# A Phase 3, Randomized, Double-blind, Multicenter Study of Dostarlimab (TSR-042) plus Carboplatin-paclitaxel versus Placebo Plus Carboplatin-paclitaxel in Patients with Recurrent or Primary Advanced Endometrial Cancer (RUBY)

Published: 10-12-2019
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This study has been transitioned to CTIS with ID 2023-506551-23-00 check the CTIS register for the current data. This study has two parts. The purpose of the first part of the study is to investigate if the investigational drug called dostarlimab (...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Uterine, pelvic and broad ligament disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52421

**Source**
ToetsingOnline

**Brief title**
RUBY / 4010-03-001 / ENGOT EN-6 / GOG-3031 / GSK 213361

### Condition

- Uterine, pelvic and broad ligament disorders

**Synonym**
endometrial cancer / uterine cancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** TESARO, Inc.
**Source(s) of monetary or material Support:** TESARO;Inc.

## Intervention

**Keyword:** Carboplatin-paclitaxel, Dostarlimab, Endometrial Cancer, Niraparib, Phase III

## Outcome measures

### Primary outcome

Primary Endpoints for Part 1:

The primary efficacy endpoint of PFS is based on the investigator assessment, which is defined as the time from the date of randomization to the earliest date of radiographic assessment of PD or death by any cause in the absence of PD, whichever occurs first. Tumor response will be evaluated using RECIST v.1.1.

The primary efficacy endpoint of overall survival is defined as the time from randomization to the date of death by any cause.

Primary Endpoint for Part 2:

The primary efficacy endpoint of PFS is based on the investigator assessment, which is defined as the time from the date of randomization to the earliest date of radiographic assessment of PD or death by any cause in the absence of PD, whichever occurs first. Tumor response will be evaluated using RECIST v.1.1.

Overall Survival (OS) is a primary endpoint for Part 1, and is defined as the time from randomization to the date of death by any cause.

**Secondary outcome**

Secondary efficacy endpoints are the following:

• OS, defined as the time from randomization to the date of death by any cause

• PFS based on BICR assessment, defined as the time from randomization to the earliest date of assessment of PD per RECIST v.1.1 or death by any cause in the absence of PD per RECIST v.1.1, whichever occurs first

• ORR based on BICR and Investigator assessment, defined as the proportion of subjects with a best overall response (BOR) of complete response (CR) or partial response (PR)

• DOR based on BICR and Investigator assessment, defined as the time from the first documentation of CR or PR until the time of the first documentation of subsequent PD per RECIST v.1.1 or death by any cause in the absence of PD per RECIST v.1.1, whichever occurs first

• DCR based on BICR and Investigator assessment, defined as the proportion of subjects who have achieved a BOR of CR, PR, or stable disease per RECIST v.1.1

• PFS2, defined as the time from treatment randomization to the date of assessment of progression on the first subsequent anticancer therapy following study treatment or death by any cause, whichever is earlier

• PRO assessment of treatment using EQ-5D-5L, EORTC QLQ-C30, and EORTC QLQ EN24

• PK and immunogenicity of dostarlimab (Part 1 and Part 2) and PK of niraparib when administered in combination with dostarlimab (Part 2 only)

# Study description

## Background summary

The use of dostarlimab and niraparib in combination with carboplatin and paclitaxel in this study are experimental or investigational, meaning that the four drugs have never been approved to be used together for this purpose.

Dostarlimab is an investigational drug, which means that it has not been approved by any regulatory authorities, including the United States Food and Drug Administration (FDA) and European Medicines Agency (EMA). At this time, dostarlimab cannot be prescribed for this disease (outside of the study).

Niraparib is a targeted therapy that has been approved by the FDA and EMA for the treatment of certain types of ovarian cancer.
Carboplatin and paclitaxel are types of chemotherapy that have been approved by the FDA and the EMA for treatment of other cancer types.
Dostarlimab belongs to a class of drugs called PD-1 inhibitors that use the own immune system to treat cancer (immuno-therapy). It is designed to stop cancer from growing by helping the immune system recognize and fight the cancer.

Dostarlimab is designed to help the immune system by attaching to a protein called PD-1 and stopping one of the signals that keeps the immune system from recognizing the cancer. This may help the immune system attack and destroy the cancer cells. Other drugs that work in a similar way have already been approved in some countries and used for the treatment of other cancers.

## Study objective

This study has been transitioned to CTIS with ID 2023-506551-23-00 check the CTIS register for the current data.

This study has two parts.

The purpose of the first part of the study is to investigate if the investigational drug called dostarlimab (also known as TSR-042) in combination with standard chemotherapy (carboplatin and paclitaxel) will improve the treatment of endometrial cancer. This part of the study is closed to new participants.

The second part is to find out if adding a medication called niraparib to dostarlimab in combination with chemotherapy (carboplatin and paclitaxel), can help delay worsening of endometrial cancer.

## Study design

This is a Phase 3, randomized, double-blind, multicenter study consisting of 2 parts. Part 1 is to evaluate the efficacy and safety of treatment with

dostarlimab plus carboplatin-paclitaxel followed by dostarlimab versus treatment with placebo plus carboplatin-paclitaxel followed by placebo in subjects with recurrent or primary advanced (Stage III or IV) endometrial cancer. Part 2 is to evaluate the efficacy and safety of treatment with dostarlimab plus carboplatin-paclitaxel followed by dostarlimab plus niraparib versus treatment with placebo plus carboplatin-paclitaxel followed by placebo in subjects with recurrent or primary advanced (Stage III or IV) endometrial cancer. Eligible subjects will be enrolled in Part 1 until enrollment is complete, then Part 2 will open for enrollment. Part 1 subjects may not enroll in Part 2. Part 1 and Part 2 will each have an experimental and control arm as follows:

Part 1: Eligible subjects will be randomized in a 1:1 ratio to the following:
• Arm 1: Subjects will receive dostarlimab intravenous (IV) plus carboplatin paclitaxel followed by dostarlimab IV .
• Arm 2: Subjects will receive placebo IV plus carboplatin-paclitaxel followed by placebo IV.

Subjects in Arm 1 and Arm 2 will be stratified by MMR/MSI status as dMMR/MSI-H or MMRp/MSS, prior external pelvic radiotherapy (yes or no), and disease status (recurrent, primary Stage III, or primary Stage IV). For local determination of MMR/MSI status, IHC, next-generation sequencing (NGS), and polymerase chain reaction (PCR) assays will be accepted. Approximately 470 subjects are planned for enrollment in Part 1.

Part 2: Eligible subjects will be randomized in a 2:1 ratio to the following:
• Arm 3: Subjects will receive dostarlimab IV plus carboplatin-paclitaxel followed by dostarlimab IV plus niraparib orally (PO).
• Arm 4: Subjects will receive placebo IV plus carboplatin-paclitaxel followed by placebo IV and placebo PO.

Subjects in Arm 3 and Arm 4 will be stratified by MMR/MSI status as dMMR/MSI H or MMRp/MSS, prior external pelvic radiotherapy (yes or no), and disease status (recurrent, primary Stage III, or primary Stage IV). Approximately 270 subjects are planned for enrollment in Part 2. The randomization schedules will be independent for Part 1 and Part 2.

This study consists of a Screening Period (Day -28 to Day -1), a Treatment Period, an End-of-Treatment (EOT) Visit, a Safety Follow-up Visit, and a Survival Assessment Period.

During the Treatment Period, study drug administration will occur in 3-week cycles for the first 6 cycles and in 6-week cycles for all following cycles starting with Cycle 7.

Part 1:
• Arm 1: Subjects will receive dostarlimab IV in combination with

carboplatin-paclitaxel every 3 weeks (Q3W) for 6 cycles starting at Cycle 1 Day 1 (Study Day 1); followed by dostarlimab IV monotherapy every 6 weeks (Q6W) starting at Cycle 7 Day 1 for up to 3 years or until progression of disease (PD), unacceptable toxicity, withdrawal of consent, Investigator*s decision, or death. Dostarlimab or placebo is to be administered prior to administration of carboplatin-paclitaxel. It is recommended that paclitaxel be administered before carboplatin; however, carboplatin may be administered first, if this is the current local institutional practice.
• Arm 2: Subjects will receive placebo IV in combination with carboplatin-paclitaxel Q3W for 6 cycles starting at Cycle 1 Day 1 (Study Day 1) followed by placebo IV Q6W starting at Cycle 7 Day 1 for up to 3 years or until PD, unacceptable toxicity, withdrawal of consent, Investigator*s decision, or death.

Part 2:
• Arm 3: Subjects will receive dostarlimab IV in combination with carboplatin-paclitaxel Q3W for 6 cycles starting at Cycle 1 Day 1 (Study Day 1); followed by dostarlimab IV Q6W in combination with niraparib PO administered daily (QD) starting at Cycle 7 Day 1, up to 3 years or until PD, unacceptable toxicity, withdrawal of consent, Investigator*s decision, or death.
• Arm 4: Subjects will receive placebo IV in combination with carboplatin-paclitaxel Q3W for 6 cycles starting at Cycle 1 Day 1 (Study Day 1); followed by placebo IV Q6W and placebo PO QD starting at Cycle 7 Day 1 for up to 3 years or until PD, unacceptable toxicity, withdrawal of consent, Investigator*s decision, or death.

Tumor imaging will be conducted Q6W (±7 days) from the randomization date until Week 25 (Cycle 8), followed by every 9 weeks (±7 days) until Week 52. Subsequent tumor imaging will be performed every 12 weeks (±7 days) until radiographic PD is documented by Investigator assessment per RECIST v1.1 followed by one additional imaging assessment 4-6 weeks later, or subsequent anticancer therapy is started, whichever occurs first. Thereafter, scans may be performed per standard of care. If a subject discontinues treatment for a reason other than PD, death, withdrawal of consent, or loss to follow-up, radiographic scans are to continue at the specified intervals.

It is required that a follow-up scan is performed a minimum of 4 weeks and up to 6 weeks after the first PD assessment by Investigator per RECIST v1.1. To continue study treatment after initial evidence of PD, subjects must be clinically stable (ie, no signs or symptoms of clinically significant PD, including worsening of laboratory values, no rapid PD, no decline in Eastern Cooperative Oncology Group (ECOG) performance status, and no progressive tumor at critical anatomical sites [eg, cord compression and intracranial tumor hemorrhage] requiring urgent medical intervention). It is highly recommended that clinically stable subjects not be discontinued until PD is confirmed.

PRO assessments (EQ-5D-5L, EORTC QLQ-C30, and EORTC-QLQ-EN24) will be collected

at every clinic visit and during every survival follow-up assessment if the questionnaires are available in the subject*s primary or preferred language.

Blood samples to assess PK and immunogenicity will be collected from all subjects before and after treatment administration. PK and immunogenicity of dostarlimab will be analyzed only in subjects administered at least 1 dose of dostarlimab and PK of niraparib (when administered in combination with dostarlimab) will be analyzed only in subjects from Part 2 who were administered at least 1 dose of niraparib. Blood samples for the analysis of exploratory
biomarkers will be collected at set timepoints during and at the end of treatment.

Collection and recording of all adverse events (AEs) for each subject will start on the day of signing the informed consent form. Nonserious AEs will be collected up until the day of the EOT Visit (see Section 7.1). Serious adverse events (SAEs) should be reported through 90 days after the last dose of study treatment or until the subject starts alternate anticancer therapy, whichever occurs first. Study drug-related SAEs will be collected through 90 days after the last dose of study treatment. Any pregnancies are to be captured through 180 days posttreatment.

**Intervention**

Part 1:
Subjects will be randomized in a 1:1 ratio to receive either dostarlimab plus carboplatin-paclitaxel or placebo plus carboplatin-paclitaxel.

Part 2:
Subjects will be randomized in a 2:1 ratio to receive either dostarlimab plus carboplatin-paclitaxel followed by dostarlimab IV plus niraparib orally or placebo plus carboplatin-paclitaxel followed by placebo IV and placebo orally.

**Study burden and risks**

For Study Drug: DOSTARLIMAB

As of January 2022, dostarlimab has been studied in about 1800 patients with advanced or recurrent solid tumors in medical research studies, with about 1160 of these patients receiving dostarlimab in combination with other medicines. 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):
• Decrease in the 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 (Anaemia)
• Underactive thyroid gland (Hypothyroidism)
• Feeling sick to the stomach (Nausea)
• Vomiting
• Frequent watery stools (Diarrhoea)
• Itchy skin
• Rash
• Fever
• Increased levels of substances in the blood produced by the liver which may be a sign of liver injury

These side effects are considered common in patients who took dostarlimab (may affect up to 1 in 10 people):
• Decreased production of adrenal hormones resulting in possible weakness and/or low blood pressure
• Overactive thyroid gland
• Inflammation of the lungs which can cause shortness of breath and difficulty breathing
• Inflammation of the pancreas causing pain in the upper abdomen. This could become severe 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

The side effects listed below require immediate medical attention or advice. Call the Investigator right away if you have any of these side effects.
• Respiratory: shortness of breath, rapid breathing, new or worse cough
• Gastrointestinal: diarrhoea, stools that are black or bloody, stomach area pain, nausea or vomiting
• 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

For Study Drug: NIRAPARIB

As of March 2021, Niraparib has been studied in more than 2244 patients in TESARO clinical trials. Niraparib capsule is marketed as ZEJULA® and is approved to treat adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in the United States and in Europe.

Niraparib is currently being studied as a single medication and as a combination therapy in a variety of cancer clinical studies.

Niraparib Side Effects experienced by patients taking niraparib as a single drug therapy:
Some of the side effects mentioned below can be life-threatening or fatal.

These side effects are considered very common in patients who took niraparib (may affect more than 1 in 10 people):
• Decrease in a type of blood cells called platelets that help stop bleeding; this may increase your risk of bleeding (thrombocytopenia)
• Decrease in red blood cells that carry oxygen; this may make you feel tired or short of breath (anemia)
• Decrease in the number of white blood cells (leukopenia) that fight infection
• Decrease in a type of white blood cells called neutrophils that fight infection; (neutropenia)
• Difficulty with emptying the bowels, often because of hard stools (constipation)
• Feeling sick to your stomach (nausea)
• Vomiting
• Reduced desire to eat (decreased appetite)
• Pain in belly (abdominal pain)
• Frequent watery stools (diarrhea)
• Upset stomach/heartburn
• Sleeplessness, trouble sleeping
• Pain or burning and frequent urination which may indicate an infection (urinary tract infection)
• Feeling weak (asthenia)
• Feeling tired, lack of energy (fatigue)
• Back pain
• Joint pain
• Breathlessness or difficulty breathing (dyspnea)
• Runny or stuffy nose (nose or upper throat infection)
• Increased blood pressure
• Feeling lightheaded or like you are about to faint (dizziness)
• Cough
• Headache
• Noticeably rapid, strong, or irregular heartbeat (palpitations)

These side effects are considered common in patients who took niraparib (may affect up to 1 in 10 people):
• Infection due to low white blood cell count (neutropenic infection)
• 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])
• Altered sense of taste; this means that foods might taste differently than you are used to

• Reduced potassium in blood
• An abnormally rapid heart rate
• Dry mouth
• Feeling anxious (anxiety)
• Mood change to feeling sad/discouraged, listless (depression)
• Impaired concentration, understanding, memory and thinking (cognitive impairment)
• Nosebleed
• Inflammation of the lining of the airways (bronchitis)
• Increased sensitivity of the skin to sunlight (photosensitivity)
• Rash
• Muscle pain
• An accumulation of fluid that causes swelling in the extremities such as lower legs, hands, and feet
• Increased liver enzyme in the blood; this may be a sign of damage to liver cells
• Increased level of creatinine in your blood; this may be a sign of kidney damage
• Decrease in weight
• Infection of the white area of the eye
• Sore, irritated, red mouth
• Swelling or irritation of the lining of the mouth, throat, esophagus, stomach, or intestines
• Allergic reaction (hypersensitivity, including anaphylaxis).

In addition to the above, the side effects below were reported by patients who were prescribed niraparib by their doctors:
• Allergic reaction (hypersensitivity*, including anaphylaxis**).
• Life-threatening allergic reaction (such as difficulty breathing, rash, localized swelling, such as tongue, throat or lips) (anaphylaxis*)
• Confusion (confusional state*: symptom that makes you feel as if you can't think clearly. You might feel disoriented and have a hard time focusing or making decisions)
• Seeing or hearing things that are not really there (hallucination**)
• Impaired concentration, understanding, memory* and thinking (cognitive impairment*)
• Inflammation of the lungs which can cause shortness of breath and difficulty breathing (non-infectious pneumonitis*)
*Observed frequency in clinical trials uncommon (may affect up to 1 in 100 people).
**No events reported in monotherapy clinical trials

Potential for new blood cancer called myelodysplastic syndrome and/or acute myeloid leukemia (MDS/AML), a new primary cancer, embolic and/or thrombotic events (blood clots):
• Niraparib belongs to a group of drugs called PARP inhibitors. This group of

drugs are suspected of causing new blood cancers known as myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Because niraparib is a PARP inhibitor there is a potential risk of developing a new blood cancer leading to leukemia.
• If you have had MDS or leukemia before entering this study, you are at increased risk for developing leukemia again and must tell your Investigator before starting this study.
• Although rare, patients in niraparib clinical trials have had MDS/AML. In a randomized trial comparing niraparib to placebo (

## Contacts

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**Scientific**
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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

Part 1 & Part 2

1. Female subject at least 18 years of age, who is able to understand the study procedures and agrees to participate in the study by providing written informed consent.
2. Subject has histologically or cytologically proven endometrial cancer with recurrent or advanced disease.
3. Subject must provide adequate tumor tissue sample at Screening for MMR/MSI status testing.
4. Subject must have primary Stage III or Stage IV disease or first recurrent endometrial cancer with a low potential for cure by radiation therapy or surgery alone or in combination, and meet at least 1 of the following criteria:
a. Subject has primary Stage IIIA to IIIC1 disease with presence of evaluable or measurable disease per RECIST v.1.1 based on Investigator*s assessment. Lesions that are equivocal or can be representative of post-operative change should be biopsied and confirmed for the presence of tumor.
b. Subject has primary Stage IIIC1 disease with carcinosarcoma, clear cell, serous, or mixed histology (containing >= 10% carcinosarcoma, clear cell, or serous histology) regardless of presence of evaluable or measurable disease on imaging.
c. Subject has primary Stage IIIC2 or Stage IV disease regardless of presence of evaluable or measurable disease.
d. Subject has first recurrent disease and is chemotherapy naïve to systemic anticancer therapy.
e. Subject has received prior neo-adjuvant/adjuvant systemic chemotherapy and had a recurrence or PD >= 6 months after completing treatment (first recurrence).
5. Subject has an ECOG performance status of 0 or 1.
6. Subject has adequate organ function, defined as follows:
a. Absolute neutrophil count >= 1,500 cells/µL
b. Platelets >= 100,000 cells/µL
c. Hemoglobin >= 9 g/dL or >= 5.6 mmol/L
d. Serum creatinine <= 1.5× upper limit of normal (ULN) or calculated CrCl >= 50 mL/min using the Cockcroft-Gault equation for subjects with creatinine levels <= 1.5× institutional ULN
e. Total bilirubin <= 1.5× ULN and direct bilirubin <= 1× ULN
f. AST and ALT <= 2.5× ULN unless liver metastases are present, in which case they must be <= 5× ULN
g. International normalized ratio or prothrombin time (PT) <=1.5× ULN and activated partial thromboplastin time <=1.5× ULN. Subjects receiving anticoagulant therapy must have a PT or partial thromboplastin within the therapeutic range of intended use of anticoagulants.
7. Contraceptive use by subjects should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
The subject is a woman of nonchildbearing potential (WONCBP) OR The subject is a woman of childbearing potential (WOCBP), using a contraceptive method that is highly effective (with a failure rate of <1% per year and, preferably, with low

user dependency) during the Treatment Period and for at least 180 days after the last dose of study treatment and agrees not to donate eggs (ova or oocytes) for the purpose of reproduction during this period.
A WOCBP must have a negative highly sensitive pregnancy test (urine or serum, as required by local guidelines) within 72 hours before the first dose of study treatment. If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.

Part 2 only:
8. Subjects must have normal BP or adequately treated and controlled hypertension (systolic BP =140 mmHg and diastolic BP =90 mmHg).
9. Subjects must be able to take medication PO.

## Exclusion criteria

Part 1 & Part 2:
1. Subject has received neo-adjuvant/adjuvant systemic anticancer therapy for primary Stage III or IV disease and:
a. has not had a recurrence or PD prior to first dose on the study OR
b. has had a recurrence or PD within 6 months of completing systemic anticancer therapy treatment prior to first dose onthe study Note: Low-dose cisplatin given as a radiation sensitizer or hormonal therapies do not exclude subjects from study participation.
2. Subject has had > 1 recurrence of endometrial cancer.
3. Subject has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent.
4. Subject has received prior anticancer therapy (chemotherapy, targeted therapies, hormonal therapy, radiotherapy, or immunotherapy) within 21 days or <5 times the half-life of the most recent therapy prior to Study Day 1, whichever is shorter.
5. Subject has a concomitant malignancy, or subject has a prior non-endometrial invasive malignancy who has been disease-free for <3 years or who received any active treatment in the last 3 years for that malignancy. Non-melanoma skin cancer is allowed.
6. Subject has known uncontrolled central nervous system metastases, carcinomatosis meningitis, or both. Note: Subjects with previously treated brain metastases may participate provided they are stable (without evidence of PD by imaging [using the identical imaging modality for each assessment, either MRI or CT scan] for at least 4 weeks prior to the first dose of study treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and have not been using steroids for at least 7 days prior to study treatment. Carcinomatous meningitis precludes a subject from study participation regardless of clinical stability.
7. Subject has a known history of human immunodeficiency virus HIV (HIV 1/2

antibodies).
8. Subject has known active hepatitis B (eg, hepatitis B surface antigen reactive) or hepatitis C (eg, hepatitis C virus ribonucleic acid [qualitative] is detected).
9. Subject has an active autoimmune disease that has required systemic treatment in the past 2 years. Replacement therapy is not considered a form of systemic therapy (eg, thyroid hormone or insulin)
10. Subject has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of systemic immunosuppressive therapy within 7 days prior to the first dose of study treatment.
11. Subject has not recovered (ie, to Grade <= 1 or to baseline) from cytotoxic therapy-induced AEs or has received transfusion of blood products (including platelets or red blood cells) or administration of colony-stimulating factors (including granulocyte colony-stimulating factor [G-CSF], granulocyte macrophage colony-stimulating factor [GM
CSF], or recombinant erythropoietin) within 21 days prior to the first dose of study drug. Note: Subjects with Grade <= 2 neuropathy, Grade <= 2 alopecia, or Grade <= 2 fatigue are an exception to this criterion and may qualify for the study.
12. Subject has not recovered adequately from AEs or complications from any major surgery prior to starting therapy.
13. Subject has a known hypersensitivity to carboplatin, paclitaxel, or dostarlimab components or excipients.
14. Subject is currently participating and receiving study treatment or has participated in a study of an investigational agent and received study treatment or used an investigational device within 4 weeks of the first dose of treatment.
15. Subject is considered a poor medical risk due to a serious, uncontrolled medical disorder, nonmalignant systemic disease, or active infection requiring systemic therapy. Specific examples include, but are not limited to, active, noninfectious pneumonitis; uncontrolled ventricular arrhythmia; recent (within 90 days) myocardial infarction; uncontrolled major seizure disorder; unstable spinal cord compression; superior vena cava syndrome; or any psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the study (including obtaining informed consent).
16. Subject is pregnant or breastfeeding or is expecting to conceive children within the projected duration of the study, starting with the screening visit through 180 days after the last dose of study treatment.
17. Subject has received, or is scheduled to receive, a live vaccine within 30 days before first dose of study treatment, during study treatment, and for up to 180 days after receiving the last dose of study treatment.

Part 2 only:
18. Subject has received prior therapy with a PARP inhibitor.
19. Subject has clinically significant cardiovascular disease.
20. Subject has any known history or current diagnosis of myelodysplastic syndrome or acute myeloid leukemia.

21. Subject is at increased bleeding risk due to concurrent conditions.
22. Subject has a known hypersensitivity to niraparib components or excipients.
23.Subject has participated in Part 1 of this study.

# Study design

## Design

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|---|---|
| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 10-07-2020 |
| Enrollment: | 25 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Jemperli (Dostarlimab) |
| Generic name: | TSR-042 / GSK4057190A |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Zejula (Niraparib) |
| Generic name: | Niraparib / GSK3985771 |
| Registration: | Yes - NL intended use |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 10-12-2019 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 03-03-2020 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 25-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-08-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 06-03-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 10-11-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 15-02-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO | |

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|---|---|
| Date: | 01-05-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 08-09-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 01-10-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-05-2023 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-09-2023 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 04-01-2024 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-01-2024 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-05-2024 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam |

(Rotterdam)

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EU-CTR | CTIS2023-506551-23-00 |
| EudraCT | EUCTR2019-001576-11-NL |
| ClinicalTrials.gov | NCT03981796 |
| CCMO | NL70807.078.19 |