 days after the last dose of study drugs. If you are male, you must agree to use 1 highly effective birth control method starting from the time you sign this consent, during the study, and for 90 days after your last dose of study drugs. Highly effective methods include:

- Combined (estrogen- and progestogen-containing) hormonal birth control, including birth control pills, patches, or intrauterine devices (IUDs)
- Progestogen-only hormonal birth control injections
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion (“tubes tied”)
- Vasectomy or vasectomized partner
- Condom used in combination with spermicide

Males: Do not donate sperm for 90 days after your last dose of the study drugs. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. If your partner/spouse becomes pregnant while you are on this study, the sponsor would like to collect information about the pregnancy. The study sponsor's contact information will be made available so that, if you and your partner wish to, you can share information about the outcome of the pregnancy with the sponsor. If you and/or your partner choose not to share this information, it will not result in any penalty or loss of benefits to which you are otherwise entitled.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. The sponsor will ask for information about the pregnancy.

Getting pregnant **will** result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, you will have a tumor tissue biopsy on Day 1 of Cycle 3 (+/- 7 days) for biomarker testing, including genetic biomarkers, and immune system tests. The collected tissue will also be used to make cell lines and will be compared to earlier samples to learn how your body responds to the study drug.

Optional Procedure #2: If you agree, blood (about 4 teaspoons) will be drawn for circulating tumor cell (CTC) testing and cell-free DNA (cfDNA) testing. CTC tests look at how many tumor cells are in the blood. cfDNA testing looks for genetic mutations, or changes, that may be related to the disease

There are no benefits to you for taking part in the optional procedure. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure.

Optional Procedure Risks

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.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have tumor tissue collected from you for biomarker and immune system testing, for use in making cell lines, and to compare with other biopsy samples?

YES **NO**

Optional Procedure #2: Do you agree to have blood samples taken from you for CTC and cfDNA testing?

YES **NO**

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Tesaro for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Carl M. Gay, at 713-792-6363) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Tesaro, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the

IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: Tesaro.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Tesaro and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by Tesaro may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Tesaro, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2020-0412**.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION