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Fred Hutchinson Cancer Center
University of Washington

Consent To Take Part in A Research Study:

A Phase 1B Trial of Niraparib and Dostarlimab (TSR-042) in Patients with BRCA-Mutated Breast, Pancreas, or Ovary Cancer

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SUMMARY

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study. Please read this consent form carefully. It may contain words that are not familiar to you. Please ask the study doctor or study staff to explain any words or information that you do not understand.

This consent form tells you why this research study is being done and what tests are involved. It describes responsibilities that you will have if you join this study. It explains any possible benefits and possible risks of taking part in this study. It also explains how your medical information will be used and who may see it.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help people in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the study will not cause you to lose any medical benefits. If you decide not to take part in this study, your regular doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard care is the treatment normally given for a certain condition or illness.

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- Other parts of this study may involve experimental (investigational) drugs, devices or procedures that are being tested for a specific condition or illness. An investigational drug is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and talking with the research staff, you should know which parts of the study are experimental and which parts are standard medical care. You should also know what parts you would receive even if you weren't in the study.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at or copied by the sponsor of this study. They may also be looked at or copied by government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a study. Taking part in a study could affect your current or future insurance coverage.

Your participation in this study is totally voluntary. If you take part in this research study, you will be given a copy of this signed and dated consent form.

WE INVITE YOU TO JOIN THIS RESEARCH STUDY

We are inviting you to join this research study because you have breast, pancreas or ovary cancer that is positive for a BRCA mutation. We will be testing a combination of investigational products called Niraparib and Dostarlimab (TSR-042) to see if these drugs slow or stop your cancer from growing or getting worse. We also want to see what side effects the combination of study drugs cause, good or bad.

Research is not the same as treatment or medical care. The purpose of a research study is to collect information and answer scientific questions.

You do not have to be in the study. You are free to say "Yes" or "No", or to stop being in the study at any time after joining. If you say "No," you would not have any penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

STUDY PURPOSE

We are doing this study to find out how the combination of niraparib and Dostarlimab (TSR-042) works in subjects who have breast, pancreatic, or ovary cancer.

We are studying niraparib (a PARP1 inhibitor) and Dostarlimab (TSR-042), (an anti-PD-1-immunotherapy). Niraparib is approved for sale in the United States by the Food and Drug Administration (FDA) for use by patients with ovarian cancer that has been treated with chemotherapy. However, niraparib and Dostarlimab (TSR-042) are experimental in combination in subjects with ovary cancer. Neither product is approved to treat breast or pancreas cancers,

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and the combination is not currently approved by the FDA for sale in the United States. We think that these study products might work together to slow or stop your cancer from getting worse.

We will also find out how your cancer reacts to niraparib alone, and to see how this study treatment works in patients who have received PARP inhibitor products before.

Up to 18 people will take part in this study.

STUDY DRUG DOSING

If you join this study, you will get the combination of niraparib and Dostarlimab (TSR-042). Niraparib is taken by mouth; you will be given a supply to take at home. Dostarlimab (TSR-042) is an intravenous (IV) product. This means you need to come to the clinic to get this study product infused directly into a vein.

All of the patients who take part in this study will take the same doses and schedule of the study products (niraparib and Dostarlimab (TSR-042)).

Patients will start the study in Cycle 1 taking niraparib alone for 28 days. If you weigh 77 kg (about 169 lbs) or more, you will take 300 mg of niraparib every day. If you weigh less than 77 kg, you will take 200 mg of niraparib every day.

Once you have completed Cycle 1 (Days 1-28) taking niraparib alone, we will ask you to come to the clinic to get an infusion of Dostarlimab (TSR-042). This will be the start of Cycle 2. You will get 500 mg intravenously (directly into a vein through a needle or tube). This will happen about every 3 weeks (21 days). During this time, you will continue to take niraparib every day by mouth.

After 5 cycles (15 weeks), if you are not having any unacceptable side effects and would like to keep taking the study drugs, you will continue to take niraparib every day by mouth, but you will get 1000mg Dostarlimab (TSR-042) once every 6 weeks (instead of 500mg every 3 weeks). You can continue this study treatment for up to 24 months.

TESTS, PROCEDURES & STUDY VISITS

We will conduct tests and procedures to see if you qualify to take part in this study and to monitor your health and safety while you take the study treatment. You will be told which tests and procedures you are going to have at each visit. If you decide to stop taking the study treatment, or the study doctor thinks it is not working well for you, we will ask you to have tests and procedures about 30 days after you stop the study drugs to see if you are safe.

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SCREENING VISIT

After signing this consent form, the study will begin with a screening visit. The purpose of this visit is to find out if you meet all of the requirements to take part in this research study. It is possible that after the screening tests are reviewed, you will not be able to take part in this study. If this happens, the study doctor will tell you why. They will discuss other treatment options with you, if available.

Within 30 days of your first dose of study drug, we have to complete the following tests and procedures:

- We will review your medical history, including your cancer history.
- We will do a physical examination. It will include an exam of major body systems and recording your height and weight.
- We will ask you how you are feeling and if your level of activity has changed.
- We will review any medications that you take, including over-the-counter drugs vitamins, and herbal products.
- We will record your blood pressure, pulse, oxygen saturation, respirations, height, weight (vital signs). Vital signs especially, blood pressure and heart rate will be monitored weekly for first 2 months, monthly for first year, and periodically thereafter.
- We will collect blood for safety tests. We will test your blood to look at your organ function, including how your thyroid is functioning, and blood cell counts. We will also need to test some blood to see if you have Hepatitis B or C infection. Your hepatitis B and C tests must be negative for you to participate in the study. State law requires that the results of positive tests for hepatitis be reported to the Washington State Department of Health.
- We will test your urine to see how your kidneys are functioning.
- If you are a woman who is able to have children, we will test your urine or blood to see if you are pregnant. If you are pregnant, planning to become pregnant, or breastfeeding, you may not take part in this study.
- If you have not had images of your cancer within 6 weeks of starting the study drug, we will ask you to repeat these scans for the study about every 12 weeks from when you start the study drug. We will use one of the tests described below. Your study doctor will decide which test is best for you. These images will include your chest, abdomen and pelvis. If you have a high risk of cancer in your head, neck, arms and legs, we may scan these areas too.
    - Computed Tomography (CT) Scan: This test uses a small amount of radiation (x-ray) to take pictures of the inside of your body. If can show a cross section, like a thin “slice” of your body, or it can show the body tissues and structures in “3-D”. For this test, the study doctor or staff may give you a contrast dye, either by mouth or injected into a vein with a needle. The study doctor or

staff can tell you more about the contrast dye.

- Magnetic Resonance Imaging (MRI) Scan: This test uses powerful magnets and radio waves to make pictures of body tissues and structures. During an MRI, you must lie on your back in the MRI scanner without moving. You may have a contrast dye given by mouth or injected into a vein with a needle. The study doctor or staff can tell you more about the contrast dye.

- Archival Tissue: We will ask to send some tumor tissue (cancer cells from your body) that has been *previously* collected from surgery or biopsy to the University of Washington. This is called "archived" tissue.
- Before you start the study treatment, we will ask you to have a new tissue sample collected for research tests. This sample must be collected within 14 days of you starting the study treatment.
- After 4 weeks of study treatment, we will ask you to have a new tissue sample collected for research tests.
- At the end of the study, you can choose to get another tissue sample collected for research tests if you want.

TREATMENT

This study is divided up into Cycles, which are a period of either 21, 28, or 42 days. Cycle 1 is 28 days long and Cycles 2 through 5 are 21 days long. Starting at Cycle 6, the cycles in this study are 42 days long and, again, you will come to the clinic on Day 1 of each cycle (every 42 days).

We will ask you to come to the clinic for some study treatments on Day 1 of each cycle (whether it is a 21-day, 28-day, or 42-day cycle). When you come to the clinic, we will perform tests and procedures. If these show that you are able to continue taking part in the study, we will give you an infusion of Dostarlimab (TSR-042) through a needle in your vein or an implanted catheter (also called a "port").

You will be given niraparib starting on Cycle 1, Day 1. You will take either 200 mg or 300 mg daily at about the same time each day. If you forget to take your dose of niraparib for more than 12 hours beyond your normal dosing time, you should skip that dose and start again the next day. If you vomit your dose of niraparib, you should not take another dose until the next day. You should keep taking niraparib until you run out or you are asked to come to the clinic to return any unused drug. We will give you a diary to take home with you to help keep track of your daily doses. We may ask you to bring your completed diary and any unused drug to your visits on Day 1 of each cycle.

If you have uncomfortable side effects, your study doctor may lower the dose of niraparib that you take. They may also tell you to stop taking the study drug. If that happens, please save the study drug and containers to return when you come to the clinic for your next visit.

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STUDY LENGTH

If you join this study, you could take part for up to 7 years. You would get the study treatment for the first 2 years. After that, you would have a safety follow-up visit in the clinic 30 days after your last dose of study drug. Once you complete the safety follow-up, the long-term follow-up period will start 6 months after your last dose of study drug and last for about 5 years depending on your future cancer treatment.

The study doctor can stop you from taking part in the study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

SAFETY FOLLOW-UP

If you finish 24 cycles of study treatment or decide to stop taking part in the study, we will ask you to come to the clinic for a "Safety Follow-up" assessment. This will take place at least 30 days after you have finished taking the study drug. We will ask about any side effects you might have and collect a blood sample for safety tests.

LONG TERM FOLLOW-UP

The study doctor and staff would like to check your medical record and contact you every 6 months to see if you have had any tumor assessments or any health concerns. This will happen until you start a new anti-cancer treatment or decide that you no longer want to take part in this study.

The table on the following page shows you what tests and procedures you will have and when these will be completed while you are in this study.

Study Procedures	Screening	Cycle 1 (28 days)				Cycle 2 (21 days)			Cycles 3-5 (21 days)	Cycle 6+ (42 days)		EOT	Safety Follow-Up	Long Term Follow-Up
		D1	D8	D15	D22	D1	D8	D15	D1	D1	D22		At least 30 days from last dose	Every 6 months for 2 years and annually thereafter

Medical History	X													
Measure Height and Weight	X													
Vital Signs Measured		X	X*	X*	X*	X	X*	X*	X	X		X	X	
Review of your ability to perform daily activities	X	X				X			X	X				
Review of Current Medications	X	X				X			X	X		X		
Physical Exam	X					X			X	X			X	
Review of any Side Effects You are Having		X				X			X	X		X	X	
Assess for MDS/AML (Blood Test)		X				X			X	X		X	X	X
Pregnancy Testing	X	X							Every 9 weeks while on study (Cycle 4, Cycle 7, etc.)			X		
Routine blood safety tests to check your blood cell counts and monitor kidney & liver function	X	X	X	X	X	X	X	X	X	X	X	X	X	
Comprehensive Metabolic Panel	X	X				X			X	X		X	X	
Coagulation (to see how your blood clots)	X												X	
Hepatitis B and C Blood Tests	X													
Thyroid Blood Tests	X					X			X	X		X	X	
Collection of Urine Sample for Routine Testing	X	X				X			X	X		X	X	
Study Procedures	**Screening**	**Cycle 1 (28 days)**				**Cycle 2 (21 days)**			**Cycles 3-5 (21 days)**	**Cycle 6+ (42 days)**		**EOT**	**Safety Follow-Up**	**Long Term Follow-Up**
		D1	**D8**	**D15**	**D22**	**D1**	**D8**	**D15**	**D1**	**D1**	**D22**		**At least 30 days from last dose**	**Every 6 months for 2 years and annually thereafter**

Fresh tissue Biopsy (optional at EOT)	X					X						X		
Bone marrow aspirate and/or biopsy		Only if your study doctor thinks it is necessary												
Follow-up contacts (may be by telephone)														X
Tumor Assessment [CT, MRI, etc.] Every 12 weeks	X								X					
Study Drug Administration														
Niraparib (300mg or 200mg)		Taken by mouth once a day throughout the study												
Dostarlimab (TSR-042) Infusion (every 21 days for Cycles 2-5, then every 42 days starting at Cycle 6)						X			X	X				

*Patients may take their blood pressure and pulse on a personal blood pressure device and report the results within one business day by phone, email or MyChart to the study staff for safety oversight.

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RISKS & SIDE EFFECTS

Any research has some risks. These can include things that could make you feel unwell, uncomfortable, or harm you. You might have side effects related to the study treatment while taking part in the study. We will watch everyone taking part in the study for any negative effects. The study team does not know all the effects that the study treatment may have on you. These side effects may be mild, moderate or severe. In some cases, these effects might be long lasting, or permanent, and may even be life threatening. The research study team may give you medicines to help reduce side effects.

If any of the side effects listed below happen to you, tell your study doctor **immediately.**

Risks Associated with Niraparib

The treatment with niraparib could result in side effects. The frequencies below are based on niraparib clinical trials.

Niraparib has moderate influence on the ability to drive or use machines. Patients who take niraparib may experience weakness, fatigue, difficulty concentrating and dizziness. Patients who experience these symptoms should observe caution when driving or using machines.

Known side effects of niraparib are listed below:

Very Common potential adverse events (may affect more than 1 in 10 people):

- Increased blood pressure (hypertension)
- Feeling like your heart is skipping beats or beating harder than usual (Heart palpitations)
- Feeling tired, lack of energy (fatigue)
- Headache
- Difficulty sleeping or falling asleep (insomnia)
- Dizziness
- Feeling sick to the stomach (nausea)
- Vomiting
- Loose/liquid stools (diarrhea)
- Difficulty passing stool (Constipation)
- Stomach area pain (abdominal pain)
- Indigestion (dyspepsia)
- Painful and frequent urination (Urinary tract infection)

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- Low number of red blood cells (anemia)
- Decrease in amount of white blood cells called neutrophils (cells that protect the body against infection and germs; neutropenia)
- Low platelet count in the blood, which may make you more likely to bruise or bleed (thrombocytopenia)
- Decrease in the number of other types of white blood cells (leukopenia) that fight infection.
- Back pain
- Joint pain, ache, stiffness (arthralgia)
- Cough
- Shortness of breath (dyspnea)
- Runny or stuff nose (nasopharyngitis)
- Feeling Weak (asthenia)
- Decreased appetite
- Fever
- Rash
- Dry mouth
- Abnormal taste in mouth (dysgeusia)
- Changes of results of standard blood tests including increased creatinine, low levels of magnesium and increased alkaline phosphatase (may indicate changes of how your organs are functioning)
- Low levels of sodium, which can be caused by fluid build-up in the body. This can cause changes to your heart function like slow or fast heartbeat, feeling like your heart is skipping beats, or beating faster or harder than usual.
- Changes of blood test results for liver function including increased AST and ALT (enzymes produced by the liver which can mean your liver function has changed)
- Swelling or collection of fluid in the arms, hands, legs and feet (peripheral edema)

Common potential adverse events (may affect up to 1 in 10 people):

- Abnormally fast heartbeat (tachycardia)
- Abnormal amount of fluid under the skin and in the body (peripheral edema)
- Depression

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- Feelings of worry, nervousness or unease (Anxiety)
- Decreased level of potassium in blood (hypokalemia)
- Increase in amount of an enzyme called gamma-glutamyltransferase (may indicate a possible negative effect on liver, bile, or a sign of worsening of cancer)
- Swelling or irritation of the lining of the mouth, throat, esophagus, stomach or intestines (mucosal inflammation/mucositis)
- Sore or red mouth (stomatitis)
- Pink eye (conjunctivitis)
- Muscle and bone pain (myalgia)
- Nosebleeds (epistaxis)
- Infection due to low white cell counts (Neutropenic infection)
- An irritation or infection in the tubes that carry air in and out of the lungs, that causes a cough (bronchitis)
- Decrease in weight.
- Increased sensitivity of the skin to sunlight (Photosensitivity)
- Increased level of creatinine in your blood (blood creatinine increase), which may be a sign of kidney damage
- Increased levels of glucose in your blood (hyperglycemia), which may mean your pancreas functions have changed
- Pain in the arms, hands, legs and feet
- Hot flashes or flushing
- Low blood cell counts due to a problem in the bone marrow or blood cancer starting from the bone marrow (Myelodysplastic Syndrome [MDS]/Acute Myeloid Leukemia [AML])
- Impaired concentration, understanding, memory and thinking (cognitive impairment)
- Allergic reaction (hypersensitivity, including anaphylaxis).

Uncommon Occurrence (may affect up to 1 in 1000 people)

- Fever with low white blood cell count (Febrile neutropenia)
- Decrease in number of all types of blood cells (Pancytopenia)

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- Severe life-threatening infection due to low white cell counts [associated with low blood pressure and possible organ failure (for example, heart, kidney and/or liver), (neutropenic sepsis)]
- Confusion (confusional state/disorientation)
- Seeing or hearing things that are not really there (hallucination)
- Inflammation of the lungs which can cause shortness of breath and difficulty breathing (non-infectious pneumonitis)
- Fluid in the chest and lungs (pleural effusion)
- Infection in the lungs (pneumonia)
- Blockage (obstruction) in the small or large intestine
- Sudden condition where the muscles of the intestines stop working, preventing food from passing through (paralytic ileus), which can lead to blockage.
- Sudden kidney injury
- Air bubble in a vein or artery (embolism)
- Seizure
- Skin cancer (squamous cell carcinoma)
- Rapid breathing (tachypnoea)

Rare Occurrence (may affect up to 1 in 1000 people):

- A brain condition with symptoms including seizures, headaches, confusion, and changes in vision (posterior reversible encephalopathy syndrome [PRES])
- Hypertensive crisis (a severe increase in blood pressure that can lead to a stroke or other complications)

The Side Effects Listed Below Require IMMEDIATE Medical Attention or Advice:

- Allergic reactions can be life-threatening. Symptoms may include difficulty breathing, shortness of breath, low blood pressure (feeling lightheaded, dizziness), tingling around the mouth, rash.
- Low platelet counts may increase your risk of bleeding and bruising. Bleeding may require urgent medical attention, including a transfusion (receiving blood or blood products by vein).
- Low red blood cell counts may make you feel tired or short of breath and symptoms may require a blood transfusion.
- Low neutrophil counts may be associated with infection, sometimes severe and life-threatening (neutropenic infection, neutropenic sepsis):.

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  - Symptoms of severe life-threatening infection may include:
    - Fever, feeling of low blood pressure (light-headedness, dizziness), decreased urination, rapid pulse, rapid breathing or shortness of breath

- Decrease in the number of all types of blood cells (pancytopenia)
- Low blood cell counts due to a problem in the bone marrow or blood cancer starting from the bone marrow (MDS or AML). MDS/AML, including fatal cases, have been reported with use of niraparib. If you experience prolonged hematological toxicities, contact your study doctor for hematologist evaluation.
- High blood pressure (hypertension) including severe increase in blood pressure (hypertensive crisis) has been reported with the use of niraparib. If you have pre-existing hypertension, the physician will determine if your blood pressure is adequately controlled before starting niraparib treatment.

  If you do not have to come to the clinic for any other reasons, you can choose to take your blood pressure on a personal blood pressure device. The device will show a result in an upper (systolic) and lower (diastolic) number like 112/67. If the results of your blood pressure show an upper number of 160 or more or the lower number is 90 or more, you should contact the study team immediately. The study investigator will need to provide you with clinical advice.

  If you and the investigator decide that self-collection of your blood pressure is appropriate for you, you will be responsible for purchasing a blood pressure measurement device. We will ask you to bring the device into the clinic for assessment by the study staff to make sure that the device will give the necessary information. The study staff and investigator will also give you important information about how to collect your blood pressure so that the results are accurate.

  When you self-collect your blood pressure, you will need to contact the study staff within 1 business day (MyChart message, phone or email are acceptable) with the results.

  - Symptoms of a severe increase in blood pressure may include:
    - Blurry vision, headache, nausea, vomiting, confusion, passing out, seizures, weakness or numbness on one side of body or in one arm or leg and/or difficulty talking (symptoms of a stroke), trouble breathing, chest pain, pain in the upper or lower back, urine that is brown or bloody
- Posterior Reversible Encephalopathy Syndrome (PRES), a rare neurological side effect, has been reported with niraparib treatment. If you have headache, vision changes, confusion or seizure with or without high blood pressure, please contact your doctor.

Class Effects:

Class effects are potential risks that are associated with a particular group of drugs. Niraparib

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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.

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, new primary cancers were seen in a small number of patients who took niraparib or placebo.

Safe Handling of Niraparib:

Niraparib may have negative effects on a fetus in a pregnant woman. Wash your hands after handling the study drug. If a caregiver is giving the study drug to you, they should wear disposable gloves. Tell your Study Doctor if it appears that the study drug is damaged or defective in any way.

Risks Associated with Dostarlimab (TSR-042)

As of April 2024, dostarlimab has been studied in about 3600 patients with advanced or recurrent solid tumors in clinical trials, with about 2700 of these patients receiving dostarlimab in combination with other medicines. Your study doctor will explain the risks, side effects, and discomforts that may be experienced related to non-study drugs which are part of usual care. Some of the side effects mentioned below can be life-threatening or fatal.

These side effects are considered very common in patients who took Dostarlimab (may affect more than 1 in 10 people):

- Low number of red blood cells that carry oxygen. Low red blood cells count may make you feel tired or short of breath and symptoms may require a blood transfusion (anemia)
- Feeling sick to the stomach (nausea)
- Vomiting
- Frequent, watery stools (diarrhea)
- Itchy skin (pruritis)
- Rash
- Fever (Pyrexia)

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- Increase in liver enzymes called aspartate aminotransferase (AST) which may be a sign of liver damage
- Increase in the liver enzyme called aspartate alanine transferase (ALT) which may be a sign of liver damage
- Underactive thyroid gland (Hypothyroidism)

These side effects are considered common potential adverse events (may affect up to 1 in 10 patients):

- Decreased production of adrenal hormones resulting in possible weakness and/or low blood pressure (Adrenal insufficiency)
- Overactive thyroid gland (Hyperthyroidism)
- Inflammation of the lungs which can cause shortness of breath and difficulty breathing (Pneumonitis)
- Inflammation of the pancreas causing pain in the upper abdomen. This could become sever and cause nausea and vomiting, fever, and rapid heart rate (pancreatitis)
- Inflammation of the colon that can cause stomach pain or diarrhoea (Colitis)
- Muscle pain (Myalgia)
- Chills
- Inflammation of the liver (Hepatitis)
- Dry skin

These side effects are considered uncommon in patients who took Dostarlimab (may affect up to 1 in 100 people):

- Destruction of red blood cells which can cause tiredness, dizziness, yellow skin or fast heart rate (Autoimmune haemolytic anaemia)
- Inflammation of the thyroid gland (Thyroiditis)
- Pituitary gland inflammation (Hypophysitis)
- Severe high blood sugar due to uncontrolled diabetes (Diabetic Ketoacidosis)
- Diabetes requiring insulin (Type 1 Diabetes Mellitus)
- Inflammation of the eye which can cause redness, blurred vision or vision loss (Uveitis)
- Muscle pain involving several muscles (Polymyalgia rheumatica)
- Kidney inflammation (Nephritis).

- Myasthenia Gravis
- Immune-mediated arthritis
- Inflammation in the brain (encephalitis)
- Inflammation of the heart muscle (myocarditis)
- Inflammation of the lining of the stomach (Gastritis)
- Inflammation of the food pipe (Esophagitis)
- Inflammation of the muscle which can cause weakness, swelling and pain (Myositis)
- Infusion-related reactions which can occur within 24 hours after receiving an intravenous infusion, or which can be delayed for up to about 2 weeks. Infusion-related reactions may include dizziness or fainting, flushing, rash, fever, chills, shortness of breath, increased or decreased blood pressure, increased heart rate, swelling of the lips, tongue or face, feeling sick to your stomach, back pain or pain at the site of infusion. Although infusion-related reactions are usually reversible, they can be severe or life threatening. (Infusion related reactions)

There are rare but serious immune-related negative side effects which have been seen when dostarlimab was used alone or in combination with other medicines:

- Overactive immune-system cells which damage body tissues and organs leading to signs of uncontrolled fever, enlarged spleen, low blood count and liver test abnormalities. This disease can be fatal. (Hemophagocytic Lymphohistiocytosis).
- A neurological disorder where the immune system attacks part of the peripheral nervous system that can cause tingling in the feet and hands, pain, muscle weakness, and problems with coordination (Guillain-Barre syndrome)
- Muscle weakness, twitching, cramping or inability to move (peripheral motor neuropathy)
- Muscle pain and weakness, swollen, red or thickened Skin (eosinophilic fasciitis)

There may be other risks called class effects that have been seen in patients receiving other drugs that work like dostarlimab. These effects could also occur with dostarlimab. They are potential risks but not known as side effects for dostarlimab so far. The most significant class related side effects are “immune-related”, meaning side effects caused by increased activity of the immune system, which can affect multiple organs of the body including bowels, hormone glands, heart, lungs, liver, skin, muscles and joints and nerves. These other immune-related side effects may be life-threatening or fatal.

The side effects listed below require immediate medical attention or advice. **Call the study doctor right away if you have any of these side effects**.

- Respiratory: shortness of breath, rapid breathing, new or worse cough
- Gastrointestinal: diarrhea, stools that are black or bloody, stomach area pain, nausea or vomiting

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- Kidneys: dark or bloody urine, urinating more often than usual
- Musculoskeletal: chest pain, muscle pain or weakness
- Cardiac: fast or unusual heartbeat
- Skin: rash, itching, blisters, pale or yellow skin
- Eyes: yellowing of the whites of your eyes, blurry vision
- Brain: abnormal thinking, confusion, personality changes, headache and neck stiffness.
- General: bleeding or bruising more easily than normal, feeling cold, hair loss. dizziness or fainting, feeling tired or weak, fever or chills.

WHAT ABOUT THE RISK OF CORONAVIRUS?

Coronavirus disease (COVID-19) is a viral infectious disease caused by a new strain of coronavirus. The virus may cause an illness with symptoms that usually include fever, dry cough, tiredness and loss of, or change in, sense of smell or taste. Some patients also get aches and pains, runny nose, sore throat and diarrhea. Most people have only a mild illness and recover without medical treatment. However, some people, particularly the elderly or those with pre-existing health problems, may also suffer shortness of breath and pneumonia, becoming seriously ill and requiring admission to a hospital, and, in some instances, die from the illness.

COVID-19 has been declared a pandemic by the World Health Organization (WHO) and is affecting nearly every community. GSK and the investigator site are taking the disease very seriously and taking precautions to protect subjects participating in this trial. Despite the additional procedures put in place by GSK, the facility, the staff and the study doctor(s) to reduce your risk of acquiring COVID-19 during your participation in the study, the potential exists that you could acquire COVID-19 while participating in the study. By signing this consent form, you acknowledge and accept this risk.

In your country, we may be required to share your health data related to COVID-19 with public health authorities.

Risks Associated with the Combination of Niraparib with Dostarlimab (TSR-042)

In patients treated with the combination of niraparib plus Dostarlimab (TSR-042), the most common (≥20% of patients) side effects were nausea, feeling tired (fatigue), low numbers of red blood cells (anemia), lowered levels of platelets in the blood, which can cause bruising and can make it hard for you to stop bleeding if you are injured (thrombocytopenia), and headache.

It is possible that you may experience an infusion-related reaction during or just after the infusion of Dostarlimab (TSR-042). Symptoms of a reaction are generally mild and improve

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when the infusion is slowed down or stopped. We will monitor you closely for signs of any infusion reaction, and when needed, the infusion is slowed down or discontinued. You may also be given medications before your infusion to help prevent such a reaction and your study doctor can tell you more about these.

In some cases, these reactions may be severe. This happens in about 1% of patients. A severe reaction could require intensive medical support. Fatal (deadly) reactions can happen.

There may be other side effects that are not known at this time. We will watch you carefully for any symptoms. Other drugs can be given to make side effects that happen less serious and less uncomfortable. Many side effects go away shortly after the drug is stopped, but in some cases side effects can be serious, long lasting or permanent. Be sure to tell your study doctor of all symptoms and side effects that you experience.

RISKS ASSOCIATED WITH STUDY PROCEDURES

Risks and possible discomforts you might experience from the study procedures include:

Biopsy: Removal of tissue can be painful and you may have pain, pressure, or discomfort in the area where the tissue was taken. Pain and discomfort can last for several hours and up to several days after the biopsy procedure. You may experience bleeding, redness, swelling, bruising, and infection in the area where the tissue was taken, and you may feel faint or dizzy. Your study doctor will explain the procedure and go over the risks with you. You may be asked to sign a separate consent form for this procedure.

Blood Draws: A blood draw via needle may cause faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight chance of infection.

Intravenous (IV) Catheter: The use of an intravenous catheter may cause pain, bruising, clotting, bleeding, leakage of study treatment solution, and possibly infection at the catheter site.

Bone Marrow Aspiration/Biopsy: Removal of bone marrow produces pain when the liquid part of the sample is collected. Medicine will be given to numb the area where the bone marrow is taken from but the sensation of pressure from the needle entering the bone and the pain with removal of the liquid bone marrow cannot be prevented. The pain may radiate down your leg but typically lasts only a few seconds. After the bone marrow test you may have redness, swelling, bruising, or there may be an infection in the area. You may be asked to sign a separate consent form for this procedure.

MRI: There are risks from an MRI if you are pregnant or have one of the following: an artificial heart valve, pacemaker, metal plate, pin, or other metallic objects in your body (including gun shot or shrapnel). You may also become anxious from lying in a tight space without moving. The MRI scan does not cause any pain and does not expose you to x-ray radiation. Please let the study doctor know if you have a fear of closed spaces (claustrophobia).

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Imaging Scans (CT): Some of the tests that you have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called "background radiation". This radiation is natural and comes from space, air, water, soil, and the food that you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below. The risk to your health from this level of radiation exposure is likely zero.

- Head CT: 2 mSv
- Chest CT: 7 mSv
- Abdominal CT: 8 mSv
- Pelvic CT: 6 mSv

You may also become anxious from lying in a tight space without moving. Please let the study doctor know if you have a fear of enclosed spaces (claustrophobia).

Contrast dye for CT scans and MRI: Contrast dye is usually injected when you get a CT scan or MRI. The contrast dye may cause pain or burning when it is injected. It could make your kidney function get worse if you already have kidney disease or if you have not had enough liquids that day and are dehydrated. The contrast dye may also cause an allergic reaction. This could be severe and life-threatening.

Genetic Research Risks: The pharmacogenomics and biomarker research that may be performed using your tissue and blood samples may involve genetic testing. Procedures have been put into place to make sure that any results from genetic research cannot be linked to you. However, there is a possibility that information from your participation in this study could negatively affect you or your family in some way if a genetic disorder were discovered.

OTHER RISKS

Since the study drug combinations are investigational, we don't know all of the risks of this treatment.

All study treatments could cause an allergic reaction. If not treated right away, this reaction could become life threatening. Get medical help and contact the study doctor **right away** if you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue, or neck. Other allergic reactions may include rash, hives, or blisters.

It is important that you tell us about all symptoms and side effects that you have as soon as they happen, whether or not you think they are caused by the study treatment. The phone numbers for the study team are on the first page of this document.

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PREGNANCY RELATED RISKS, USE OF BIRTH CONTROL, & BREASTFEEDING

Niraparib and Dostarlimab (TSR-042) may cause harm to unborn babies when given to a pregnant woman. You should not join this study if you are breastfeeding.

Niraparib

Niraparib may have negative effects on an unborn baby. ***You should not join this study if you are pregnant or planning to become pregnant***. In addition, you should not get pregnant for 180 days after your last dose of Niraparib.

We do not know all of the effects of niraparib at this time. Animal studies in a drug similar to niraparib have been shown to cause a decrease in the number of cells that produce eggs in women's ovaries (reproductive organs).

If you are a woman who can get pregnant, you will need to use high effective birth control while in this study and for 180 days after your last dose of niraparib. You will have a pregnancy test before you can enter the study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods of birth control may not be allowed to be used during this study.

Tell your study doctor if you are pregnant. If you get pregnant during the study, you will not receive any more niraparib, but you may stay in the study for follow-up. You must not breastfeed an infant (or store breastmilk for use) while taking the Study Drug and for 30 days after your final dose of niraparib.

Male Participants

- To be in the study, male participants must closely follow the contraception (methods or ways to prevent pregnancy) requirements.
- You must use a condom and must not donate sperm during niraparib therapy and for 90 days after receiving the last dose.
- If you are sexually active with a woman who can become pregnant, you and your partner must use a highly effective method of birth control while you are participating in this study and for 90 days after your last dose of niraparib. You must not donate sperm for 90 days after your last dose.
- Animal studies have shown that niraparib can cause a reversible decrease in sperm count. If you agree to participate in this study, you are expected to fully inform your female sexual partner(s) that you are in a clinical research study of an investigational drug, and that the effects of the drug on human sperm, an unborn baby and on a pregnant woman are unknown. You are also expected to provide your female sexual partner(s) with the information on the acceptable birth control methods described by your Study Doctor and to provide her with

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contact information for the Study Doctor for any additional questions. There have been no studies of these study treatments in pregnant women. The effects on sperm, a pregnancy, or a nursing child are not fully known.

If your female partner gets pregnant while you're in this study or within 90 days after your last dose of study drug, tell your Study Doctor or study nurse right away as they are required to follow up and document the course and the outcome of all pregnancies. Your Study Doctor may ask the pregnant woman's permission to review her medical records and the infant's medical records up to delivery, if applicable. Your Study Doctor will share the information about your pregnant partner and the baby with the Sponsor to help understand the effects, if any, that the Study Drug may have on the pregnancy and maybe the child.

Female Patients

If you are able to have children, you will be given a pregnancy test at Screening, and if the result is positive, you will not be able to be in this study.

To participate in the study, female study patients who can become pregnant must follow the birth control requirements. ***In order to reduce the chance of pregnancy, you must use 2 highly effective method of birth control throughout the study and for 180 days after your last dose of study drug***.

If you are already using a method of birth control, your Study Doctor or the study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

Your study doctor will talk to you about the types of birth control that you can use while taking part in this study. They will help you select birth control that is the best choice for you. The study doctor will instruct you in correct use of your selected birth control methods. They will review your responsibility to use this birth control consistently and correctly at each visit.

Birth control methods, even when used properly, are not perfect. If you or your partner becomes pregnant during the study, or you want to stop using birth control during the study, you should tell the study doctor immediately. Your doctor will remove you from the study if you stop using birth control or you become pregnant.

<u>Acceptable Birth Control Methods Include:</u>

- Combined (estrogen and progestogen containing) hormonal birth control; birth control pill or patch, device inserted into vagina,
- Progestogen-only hormonal birth control by injection,
- Intrauterine device (IUD),
- Intrauterine hormone-releasing system (IUS),

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- Tubes tied,
- Vasectomy for male partner,
- Condom with spermicide for male partner,
- Sexual abstinence, if this is your preferred and usual lifestyle

You should talk with your doctor which of these birth control methods are best for you.
If you become pregnant or think you may be pregnant during the study, you must stop taking the study drugs and contact the study site right away. You will be asked to withdraw from the study. The Study Doctor is required to follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished.

Pregnancy Follow Up

If your female partner becomes pregnant while you are in this study or within 90 days after your last dose of study drug, tell your Study Doctor right away as they are required to follow up and document the course and the outcome of all pregnancies. We will follow-up with you or your pregnant partner until the delivery of the baby. Your Study Doctor may seek the pregnant woman's permission to review her medical records and the infant's medical records up to delivery, if applicable. Your Study Doctor will share the information about your pregnant partner and the baby with the Sponsor to help understand the effects, if any, that the Study Drug may have on the pregnancy and/or the baby.

BENEFITS

It's possible that your cancer or cancer symptoms may improve because you are taking part in this study, but there is no guarantee that you'll benefit in any way. Your participation in this research may help future cancer patients.

If a commercial product is developed from this research study, rights to the commercial product will belong to GlaxoSmithKline (GSK) and its collaborators (persons or companies partnering with GSK). You and your family will not receive any financial benefits or compensation from, or have rights in any developments, inventions, or other discoveries that might come out of this research.

ALTERNATIVE TREATMENTS

Instead of taking part in this study, you may choose to have treatment with other cancer drugs or treatment methods. These options may include any current standard treatment for your type of cancer. Your study doctor will talk with you about alternate treatments available for your form of cancer. They will talk with you about the risks and benefits of the alternative treatments.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

Enrollment in this study may keep you from being in other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- GSK (the manufacturer of the study product) and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and University of Washington.
- Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If you authorize others to see your medical record, they would see a copy of this consent form.

How Is My Genetic Information Protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevent health insurance companies or group health plans from

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

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PAYMENT FOR PARTICIPATION

There is no payment for being in this study.

COSTS

If you join this study, you may have some extra costs. Your insurance company might pay these costs, but some insurance policies do not cover these costs. We could help find out whether your insurance company would cover these costs.

The extra costs are:

- Cost of tests that are given more often than usual,
- Cost of standard doctor visits, the costs of giving you the study drugs, scans, tissue collections (biopsies) and lab tests,
- Cost of any other medical care needed, including treatment of side effects, because of this study.
- Cost of purchasing a blood pressure device (if needed)

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

You would **not** be billed for:

- Niraparib or Dostarlimab (TSR-042)
- The cost of collecting any fresh tumor biopsies or blood samples to be used for research tests

WHAT IF YOU GET SICK OR HURT AFTER YOU JOIN THIS STUDY?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact Elizabeth Swisher, MD. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You do not lose any legal right(s) to seek payment for treatment if you sign this form.

YOUR RIGHTS AS A PARTICIPANT

Taking part in this study is your choice. You can change your mind and drop out (withdraw) at any time. If you do not to participate or decide to withdraw, there will be no penalty. You won't lose any benefits you receive now or have a right to receive.

The research study team will also tell you if we learn new information that could change your mind about taking part or continuing in this research study.

If you want to drop out, you need to tell the study team so that you end the study in the safest way. The study team will also talk to you about follow-up care, if needed. They will discuss the different withdrawal options and your responsibilities with you. The study doctor may ask you to have more tests for safety reasons. You may also be asked if you would agree to take part in the follow up portion of the research study. If you agree to continue with the follow up part of the study, we will continue to collect information about your health as described above.

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.

YOUR RESPONSIBILITIES

If you join this study, you would have some responsibilities:

- Follow the schedule of study visits and procedures,
- Takes study medications as directed,
- Prevent pregnancy
- Tell us about any side effects or changes to your health

FOR MORE INFORMATION:

If you have questions or concerns about this study, you could talk to your doctor anytime. Other people you could talk to are listed below.

If You Have Questions About:	**Call:**
This study (including complaints and requests for information)	206-543-3669 (Dr. Elizabeth Swisher) 206-606-7551 (Phase 1 Research Coordinator)

If you get sick or hurt in this study	206-598-6190 (Dr. Elizabeth Swisher or Oncology Fellow on-call)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-1113 (Patient Finance, FHCC)

Emergency number (24 hours): 206-598-6190

Please read the following statements, mark your choice, and write your initials.

Optional Blood Samples:

I agree to allow samples of my blood to be collected for research testing for this study.

☐ Yes _____ (Subject's Initials)

☐ No _____ (Subject's Initials)

Optional Tumor Tissue Biopsy at Progression:

I agree to have an additional tumor biopsy to be collected for research testing if my cancer gets worse (progresses).

☐ Yes _____ (Subject's Initials)

☐ No _____ (Subject's Initials)

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FUTURE RESEARCH:

Researchers would like to keep your unused blood and tissue for future research related to this study. In the future, new tests may become available in areas such as genetics, molecular and cellular biology, or immunology to study the nature of disease. Blood and tissue leftover from this study will be kept and used in future research to learn more about breast, ovarian, and pancreatic cancer. Your samples will be collected and stored for future research at the University of Washington. Any test results or data gathered from this research in the future will not be available to you. If any discoveries, patents, or products come from these future tests, you will not have any rights to payment or be given credit for them.

Subject identifiers will be removed from any samples that are stored for future testing. Your samples will be given a code that does not identify you personally and any information that is kept that links to these codes will be stored securely in the laboratory that performs the testing. After all identifiers are removed, your samples could be used for future research studies or distributed to another investigator for future research studies without requesting additional informed consent from you.

This choice is optional and is not required for you to participate in the treatment portion of the study. If you choose to allow storage of your leftover samples, we will keep them for an unlimited period of time. If you decide you do not want to have your samples used for this research, you will need to contact the University of Washington in writing. Please read the following statement, mark your choice and write your initials:

I agree to allow my leftover samples to be stored and used for future cancer research.

☐ Yes _____ (Subject's Initials)

☐ No _____ (Subject's Initials)

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SIGNATURES

Subject: If you have read this form (or had it read to you), asked any questions, and agree to participate, please sign:

_____
Participant / Printed Name

_____ _____
Participant Signature Date

Witness: If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

_____
Witness or Interpreter / Printed Name, Signature, and Date

Researcher's Statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

_____
Person obtaining consent signature / Printed Name

_____ _____
Person obtaining consent / Signature Date

Protocol: CC10020
Current version date: 05Dec2024
Previous version date: 26Sep2024
Copies to: Subject
Subject's Medical Record