NIRAPARIB (GSK3985771); DOSTARLIMAB (TSR-042)

3000-03-005/ENGOT-OV44/ GSK 213350 (FIRST)

The FIRST (**F**irst-line ovarian cancer treatment with N**ir**aparib plu**s** **T**SR-042) Study:

A RANDOMIZED, DOUBLE-BLIND, PHASE 3 COMPARISON OF PLATINUM-BASED THERAPY WITH TSR-042 AND NIRAPARIB VERSUS STANDARD OF CARE PLATINUM-BASED THERAPY AS FIRST-LINE TREATMENT OF STAGE III OR IV NONMUCINOUS EPITHELIAL OVARIAN CANCER

Sponsor:	TESARO, Inc., a Glaxo Smith Kline Company 1000 Winter Street, Suite 3300 Waltham, MA 02451	TESARO Bio Netherlands B.V, a Glaxo Smith Kline Company Joop Geesinkweg 901 1114AB Amsterdam-Duivendrecht The Netherlands
Medical Monitor:	PPD PPD, MD PPD Direct Phone: PPD	PPD
Principal Investigator:	Anne-Claire Hardy-Bessard, MD, GINECO	
Scientific Coordinator:	PPD, MD, PhD, GINECO	
Biostatistician:	PPD, Project Statistician, GSK PPD, MD, PhD, GINECO	
CRO:	CCI	
IND No.:	126,472	
EudraCT No.:	2018-000413-20	
EU CT No.:	2024-510605-28	
NCT No.:	NCT03602859	
Development Phase:	3	
Date of Original Protocol:	27 April 2018 (Version 1.0), 07 May 2018 (Version 2.0)	
Date of Amendment 1:	11 July 2018	
Date of Amendment 2:	01 November 2018	
Date of Amendment 3:	17 July 2019	
Date of Amendment 4:	14 January 2020	
Date of Amendment 5:	19 August 2020	
Date of Amendment 6:	01 February 2022	
Date of Amendment 7:	07 June 2024	
Date of Amendment 8:	24 October 2024	
Date of Amendment 9:	03 March 2025	
Date of Amendment 10:	08 Aug 2025	
Version of Protocol:	Version 12.0	

SPONSOR SIGNATURE PAGE

Declaration of Sponsor or Responsible Medical Officer

Title (Study Number): A Randomized, Double-Blind, Phase 3 Comparison of Platinum-Based Therapy with TSR-042 and Niraparib Versus Standard of Care Platinum-Based Therapy as First-line Treatment of Stage III or IV Nonmucinous Epithelial Ovarian Cancer (3000-03-005/ENGOT-OV44/GSK 213350 [FIRST])

This study protocol was subjected to critical review and has been approved by the Sponsor. The information it contains is consistent with the current risk/benefit evaluation of the investigational products and other study treatments as well as with the moral, ethical, and scientific principles governing clinical research as set out in the Declaration of Helsinki and the guidelines on Good Clinical Practice.

_____

_____

Rébécca Phaëton, MD Date DD Month YYYY

Senior Medical Director, GSK

The signed page is a separate document.

INVESTIGATOR'S AGREEMENT

I have received and read the Investigator's Brochures for niraparib and dostarlimab (formerly referred to as TSR-042). I have read the 3000-03-005/ENGOT-OV44/GSK 213350 (FIRST) protocol and agree to conduct the study as outlined. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

_____

Printed Name of Investigator

_____

Signature of Investigator

_____

Date

PROTOCOL AMENDMENT SUMMARY OF CHANGES

Table 1: Document History

Document	Date	Document Number
Amendment 10 (Version 12.0)	08 Aug 2025	TMF-22277333
Amendment 09 (Version 11.0)	03 March 2025	TMF-21225961
Amendment 08 (Version 10.0)	24 October 2024	TMF-19990252
Amendment 07 (Version 9.0)	07 June 2024	TMF-16341903
Amendment 06 (Version 8.0)	01 February 2022	TMF-14338694
Amendment 05 (Version 7.0)	19 August 2020	TMF-11847898
Amendment 04 (Version 6.0)	14 January 2020	TMF-19350677
Amendment 03 (Version 5.0)	17 July 2019	TMF-1903499
Amendment 02 (Version 4.0)	01 November 2018	TMF-14456931
Amendment 01 (Version 3.0)	11 July 2018	TMF-19350665
Original Protocol (Version 2.0)	07 May 2018	TMF-11847688
Original Protocol (Version 1.0)	27 April 2018	TMF-19361612

Overall rationale for the current Amendment: This is a substantial amendment to CCI [redacted]

CCI [redacted]

Table 2: Summary of Changes for Amendment 10

Section(s) Affected	Description of Change	Brief Rationale
Headers, cover page, Protocol Amendment Summary of Changes, and throughout	Headers and cover page were updated with new document number and amendment information; Protocol Amendment Summary of Changes section was updated to include rationale for this amendment; editorial revisions for consistency with Sponsor's ways of working and to add clarification and/or remove discrepancies.	Editorial changes to align with the Sponsor's standard protocol template and ways of working and for accuracy, clarity, conformity, flow, and typographical error correction.
Throughout	Editorial, administrative, and document formatting revisions.	Minor changes for consistency, clarifications, and corrections to text.
Synopsis	Update of estimated date last participant completed to Q3 2029.	Update of study completion date following the incorporation of the PACT phase.
Synopsis, Section 3.1.1 Adaption to Study Design, Section 9.6 Interim Analyses, Appendix 1 Schedule of Events	Information added to reflect no further efficacy analyses will be conducted following analysis at DCO date 31 October 2024 prior to PACT phase for all ongoing patients. Consequently, scope of data collection is reduced. Adjustments to EOT Visit and Safety Follow-up visits prior to PACT reflected in the revised schedule of events (Table 15).	To provide information on the reduction of scope of data collection as a consequence of no further efficacy analysis will be carried out post DCO date 31 October 2024.
CCI [redacted]		

Section(s) Affected	Description of Change	Brief Rationale
CCI	[redacted]	[redacted]

Section(s) Affected	Description of Change	Brief Rationale
CCI		

Section(s) Affected	Description of Change	Brief Rationale
CCI		

SYNOPSIS

Name of Sponsor/Company: TESARO, Inc., a Glaxo Smith Kline Company
Name of Investigational Treatment Combination: Niraparib and dostarlimab (formerly referred to as TSR-042)
Name of Active Ingredients: Niraparib and dostarlimab
TITLE OF STUDY: A Randomized, Double-Blind, Phase 3 Comparison of Platinum-Based Therapy with TSR-042 and Niraparib Versus Standard of Care Platinum-Based Therapy as First-line Treatment of Stage III or IV Nonmucinous Epithelial Ovarian Cancer (3000-03-005/ENGOT-OV44/GSK 213350) (FIRST)
Study Center(s): Approximately 225 sites in approximately 25 countries
Principal Investigator: Anne-Claire Hardy-Bessard, MD, GINECO

Studied Period (years):	**Phase of Development:**
Estimated date first participant enrolled: Q3 2018 Estimated date last participant completed: Q3 2029	Phase 3

Objectives:

Primary Objective

- To compare the progression free survival (PFS) of platinum-based combination therapy, dostarlimab, and niraparib treatment (Arm 3) to platinum-based combination therapy and niraparib treatment (Arm 2) in participants with Stage III or IV high-grade nonmucinous epithelial ovarian cancer.

CCI [redacted]
CCI [redacted]

Secondary Objectives

CCI [redacted]
CCI [redacted]

- Overall survival (OS, CCI [redacted]
- Blinded Independent Central Review (BICR)-determined PFS per RECIST v1.1 criteria
- Health related quality of life (HRQoL)
- Time to first subsequent therapy (TFST)
- Time to second subsequent therapy (TSST)
- Time from randomization to the earliest date of assessment of progression after initiation of subsequent anticancer therapy following study treatment or death by any cause (PFS2)

- Objective response rate (ORR) per CCI [redacted]
- Duration of response (DOR) per CCI [redacted] CCI [redacted]
- Disease control rate (DCR) per CCI [redacted] CCI [redacted]
- Pharmacokinetics (PK) and immunogenicity of dostarlimab
- PK of niraparib

Secondary objectives for platinum-based combination therapy (Arm 1), platinum-based combination therapy and niraparib (Arm 2) and platinum-based combination therapy, dostarlimab, and niraparib (Arm 3) for all participants will evaluate:

- Safety and tolerability

Exploratory Objectives

CCI [redacted]

Methodology:

Overall Study Design

This is a global, multicenter, randomized, double-blind, controlled Phase 3 study in participants with newly diagnosed, Stage III or IV high-grade nonmucinous epithelial ovarian, fallopian tube, or peritoneal cancer (collectively referred to as "ovarian cancer"). The currently recommended standard-of-care (SOC) for the first-line treatment of Stage III or IV ovarian cancer is a combination of paclitaxel-carboplatin, with or without concurrent and maintenance bevacizumab. The use of bevacizumab must be determined prior to randomization.

The study is open to participants with inoperable ovarian cancer, participants who have macroscopic residual disease at the end of the primary debulking surgery (PDS) and have recovered from PDS and participants for whom platinum-based combination neoadjuvant chemotherapy (NACT) is planned. Participants with Stage IIIC disease that has been completely resected (also known as complete cytoreduction score of '0' [CC0]) are eligible if the following criteria is present: aggregate ≥5 cm extra-pelvic disease during PDS as assessed by the Investigator. The use of bevacizumab is optional and permitted if considered SOC per local treatment guidelines and/or practices.

All eligible enrolled participants will receive SOC during the Cycle 1 Chemotherapy Run-In Period before randomization at Cycle 2.

Treatment Arm 1 consists of SOC and intravenous (IV) dostarlimab placebo followed by oral niraparib placebo and IV dostarlimab placebo in the maintenance phase of treatment. Arm 2 consists of SOC and IV dostarlimab placebo followed by oral niraparib and IV dostarlimab placebo maintenance therapy. Arm 3 consists of SOC and IV dostarlimab followed by oral niraparib and IV dostarlimab maintenance therapy.

CCI [redacted]

This study is designed to enable rapid adaptation to evolving treatment paradigms for participants with advanced ovarian cancer. This ensures that study participants will have access to the most current regimen with or without investigational treatment while maintaining the integrity of the study. Full details on adaptations to the study design are located in the protocol.

In Amendment 2, dated 01 November 2018, CCI [redacted] There was no change to participants with *BRCA*wt HRRpos and *BRCA*wt HRRneg/not determined status; they continued to be randomized to Arm 1, Arm 2, or Arm 3. Arm 1 *BRCA*mut participants who were in the Chemotherapy Treatment Period when the amendment was implemented completed the 6 cycles of chemotherapy. Following completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, these participants were allowed to start niraparib maintenance therapy as "follow-up anticancer treatment" at the Investigator's discretion. Arm 1 *BRCA*mut participants who were in the Maintenance Treatment Period when the amendment was implemented were allowed to start niraparib maintenance therapy as "follow-up anticancer treatment" if the time after Cycle 6 Day 1 of the Chemotherapy Treatment Period was ≤12 weeks. In order to facilitate this adaptation, Investigators were unblinded for Arm 1 *BRCA*mut participants enrolled prior to implementation of this amendment.

CCI [redacted] Therefore, the SOC for treatment of Stage III or IV ovarian cancer was updated to include the administration of a PARP inhibitor with or without bevacizumab during the maintenance period.

As a result, following Sponsor and Steering Committee discussions, participants were not enrolled into Arm 1 after Amendment 4 was approved at each site. Participants in Arm 1, Chemotherapy Treatment Period who are receiving bevacizumab when Amendment 4 is implemented, may continue the 6 cycles of chemotherapy. Following completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants may start bevacizumab maintenance therapy at the Investigator's discretion. Participants in Arm 1, Maintenance Treatment Period who are receiving bevacizumab when Amendment 4 is implemented may continue bevacizumab maintenance therapy at the

Investigator's discretion. Investigators will remain blinded for those participants enrolled in Arm 1 and receiving bevacizumab at the time of implementation of Amendment 4.

Participants in Arm 1, Chemotherapy Treatment Period not receiving bevacizumab when Amendment 4 is implemented, may continue the 6 cycles of chemotherapy. Following completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants may start niraparib maintenance therapy as "follow-up anticancer treatment" at the Investigator's discretion. Participants in Arm 1, Maintenance Treatment Period not receiving bevacizumab when Amendment 4 is implemented may start niraparib maintenance therapy as "follow-up anticancer treatment" if the time after Cycle 6 Day 1 of the Chemotherapy Treatment Period is ≤12 weeks. Participants will be permitted to remain on study until withdrawal of consent, sponsor decision to terminate study or death. Participants who do not elect to receive niraparib or bevacizumab maintenance will be discontinued from the study treatment and given the option to stay in the study for follow up. Investigators will be unblinded for those participants enrolled in Arm 1 and not receiving bevacizumab at the time of implementation of Amendment 4. The schedule of events for these participants is shown in Table 18.

In total, CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]

Following the analysis conducted at the 31 October 2024, DCO date, no further efficacy analyses will be conducted for the study. Consequently, the scope of data collection is reduced for those ongoing participants still receiving study treatment and in follow-up, aligning with the prior to PACT schedule of events.

Participants may access the treatment outside of the study protocol prior to PACT by the DCO date for the final analysis by a rollover study, Managed Access route, or other potential mechanisms of access, or if commercially available and accessible. Following the DCO date for the final analysis, Study 213350 (FIRST) may move into the PACT phase where the study remains open only to provide continued access to study treatment for participants who are continuing to derive clinical benefit in the opinion of the Investigator and cannot access the treatment outside of the study protocol by the time of the final analysis DCO date. At that time, the collection of new data for participants who no longer receive study intervention will stop entirely and will be considered to have completed the study. The clinical study database will be closed to new data following the DCO date for the final analysis. Participants still clinically benefiting from study intervention at the time of the PACT phase may continue to receive study treatment and only serious adverse events (SAEs), AEs leading to study intervention discontinuation, overdose, adverse events of special interest (AESIs), and pregnancy cases will be reported directly to the sponsor. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

[b] All participants previously randomized to placebo and not receiving bevacizumab will be unblinded and provided the option to receive niraparib maintenance if they have received chemotherapy or discontinued chemotherapy ≤12 weeks.

Pre-Screening Period

During the Pre-Screening Period, participants may sign a pre-Screening informed consent form consenting to collection of the required tumor tissue sample The Pre--Screening Period can take place within the 14 days prior to the Screening Period, defined as the date of signing the main informed consent, but does not have to encompass the full period. A participant can move to the Screening Period once deemed able.

Screening Period

During the Screening Period, participants will sign the main consent form and complete all assessments required to determine eligibility into the study. The Screening Period is within 28 days prior to Cycle 1 Day 1 (C1D1) of the Chemotherapy Run-In Period.

Chemotherapy Run-In Period (Cycle 1)

Prior to randomization, all participants will receive 1 cycle of paclitaxel-carboplatin during a Chemotherapy Run-In Period. Participants may also receive bevacizumab with paclitaxel-carboplatin as part of SOC per local practice. However, bevacizumab must not be administered

less than 28 days before or 28 days following major surgery, and post-operative incisions must be fully healed. The determination to use bevacizumab must be made prior to randomization. Participants will be randomized following Cycle 1, prior to treatment in Cycle 2 during the Chemotherapy Treatment Period. Randomization may occur up to one week prior to Cycle 2 Day 1.

Intraperitoneal (IP) chemotherapy and weekly paclitaxel will not be allowed.

Chemotherapy Treatment Period (Cycles 2 to 6)

Prior to the chemotherapy administration of Cycle 2, all of the following criteria must be met:

- Absolute neutrophil count (ANC) ≥1,500 cells/μL, or ≥1,000 cells μL if granulocyte-colony stimulating factor (G-CSF) is to be administered
- Platelet count ≥100,000 cells/μL
- Hemoglobin ≥8 g/dL

Thereafter, re-treatment criteria for remaining chemotherapy Cycles 3 to 6 should be in accordance with treatment guidelines per local practice.

Following randomization, participants who have inoperable disease or who have undergone PDS will receive cycles 2 to 6 of paclitaxel-carboplatin, for a total of 6 cycles of chemotherapy inclusive of Cycle 1. Participants will also receive dostarlimab/placebo in combination with paclitaxel-carboplatin started with Cycle 2 of chemotherapy, for a total 5 cycles. Bevacizumab may continue per local practice.

Participants for whom NACT is planned will receive 3 to 4 cycles of paclitaxel-carboplatin prior to interval debulking surgery (inclusive of Cycle 1) and 2 to 3 additional cycles of paclitaxel-carboplatin following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor. These participants will also receive dostarlimab/placebo, which will be started with Cycle 2 of chemotherapy, for a total of 5 cycles. Chemotherapy and dostarlimab/placebo will resume upon recovery of surgery. Participants for whom NACT is planned may receive bevacizumab with paclitaxel-carboplatin per local practice; however, bevacizumab must not be administered less than 28 days before or 28 days following major surgery, and post-operative incisions must be fully healed.

IP chemotherapy and weekly paclitaxel will not be allowed.

Maintenance Treatment Period

Participants who complete the Chemotherapy Treatment Period without progressive disease (PD) will start the Maintenance Treatment Period 3 weeks after Cycle 6 Day 1. Dostarlimab/placebo ± bevacizumab will also continue in the Maintenance Treatment Period in combination with oral niraparib maintenance treatment, per study schedule. However, the start of niraparib will be delayed at least 6 weeks after Cycle 6 Day 1 and up to 9 weeks after to allow for adequate recovery of hematologic toxicity.

Prior to starting the first dose of oral niraparib maintenance treatment, participants must have a complete blood count (CBC) that demonstrate adequate recovery from hematologic toxicity from chemotherapy:

- Absolute neutrophil count ≥1,500 cells/µL
- Platelet count ≥100,000/µL
- Hemoglobin ≥9 g/dL
- Blood pressure (BP) <150/100 mmHg

Weekly CBC is to be performed for the first 4 weeks from the start of niraparib in the Maintenance Treatment Period.

The recommended order of administration is provided below, unless local clinical practice or institutional policies differ:

- During the Chemotherapy Treatment Period, CCI [redacted] CCI [redacted] CCI [redacted].
- During the Maintenance Treatment Period, CCI [redacted] CCI [redacted]

Study Conduct

Treatment Cycles

Treatment cycles are 21 days long.

Visits should occur within ±3 days of the scheduled visit. This window also applies to study procedures, with all procedures allowed to be performed up to ±3 days of the scheduled visit. All times should be recorded using the 24-hour clock (e.g., 23:20, not 11:20 PM).

Interval Debulking Surgery (IDS)

Participants for whom NACT is planned will receive 3 to 4 cycles of chemotherapy treatment prior to IDS (inclusive of Cycle 1) and an additional 2 to 3 cycles following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor. Initiation of the subsequent cycles post-IDS will be upon post-operative recovery of the participant. Bevacizumab should not be administered less than 28 days before or 28 days following major surgery. Additionally, participants indicated for IDS will also have a pre-operative scan during the chemotherapy period.

Radiographic Evaluation for Primary Outcome

All participants are required to undergo radiographic evaluation throughout the study. RECIST v1.1 tumor assessment via computed tomography (CT) or magnetic resonance imaging (MRI) scan of the chest/abdomen/pelvis and clinically indicated areas is required at Screening, prior to IDS (if applicable), prior to the start of the maintenance period, and at regular intervals throughout the maintenance. If there are lesions in the chest and/or clinically indicated areas at Screening, then these areas should be scanned at each subsequent timepoint. Otherwise, only

abdomen/pelvis are required after Screening. During the Maintenance Treatment Period, imaging to assess disease status must occur at C1D1 (±14 days) of the Maintenance Treatment Period and then every 4 months (±7 days) for 24 months, followed by every 6 months (±7 days) during the third year and every year thereafter until PD or initiation of follow-up anticancer therapy. Tumor assessments should occur according to this schedule, regardless of whether study treatment is discontinued (i.e., counting from C1D1 of the Chemotherapy or Maintenance Treatment Period, as appropriate). Additional unscheduled RECIST v1.1 CT or MRI scans (of any anatomical region that may be clinically indicated) must be performed whenever disease progression is suspected based on increasing cancer antigen 125 (CA 125) values or other suspicious symptoms. PD will not be diagnosed in the case of CA 125 progression or suspicious symptoms in the absence of radiologic evidence of PD. Following completion of 3 years of maintenance therapy, participants will be evaluated clinically with annual scans and additional unscheduled scans for suspicion of disease progression based on increases in CA 125 or other suspicious symptoms. Participants may be considered for treatment beyond 3 years in consultation with the Sponsor. Prior to PACT (included in Amendment 10), RECIST v1.1. scans may occur at the time of clinical suspicion of disease progression or at an annual interval, whichever occurs first according to the PI discretion and local practice guidelines.

CCI [redacted] Clinically stable participants are those with no signs or symptoms of clinically significant or rapid progression of disease, including worsening of laboratory values or decline in performance status (ECOG) and no progressive tumor at critical anatomical sites [e.g., cord compression, intracranial tumor hemorrhage] requiring urgent medical intervention. CCI [redacted]

Patient-Reported Outcomes and Health-related Quality of Life

The following HRQoL assessments will be obtained: the European Quality of Life 5-Dimension 5-Level Scale (EQ-5D-5L), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30), and the EORTC-QLQ Ovarian Cancer Module OV28 (EORTC-QLQ-OV28). These will be collected at the following time points:

- Chemotherapy Run-In (21-day cycle): C1D1.
- Chemotherapy Treatment (21-day cycles): Cycle 2/Day 1, and every 2 cycles thereafter (Cycle 4/Day 1, ending Cycle 6/Day 1).
- Maintenance Treatment (21-day cycles): Day 1 of every cycle (i.e., every 21 days [Q21D]) ±7 days) for the first 3 cycles, Day 1 of every 3 cycles (i.e., every 9 weeks ±7 days) through 15 cycles, Cycle 17 and every 6 cycles thereafter until PD or end of study treatment. Not applicable prior to PACT (included in Amendment 10).
- Post-treatment: For participants who discontinue treatment, HRQoL assessments should be collected at the end of treatment (EOT) Visit, 30-day post EOT (±7 days) Safety Follow-up Visit, 90-day post EOT (±14 days) Long-Term Follow-up Visit, and every 180 days (±14 days) after the Long-Term Follow-up Visit (every other post-treatment assessment), which will continue until death or

the end of study data collection. Not applicable prior to PACT (included in Amendment 10).

All HRQoL assessments during the Chemotherapy Treatment and Maintenance Periods should be collected in clinic, on the day of study drug administration, prior to dosing or clinical procedures. They may be completed remotely if the participant is no longer actively returning to the site.

Biomarker, Pharmacokinetic, and Immunogenicity Assessment

CCI [redacted]

PACT Phase

Following the final DCO date, the study may move into the PACT phase. Participants who continue to receive study treatment during the PACT phase will be monitored and will receive follow-up care in accordance with standard local clinical practice. Assessments will revert to the standard of care at a participant's particular study site. Study treatment will continue for up to 3 years from the final DCO date, or until transition to an alternative method of continued treatment access (outside of the study), or manufacturing of the product ceases, or the study intervention discontinuation criteria are met, whichever occurs first. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

End of Treatment Visit and Safety Follow-up Visit

All participants will undergo an EOT visit within 7 days after the last dose of study treatment or at the time of disease progression, whichever occurs first. A safety follow-up visit will be conducted 30 days (±7 days) after the last dose of study treatment or before the initiation of follow-up anticancer therapy. Safety follow-up visits are required only for those participants who have not started a follow-up anticancer therapy. After the 30-day (±7 days) safety follow-up visit, all participants will enter the post-treatment follow-up period of telephone assessment for survival status, documentation and management of any AEs/SAEs), adverse event of special interest (AESI), and follow-up anticancer therapy every 90 (±14) days until participant discontinuation of study, withdrawal of consent, or death. CCI [redacted]
CCI [redacted]
CCI [redacted] If a participant

discontinues treatment within 28 days of the scan that indicates PD, then the EOT scan will not be performed.

A safety follow-up visit is not carried out for a participant who transitions to continue treatment outside of the study prior to PACT. For a participant discontinuing treatment in the PACT phase, no end of treatment or safety follow-up visit is required.

Safety Assessments

Safety assessments conducted throughout the Chemotherapy Treatment Period and Maintenance Treatment Period include collection of treatment emergent adverse events (TEAEs), serious adverse events (SAEs), treatment discontinuations or dose delays or reductions due to adverse events (AEs), ECOG performance, clinical laboratory results (hematology and chemistry), vital sign measurements, observations during physical examination, and use of concomitant medications.

All AEs are required to be captured through 30 days after cessation of study treatment. SAEs are required to be captured through 90 days after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy). Investigators must continue to directly report AESIs during treatment with niraparib and for 90 days after the last dose of niraparib. If the Investigator learns of an AESI after the last dose of niraparib, the Investigator must promptly notify the Sponsor. Any pregnancies that occur within 180 days post-treatment discontinuation will be captured for all participants (not only participants in PACT Phase). If applicable, when a patient transitions off study to continue treatment prior to PACT, safety reporting should be via the reporting mechanism applicable to the access route outside the study. Once the specified safety reporting period has elapsed, investigators are not obliged to actively seek information on AEs, SAEs or AESIs, however if the Investigator learns of an AESI or an SAE that is considered reasonably related to the study, the Investigator must promptly notify the Sponsor. All AEs and SAEs experienced by a participant, regardless of the suspected causality, will be monitored until the AE or SAE has resolved, until any abnormal laboratory values have returned to baseline or normalized, until there is a satisfactory explanation for the change(s) observed, until the participant is lost to follow-up or withdraws consent, or until the participant has died.

The niraparib AESIs for this study are myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and secondary cancers (new malignancies other than MDS/AML). There are no AESIs for dostarlimab. AESIs must be reported to the Sponsor as soon as the Investigator becomes aware of them.

For PACT, Investigators must report all SAEs, AEs leading to study treatment discontinuation, overdose, AESIs, and pregnancy cases via paper forms directly to the Sponsor.

Number of Participants (Randomized): CCI [redacted]

Criteria for Inclusion:

To be considered eligible to participate in this study the following requirements must be met:

1. Participants must be female, ≥18 years of age, able to understand the study procedures, and agree to participate in the study by providing written informed consent.
2. Participants with a histologically confirmed diagnosis of high-grade nonmucinous epithelial ovarian (serous, endometrioid, clear cell, carcinosarcoma, and mixed

pathologies), fallopian tube, or primary peritoneal cancer that is Stage III or IV according to the International Federation of Gynecology and Obstetrics (FIGO) or tumor, node and metastasis (TNM) staging criteria [i.e., American Joint Committee on Cancer].

3. All participants with Stage IV disease are eligible. This includes those with inoperable disease, those who undergo PDS (R0 or macroscopic disease), or those for whom NACT is planned.
4. Participants with Stage III are eligible if they meet one or more of the following criteria:
   a. Stage IIIC participants with CC0 resection if they meet the following criteria: aggregate ≥5 cm extra-pelvic disease during PDS as assessed by the Investigator
   b. All participants with inoperable Stage III disease
   c. All Stage III participants with macroscopic residual tumor (per Investigator judgment) following PDS
   d. All Stage III participants for whom NACT is planned.
5. Participant must provide a blood sample for CCI [redacted] at Pre-Screening or Screening.
6. Participant must provide sufficient tumor tissue sample CCI [redacted] CCI [redacted] CCI [redacted]
7. Participants of childbearing potential must have a negative serum or urine pregnancy test (beta human chorionic gonadotropin) within 3 days prior to receiving the first dose of study treatment.
8. Participants must be postmenopausal, free from menses for >1 year, surgically sterilized, or willing to use highly effective contraception to prevent pregnancy or must agree to abstain from activities that could result in pregnancy throughout the study, starting with enrollment through 180 days after the last dose of study treatment.
9. Participants must have adequate organ function, defined as follows (Note: CBC test should be obtained without transfusion or receipt of stimulating factors within 2 weeks before obtaining Screening blood sample):
   a. Absolute neutrophil count ≥1,500/µL
   b. Platelet count ≥100,000/µL
   c. Hemoglobin ≥9 g/dL
   d. Serum creatinine ≤1.5×upper limit of normal (ULN) or calculated creatinine clearance ≥60 mL/min using the Cockcroft-Gault equation
   e. Total bilirubin ≤1.5×ULN or direct bilirubin ≤1.5×ULN
   f. Aspartate aminotransferase and alanine aminotransferase (ALT) ≤2.5×ULN unless liver metastases are present, in which case they must be ≤5×ULN
10. Participants must have an ECOG score of 0 or 1.
11. Participants must have normal BP or adequately treated and controlled hypertension (systolic BP ≤140 mmHg and/or diastolic BP ≤90 mmHg).

12. Participants must agree to complete HRQoL questionnaires throughout the study.
13. Participants must be able to take oral medication.

Criteria for Exclusion:

Participants will not be eligible for study entry if any of the following criteria are met:

1. Participant has mucinous, germ cell, transitional cell, or undifferentiated tumor.
2. Participant has low-grade or Grade 1 epithelial ovarian cancer.
3. Stage III participant with CC0 resection after PDS (i.e., no macroscopic residual disease, unless inclusion criterion #4a is met).
4. Participant has not adequately recovered from prior major surgery.
5. Participant has a known condition, therapy, or laboratory abnormality that might confound the study results or interfere with the participant's participation for the full duration of the study treatment in the opinion of the Investigator.
6. Participant is pregnant or is expecting to conceive children while receiving study drug or for up to 180 days after the last dose of study drug. Participant is breastfeeding or is expecting to breastfeed within 30 days of receiving the final dose of study drug (women should not breastfeed or store breastmilk for use, during niraparib treatment and for 30 days after receiving the final dose of study treatment).
7. Participant has known active central nervous system metastases, carcinomatous meningitis, or both.
8. Participant has clinically significant cardiovascular disease (e.g., significant cardiac conduction abnormalities, uncontrolled hypertension, myocardial infarction, uncontrolled cardiac arrhythmia or unstable angina <6 months to enrollment, New York Heart Association Grade 2 or greater congestive heart failure, serious cardiac arrhythmia requiring medication, Grade 2 or greater peripheral vascular disease, and history of cerebrovascular accident within 6 months).
9. Participant has a bowel obstruction by clinical symptoms or CT scan, subocclusive mesenteric disease, abdominal or gastrointestinal fistula, gastrointestinal perforation, or intra-abdominal abscess.
10. Participant initiating bevacizumab as SOC has proteinuria as demonstrated by urine protein:creatinine ratio ≥1.0 at Screening or urine dipstick for proteinuria ≥2 (participants discovered to have ≥2 proteinuria on dipstick at baseline should undergo a 24-hour urine collection and must demonstrate <2 g of protein in 24 hours to be eligible).
11. Participant has any known history or current diagnosis of MDS or AML.
12. Participant has been diagnosed and/or treated with any therapy for invasive cancer <5 years from study enrollment, completed adjuvant chemotherapy and/or targeted therapy (e.g., trastuzumab) less than 3 years from enrollment, or completed adjuvant hormonal therapy less than 4 weeks from enrollment. Participants with definitively treated non-invasive malignancies such as cervical carcinoma in situ, ductal carcinoma in situ, Grade 1 or 2, Stage I endometrial cancer, or non-melanomatous skin cancer are allowed.
13. Participant is at increased bleeding risk due to concurrent conditions (e.g., major injuries or major surgery within the past 28 days prior to start of study treatment and/or

history of hemorrhagic stroke, transient ischemic attack, subarachnoid hemorrhage, or clinically significant hemorrhage within the past 3 months).

14. Participant is immunocompromised. Participants with splenectomy are allowed. Participants with known human immunodeficiency virus (HIV) are allowed if they meet all of the following criteria:
    a. Cluster of differentiation 4 ≥350/μL and viral load <400 copies/mL
    b. No history of acquired immunodeficiency syndrome-defining opportunistic infections within 12 months prior to enrollment
    c. No history of HIV-associated malignancy for the past 5 years
    d. Concurrent antiretroviral therapy as per the most current National Institutes of Health (NIH) Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV started >4 weeks prior to study enrollment.
15. Participant has known active hepatitis B (e.g., hepatitis B surface antigen reactive) or hepatitis C (e.g., hepatitis C virus ribonucleic acid [qualitative] is detected).
16. Participant is considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease, or uncontrolled infection. Specific examples include, but are not limited to, history of non-infectious pneumonitis that required steroids, current pneumonitis, uncontrolled autoimmune disease, uncontrolled ventricular arrhythmia, recent myocardial infarction within 90 days of consent, 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).
17. Participant has had investigational therapy administered within 4 weeks or within a time interval less than at least 5 half-lives of the investigational agent, whichever is longer, prior to the first scheduled day of dosing in this study.
18. Participant has received a live vaccine within 14 days of planned start of study therapy. Seasonal influenza vaccines that do not contain live viruses are allowed.
19. Participant has a known contraindication or uncontrolled hypersensitivity to the components of paclitaxel, carboplatin, niraparib, bevacizumab, dostarlimab, or their excipients.
20. Prior treatment for high-grade nonmucinous epithelial ovarian, fallopian tube, or peritoneal cancer (immunotherapy, anticancer therapy, radiation therapy).
21. Participant 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 (e.g., thyroid hormone or insulin).
22. Participant 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.

Duration of Treatment:

Planned Study Duration: Approximately 94 months (time from first patient enrolled until last patient last visit).

Planned Treatment Duration: Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor. Bevacizumab (administered during the chemotherapy portion and maintenance portion) may be continued for up to 15 months or a total of 22 consecutive or non-consecutive cycles (inclusive of bevacizumab administered during the Chemotherapy Treatment Period) as per local practice and in the absence of PD, unacceptable toxicity, participant withdrawal, or Investigator's decision.

For PACT, study treatment will continue for up to 3 years from the final DCO date, or until transition to an alternative method of continued treatment access (outside of the study), or the manufacturing of the product ceases, or a study intervention discontinuation criteria is met including unacceptable toxicity, participant withdrawal, or Investigator's decision, whichever occurs first. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

Criteria for Evaluation:

Efficacy Analysis

The comparison of interest in this study is Arm 3 to Arm 2. CCI [redacted]
CCI [redacted]

Primary Efficacy Endpoint

The primary efficacy endpoint PFS, is defined as the time from the date of randomization to the date of first documentation of progression or death by any cause, whichever occurs first.
CCI [redacted]

Secondary Efficacy Endpoints

The following secondary efficacy endpoints will be evaluated:

- Overall survival (OS, CCI [redacted]
- BICR CCI [redacted]
- The absolute scores and change from baseline in the EQ-5D-5L Visual Analogue Score (VAS) and Health Utility Index (HUI) HRQoL assessments
- The absolute scores and change from baseline in the EORTC-QLQ-C30, and EORTC-QLQ-OV28 HRQoL assessments
- TFST, defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy or death by any cause, whichever occurs first
- TSST, defined as the time from the date of randomization to the start date of the second subsequent anticancer therapy or death by any cause, whichever occurs first

- PFS2, defined as the time from the date of randomization to the date of first PD per Investigator's assessment after initiation of subsequent anticancer therapy or death by any cause, whichever occurs first
- ORR, CCI [redacted]
- DOR, CCI [redacted]
- DCR, CCI [redacted]

Safety Analysis (Secondary Endpoint)

CCI [redacted]

Interim Analysis

Planned periodic safety analyses will be conducted by the Independent Data Monitoring Committee (IDMC) CCI [redacted]

CCI [redacted]

Final Analysis

A final analysis focusing on safety at the time of final DCO will be performed.

Biomarker Analysis

CCI [redacted]

CCI [redacted]

Immunogenicity Analysis

CCI [redacted]

PK Analysis

CCI [redacted]

Statistical Methods:

Sample Size Considerations

CCI [redacted]

CCI [redacted]

Analysis Populations:

- The Intent to Treat (ITT) Population consists of all randomized participants. Any deceased participants randomized in error with death prior to randomization will be excluded from the population. Participants will be analyzed as randomized.
- The Safety Analysis Population includes all randomized participants who received at least 1 dose of study treatment after randomization. Participants will be analyzed according to the treatment that they actually received.
- The PK Analysis Population is defined as all participants in Arm 2 (niraparib only) and Arm 3 (both niraparib and dostarlimab) who received at least 1 dose of either drug and have at least 1 measurable post dose PK result. PK populations are defined separately for niraparib and dostarlimab.
- CCI [redacted]
  CCI [redacted]

Primary Efficacy Analysis

CCI [redacted]

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Table 3: Abbreviations and Specialist Terms

Abbreviation or Specialist Term	Explanation
CCI	CCI
ADP	adenosine diphosphate
ADR	adverse drug reaction; an adverse event where a causal relationship between a medicinal product and the adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. a. In the context of a clinical trial, an ADR can be serious or non-serious. Serious ADRs may be subject to expedited reporting if they are considered unexpected (see SUSAR definition). b. For marketed products, ADRs are subject to expedited reporting within the country where they are authorized.
AE	adverse event
AESI	adverse event of special interest
ALT	alanine aminotransferase
AML	acute myeloid leukemia
ANC	absolute neutrophil count
anti-mPD-1	anti-mouse-anti-PD-1
anti-PD(L)-1	anti-programmed death (ligand)-1
anti-PD-1	anti-programmed death-1
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
AUC_{ss}	AUC at steady state
AxMP a. Authorized AxMP	Auxiliary Medicinal Product; medicinal products used in the context of a clinical trial but not as investigational medicinal products, such as medicinal products used for background treatment, challenge agents, rescue medication, or used to assess end-points in a clinical trial. Auxiliary medicinal products should not include concomitant medications, that is medications unrelated to the clinical trial and not relevant for the design of the clinical trial. Medicinal product authorized in accordance with Regulation (EC) No 726/2004, or in any Member State concerned in accordance with Directive 2001/83/EC, irrespective of changes to the labelling of the medicinal product. 1. Safety reporting with regard to auxiliary medicinal products shall be made in accordance with Chapter 3 of Title

Abbreviation or Specialist Term	Explanation
b. Unauthorized AxMP	IX of Directive 2001/83/EC. a. Medicinal product not authorized in accordance with Regulation (EC) No 726/2004 1. Safety reporting for unauthorized auxiliary medicinal products will follow the same processes and procedures as SUSAR safety reporting.
Background treatment	Type of medicinal product administered to each of the clinical trial participant, regardless of randomization group, to treat the indication that is the object of the study. Background treatment is generally considered to be the current standard care for the particular indication. In these trials, the IMP is given in addition to the background treatment and safety efficacy are assessed. The protocol may require that the IMP plus the background treatment is compared with an active comparator or with placebo plus background treatment.
BICR	Blinded Independent Central Review
BIW	twice weekly
BP	blood pressure
BRCA	breast cancer susceptibility gene
*BRCA*mut	*BRCA* mutated
*BRCA*wt	*BRCA* wild-type
*BRCA*wt HRRneg/not determined	*BRCA* wild-type homologous recombinant repair negative or not determined
*BRCA*wt HRRpos	*BRCA* wild-type homologous recombinant repair positive
CA 125	cancer antigen 125
CBC	complete blood count
CC0	complete cytoreduction score of 0
Challenge agents	A product given to trial participants to produce a physiological response that is necessary before the pharmacological action of the IMP can be assessed.
CI	confidence interval
Co-administered (concomitant) products	A product given to clinical trial participants as required in the protocol as part of their standard care for a condition which is not the indication for which the IMP is being tested and is therefore not part of the objective of the study.

Abbreviation or Specialist Term	Explanation
Comparator	Any product used as a reference (including placebo, marketed product, GSK or non-GSK) for an investigational product being tested in a clinical trial. This is any product that is being used to assess the safety, efficacy, or other measurable value against the test product (IMP).
CR	complete response
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CCI	CCI
CYP	cytochrome P450
DCR	disease control rate
DLT	dose-limiting toxicity
DNA	deoxyribonucleic acid
DOR	duration of response
EC	endometrial cancer
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EMA	European Medicines Agency
EORTC-QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30
EORTC-QLQ-OV28	EORTC-QLQ Ovarian Cancer Module OV28
EOS	End of study
EOT	End of treatment
EQ-5D-5L	European Quality of Life 5-Dimension 5-Level Scale
ESMO	European Society for Medical Oncology
EU	European Union
FDA	Food and Drug Administration
CCI	CCI
FIGO	International Federation of Gynecology and Obstetrics
FiH	First in Human
CCI	
GCP	Good Clinical Practice

Abbreviation or Specialist Term	Explanation
G-CSF	Granulocyte-colony stimulating factor
GLP	Good Laboratory Practice
GSK	Glaxo Smith Kline
HBV/HCV	Hepatitis B virus/Hepatitis C virus
HIV	human immunodeficiency virus
HR	hazard ratio
HRD	homologous recombination deficiency
HRDpos	HRD positive
HRQoL	health-related quality of life
HRR	homologous recombinant repair
HUI	Health Utility Index
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICI	immune checkpoint inhibitor
IDMC	Independent data monitoring committee
IDS	Interval debulking surgery
IEC	Independent Ethics Committee
IgG4	immunoglobulin G4
Investigational Product	A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
IP	intraperitoneal
irAE	immune-related adverse event
irAEI	immune-related adverse event of interest
IRB	Institutional Review Board
IV	intravenous
LSLV	Last Subject Last Visit (the date of the last subject to complete the study[i.e., assessments as defined in the Schedule of Events or last dose plus, if applicable, 90 day AE reporting period])

Abbreviation or Specialist Term	Explanation
mAb	monoclonal antibody
MDS	myelodysplastic syndrome
MDSC	myeloid-derived suppressor cell
MedDRA	Medical Dictionary for Regulatory Activities
Medicinal products used to assess end-points	A product given to the participant in a Clinical Trial as a tool to assess a relevant clinical trial endpoint; it is not being tested or used as a reference in the clinical trial.
MRI	magnetic resonance imaging
MSI-H	microsatellite instability-high
MSS	microsatellite stable
N/A	not applicable
NACT	neoadjuvant chemotherapy
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NCI-CTCAE	National Cancer Institute - Common Terminology Criteria for Adverse Events
neg	negative
NIH	National Institutes of Health
CCI [redacted]	CCI [redacted]
NSCLC	non-small cell lung cancer
OC	ovarian cancer
ORR	objective response rate
OS	overall survival
PACT	post-analysis continued treatment
PARP	poly(ADP-ribose) polymerase
PD	progressive disease
PD-1	programmed death-1
PD-L1/PD-L2	programmed death-ligand 1/2
PDS	primary debulking surgery
PFS	progression-free survival
PFS2	progression on next-line therapy
PI	Principal investigator
PK	pharmacokinetics

Abbreviation or Specialist Term	Explanation
PO	oral, orally
pos	positive
PP	per-protocol
PR	partial response
PRES	posterior reversible encephalopathy syndrome
Q21D	every 21 days
Q3W	every 3 weeks
Q6W	every 6 weeks
QD	once daily
RB	retinoblastoma gene
RBC	red blood cell
RECIST	Response Evaluation Criteria in Solid Tumors
Rescue medication	Medicines identified in the protocol as those that may be administered to the participants when the efficacy of the IMP is not satisfactory, or the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation
RP2D	recommended Phase 2 dose
SAE	serious adverse event
SAP	statistical analysis plan
SD	stable disease
SOC	standard of care
Standard of Care	Medicine(s) for a specific indication, or a component of the standard care for a particular medical indication, based on national and/or international consensus; there is no regulatory significance to this term. 1. Products/regimens considered standard of care may differ country to country, depending on consensus in individual countries
SUSAR	Suspected Unexpected Serious Adverse Reaction; Suspected Unexpected Serious Adverse Reaction; in a clinical trial, a serious adverse reaction that is considered unexpected, i.e., the nature or severity of which is not consistent with the reference safety information (e.g., Investigator's Brochure for an unapproved investigational medicinal product). All adverse drug reactions (ADRs) that are both serious and unexpected are subject to expedited reporting.
T1DM	type 1 diabetes mellitus

Abbreviation or Specialist Term	**Explanation**
t*BRCA*mut	tumor *BRCA* mutation
t*BRCA*wt	tumor *BRCA* wild type
TEAE	treatment-emergent adverse event
TFST	time to first subsequent therapy
TSH	thyroid stimulating hormone
TSST	time to second subsequent therapy
ULN	upper limit of normal
US	United States
VAS	visual analogue score
VEGF	vascular endothelial growth factor
WHO	World Health Organization
WMA	World Medical Association

1. INTRODUCTION

Niraparib is an orally available, potent, and highly selective poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP)-1 and PARP-2 inhibitor. Niraparib was approved for the maintenance treatment of women with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete response (CR) or partial response (PR) to platinum-based combination chemotherapy by the United States (US) Food and Drug Administration (FDA) on 27 March 2017 and received a Marketing Authorization in the European Union (EU) on 16 November 2017.

CCI

The objective of the proposed study is to evaluate the efficacy of a adding the anti-PD-1, dostarlimab during both the chemotherapy and maintenance periods to the standard-of-care (SOC) regimen consisting of platinum based- combination chemotherapy ± concurrent and maintenance bevacizumab plus niraparib in maintenance in participants with newly diagnosed Stage III or IV nonmucinous epithelial cancer of the ovary, fallopian tube, or primary peritoneum (collectively referred to as “ovarian cancer”).

1.1. Biology of Ovarian Cancer

Ovarian cancer is the fifth overall cause for cancer death in women, representing 5% of all cancer deaths in women [ACS, 2016]. It is also the deadliest of gynecologic cancers: in 2017, 14,080 women in the US [National Cancer Institute, 2016] and in 2018, 44,576 women in Europe [WHO, 2018] died from ovarian cancer.

Epithelial OC is histologically divided into five main subtypes: high grade serous (HGS), endometrioid, clear cell (CC), low grade serous (LGS) and mucinous OC. These subtypes have distinct developmental origins: HGS OC predominantly arises from the epithelium of the distal fallopian tubes, while CC and endometrioid OC are associated with endometriosis [Hollis, 2016]. Through the Cancer Genome Atlas project, researchers have identified key molecular aberrations in patients with high-grade serous or endometrioid ovarian cancer [Cancer Genome Atlas Research Network, 2011]. In addition, clear cell ovarian cancer appears to have breast cancer susceptibility gene (*BRCA*)-like DNA repair dysfunction [Kawahara, 2017]. Key characteristics of the 5 main histological subtypes of ovarian cancer are presented in Table 4.

Table 4: Characteristics of the 5 Main Histological Subtypes of Ovarian Cancer

	High Grade Serous	Endometrioid	Clear Cell	Mucinous	Low Grade
Approximate proportion of OC cases	70%	10%	10%	<5%	<5%
Overall prognosis	Poor	Favorable	Intermediate	Intermediate	Intermediate
Tissue of origin / precursor lesion	Distal fallopian epithelium	Endometriosis	Endometriosis	Poorly defined	Serous borderline tumor
Intrinsic chemosensitivity	High	High	Low	Low	Low
Associated hereditary syndromes	Germline *BRCA1/2*	Lynch syndrome	Lynch syndrome		
Typical stage at diagnosis	80% advanced stage	50% early stage	60% early stage	80% early stage	Typically advanced stage
Frequent molecular abnormalities	Chromosome instability *BRCA1, BRCA2, TP53, NF1, RB1, CCNE1 amplification*	*PTEN*, *PIK3CA*, *ARID1A*, *CTNNB1*	*PTEN*, *PIK3CA*, *ARID1A*, chr20q13.2, *amplification*	*KRAS*, *HER2 amplification*	*KRAS*, *BRAF*

Abbreviations: *ARID1A*=AT-rich interaction domain 1A gene; *BRAF*=rapidly accelerated fibrosarcoma-B gene; *BRCA1/ 2*=breast cancer susceptibility gene 1, 2 ; *CCNE1 amplification*=cyclin E gene amplification; *CTNNB1*=catenin beta 1 (human) gene; *HER2 amplification*=human epidermal growth factor receptor 2 amplification; *KRAS*=Kirsten rat sarcoma oncogene; *NF1*=neurofibromatosis type 1; OC=ovarian cancer; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog gene; *RB1*=retinoblastoma gene; *TP53*=tumor protein gene.
Source: [Hollis, 2016].

Besides the malignant epithelial cell itself, the tumor microenvironment in ovarian cancer offers additional opportunities to improve patient outcomes from ovarian cancer. Angiogenesis is essential for both tumor growth and metastases, making it one of the hallmarks of cancer and an actionable target for drug development [Yang, 2020]. The activity of bevacizumab is established in the treatment of newly diagnosed ovarian cancer, platinum sensitivity recurrent ovarian cancer, and platinum resistant ovarian cancer [Aghajanian, 2012; Pujade-Lauraine, 2014].

Immune cells represent a critical component of the tumor microenvironment [Yang, 2020] The presence of intratumoral T-cells in newly diagnosed ovarian cancer patient is associated with improved progression-free survival (PFS) and overall survival (OS) in patients [Zhang, 2003]. Consistent with this, it has been reported that *BRCA* deficient tumors are associated with an immunoreactive molecular subtype characterized by intense intratumoral T-cell infiltration in high-grade serous ovarian cancer patients. Programmed cell death-ligand (PD-L1) expression in tumors results in T-cell inactivation/anergy. Survival outcomes are negatively impacted in tumors with high PD-L1 expression regardless of tumor stage, histologic type, residual tumor burden, and chemotherapy [Hamanishi, 2007]. Preliminary efficacy rates for single-agent PD-1 or PD-L1 inhibitors range from 5.9% to 15% in unselected recurrent ovarian cancer patients, in clinical studies that include patients with platinum-sensitive disease [Hamanishi, 2015; Varga, 2015; Disis, 2016; Infante, 2016]. These data support the incorporation of dostarlimab and niraparib into the first-line treatment of advanced ovarian cancer.

1.2. First-Line Chemotherapy for Advanced Ovarian Cancer

Most women with ovarian cancer present with Stage III or IV disease, contributing to its high mortality rate. In spite of its widespread nature, debulking surgery still plays a major role in the treatment of newly diagnosed ovarian cancer patients. Five-year survival rates are significantly improved in those patients who have undergone optimally debulked disease (i.e., residual tumor nodules <1 cm) compared to patients who have undergone suboptimal debulking (i.e., residual tumor nodules ≥1 cm) (47% and 35%, respectively) [Chi, 2009]. Overall, depending upon stage and post-operative tumor burden, 5-year survival rates for advanced ovarian cancer patients following surgery and platinum-based combination therapy in advanced ovarian cancer patients have remained relatively stable at 26% to 42% [Torre, 2018].

A pivotal study conducted by European Organization for Research and Treatment of Cancer (EORTC) Investigators compared primary debulking surgery (PDS) followed by at least 6 cycles of platinum-based combination chemotherapy to 3 cycles of neoadjuvant chemotherapy (NACT), plus interval debulking surgery (IDS) and 3 cycles of chemotherapy post-operatively in patients with Stage IIIC or IV ovarian cancer. NACT patients had noninferior outcomes to PDS patients based upon the primary study endpoint of OS (median survival: 30 months versus 29 months) and PFS (median PFS of 12 months in both arms). Furthermore, the use of NACT was associated with lower rates of post-operative morbidity (e.g., hemorrhage, infection, venous complications) and mortality (0.7 versus 2.5%). This study also demonstrated that the most favorable outcomes were observed in patients with complete macroscopic resection (median survival: 39 months for NACT patients and 45 months for PDS patients) [Vergote, 2010]. Based upon these results, the use of NACT is increasingly administered in patients with large volume Stage IIIC/IV disease.

For patients with inoperable disease, sub-optimally debulked disease following PDS or the presence of significant upper abdominal disease (e.g., disease present on the surface of the liver, diaphragmatic peritoneum, stomach, pancreas, and large volume ascites which indicate a high likelihood of unresectable disease or residual disease after surgery), intravenous (IV) paclitaxel in combination with carboplatin is the SOC based upon a

superior toxicity profile and comparable efficacy when compared to IV paclitaxel in combination with cisplatin [Ozols, 2003; du Bois, 2003]. Per European Society for Medical Oncology (ESMO) guidelines, paclitaxel 175 mg/m^2 and carboplatin at an area under the concentration-time curve (AUC) of 5 to 6 mg/mL/min administered every 3 weeks (Q3W) have been the clinical and research SOC in first-line ovarian cancer patients for more than 15 years [Ledermann, 2013]. For patients with optimally cytoreduced ovarian cancer following PDS, intraperitoneal (IP) therapy is an option. However, this type of therapy remains controversial [Walker, 2016].

Dose dense strategies, in which either carboplatin or the combination of carboplatin and paclitaxel was administered on a weekly schedule with or without bevacizumab, have yielded conflicting results [Katsumata, 2013; Chan, 2016; Pignata, 2014]. Bevacizumab has been evaluated in multiple clinical studies, including in 1,873 patients with newly diagnosed, Stage III (incompletely resected) or Stage IV epithelial ovarian cancer who had undergone debulking surgery as part of a Phase 3 study (GOG218) [Burger, 2011]. Patients receiving bevacizumab administered concurrently with chemotherapy and as a maintenance treatment showed statistically significant improvement in PFS compared to placebo (18.2 months vs 12.0 months; hazard ratio [HR], 0.62; p<0.0001) [AVASTIN®, 2016].

Bevacizumab was also evaluated in 1,528 patients with ovarian cancer, regardless of International Federation of Gynecology and Obstetrics (FIGO) stage as part of a Phase 3 study (ICON7). Patients receiving bevacizumab administered concurrently with chemotherapy and as a maintenance treatment showed statistically significant improvement in PFS compared to chemotherapy alone (19.0 months vs 17.3 months; HR, 0.81; p=0.004), with maximum improvement compared to chemotherapy alone at 12 months (15.1%; 95% confidence interval [CI], 10.7-19.5). The improvement was even more pronounced in patients at high risk of progression (i.e., FIGO Stage IV or FIGO Stage III and >1.0 cm of residual disease after debulking surgery; 15.9 months vs 10.5 months; HR, 0.68; p≤0.001) [Perren, 2011].

The National Comprehensive Cancer Network (NCCN) provides Level 2A recommendation for Q3W paclitaxel-carboplatin ± bevacizumab, dose dense weekly carboplatin with Q3W paclitaxel, dose dense weekly carboplatin and paclitaxel, and systemic and IP paclitaxel with systemic cisplatin in optimally debulked patients, ESMO guidelines recommend Q3W paclitaxel-carboplatin [Ledermann, 2013]. Bevacizumab, in combination with carboplatin and paclitaxel, followed by bevacizumab maintenance as a single agent, is approved by the FDA and European Medicines Agency (EMA) for the treatment of patients with Stage III or IV epithelial, ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.

The introduction of PARP inhibitors into the first-line maintenance setting is warranted based on experience in platinum sensitive recurrent ovarian cancer. In a pivotal double-blind placebo-controlled study of niraparib maintenance in patients in CR or PR to their last platinum therapy, PFS was significantly improved in germline *BRCA* mutated (g*BRCA*mut) patients as well as non-*gBRCAmut* patients [Mirza, 2016]. Significant improvement in PFS was also reported in patients with *BRCA* mutated (*BRCA*mut) ovarian cancer treated with olaparib or all-comers treated with rucaparib in the

maintenance setting [Pujade-Lauraine, 2017; Coleman, 2017]. Based on the results of these pivotal studies (NCT01844986, NCT02477644, and NCT02655016), niraparib and olaparib are currently being studied in the Phase 3 setting as maintenance therapy following first-line platinum-based combination therapy in participants with homologous recombination deficiency (HRD) positive and negative tumors (niraparib), or participants with g*BRCA*mut ovarian cancer (olaparib), or added to continuation bevacizumab therapy in all comers (olaparib) [González-Martín, 2019; Moore, 2018; Ray-Coquard, 2019b].

In 2018, the Phase 3 study investigating olaparib monotherapy maintenance versus placebo following frontline platinum-based chemotherapy (SOLO-1) reported that PARP inhibitor maintenance provided significant clinical benefits. Olaparib demonstrated a PFS HR of 0.30 (95% CI: 0.23-0.41, p<0.001) in 391 randomized participants with advanced ovarian cancer and a *BRCA*1/2 mutation. The median progression free survival (mPFS) at 41 months was 49.9 months for olaparib versus 13.8 months for placebo (data maturity, 51%) [Moore, 2018]. Olaparib received approval in the US and EU in December 2018 and June 2019, respectively.

In 2019, two Phase 3 studies demonstrated the efficacy of PARP inhibitor maintenance therapy in all participants regardless of *BRCA* status in newly diagnosed advanced ovarian cancer. The Phase 3 PRIMA study demonstrated a PFS HR of 0.62 (95% CI: 0.50 to 0.76, p<0.001) in participants who received niraparib as compared to placebo in participants who responded to first-line platinum based chemotherapy and this regimen was approved in the US on 29 April 2020 and in EU on 27 October 2020 [González-Martín, 2019]. A summary of PFS in participants with ovarian cancer by study is presented in Table 5.

Table 5: Progression-Free Survival in Participants with Ovarian Cancer by Study

Study	PRIMA[1]	SOLO-1[2]	PAOLA[3]
Data	HR (95% CI)	HR (95% CI)	HR (95% CI)
Overall	0.62 (0.50-0.76)	NA	0.59 (0.49-0.72)
HR-deficient (all)	0.43 (0.31-0.59)	NA	0.33 (0.25-0.45)
*BRCA*mut	0.40 (0.27-0.62)	0.30 (0.23-0.41)	0.31 (0.20-0.47)
*BCRA*wt	0.50 (0.31-0.83)	NA	0.43 (0.28-0.66)
HR-proficient	0.68 (0.49-0.94)	NA	1.00 (0.75-1.35)

Abbreviations: *BRCA*mut=mutation in the *BRCA* gene; *BRCA*wt=wild-type *BRCA* gene; CI=confidence interval; HR-deficient=homologous recombination deficient; HR=hazard ratio; HR-proficient=homologous recombination proficient; NA=not applicable.
[1][González-Martín, 2019]; [2][Moore, 2018]; [3][Ray-Coquard, 2019a].

Key findings presented at ESMO, 27 September 2019 from the PAOLA-1 study, a randomized Phase 3 study of olaparib maintenance therapy or placebo added to bevacizumab maintenance treatment following first-line platinum therapy for Stage III/IV ovarian cancer, showed an improved PFS in participants who receive bevacizumab plus olaparib, HR 0.59 (95% CI: 0.49-0.72; p<0.0001) [Ray-Coquard, 2019b]. Based on results from PAOLA-1, olaparib in combination with bevacizumab in HR-deficient participants received approval in the US and EU in the frontline maintenance setting.

The FIRST study design will enable Investigators to provide participants with the current SOC for advanced ovarian cancer should it change during study conduct as results are anticipated from pivotal studies of first-line PARP inhibitor maintenance therapy that may lead to the incorporation of PARP inhibitors into first-line treatment of advanced ovarian cancer.

1.3. Background of Niraparib

Niraparib is an orally available, potent, and highly selective PARP1 and PARP2 inhibitor that is approved for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy, and additionally for adult patients with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. The inhibition of PARP by niraparib has been confirmed by a battery of in vitro and in vivo nonclinical studies using models that are HRD through silencing or mutation of *BRCA1* or *BRCA2*. Notably, PARP inhibition in tumor tissue is greater and more durable than PARP inhibition in nontumor tissue from the same animals.

The initial niraparib study, PN001, was a Phase 1 multiple ascending dose study. In this study, 300-mg niraparib administered orally once daily (QD) was the maximum tolerated dose of niraparib monotherapy, in consideration of clinical, pharmacokinetic (PK), and pharmacodynamic data. The clinical activity of niraparib was observed among participants with various advanced and refractory tumor types, particularly among those with ovarian or prostate cancer with and without *BRCA* mutations.

The clinical efficacy of niraparib was demonstrated in a randomized, double-blind, placebo-controlled Phase 3 trial (ENGOT-OV16/NOVA) [Mirza, 2016]. To assess the impact of tumor genotype upon the efficacy of niraparib, participants were analyzed by subpopulation: g*BRCA*mut bearing versus those with high-grade serous histology non-g*BRCA*mut. Participants in the non-g*BRCA*mut subpopulation were further subdivided by tumor HRD status (positive or negative). In this study, PFS was significantly longer for participants who received niraparib compared to those who received placebo regardless of *gBRCA*mut status. Median PFS was 21.0 months for *gBRCA*mut participants receiving niraparib versus 5.5 months for those receiving placebo (Table 6).

Participants without *gBRCA* mutations also benefitted from niraparib therapy (median PFS: 9.3 months, niraparib; 3.9 months, placebo) regardless of tumor HRD status. Progression-free survival was also significantly longer for participants receiving niraparib than for those treated with placebo in the HRD positive (HRDpos) subgroup of the non-*gBRCA*mut subpopulation (median PFS: 12.9 months, niraparib; 3.8 months, placebo). There was no evidence for the detrimental impact of niraparib treatment on OS. Importantly, niraparib dose reduction had no impact on PFS outcomes.

Table 6: Progression-Free Survival in Participants with Ovarian Cancer in NOVA

	g*BRCA*mut		non-g*BRCA*mut (regardless of HRD status)		non-g*BRCA*mut + HRDpos	
	Niraparib (N=138)	**Placebo (N=65)**	**Niraparib (N=234)**	**Placebo (N=116)**	**Niraparib (N=106)**	**Placebo (N=56)**
Median PFS[a] (95% CI)	21.0 (12.9, NR)	5.5 (3.8, 7.2)	9.3 (7.2, 11.2)	3.9 (3.7, 5.5)	12.9 (8.1, 15.9)	3.8 (3.5, 5.7)
***p* value**	<0.0001		<0.0001		<0.0001	
Hazard Ratio[b] (95% CI)	0.27 (0.173, 0.410)		0.45 (0.338, 0.607)		0.38 (0.243, 0.586)	

Abbreviations: CI=confidence interval; g*BRCA*mut=germline breast cancer susceptibility gene mutated; HRD=homologous recombination deficient; HRDpos=HRD positive; N=number of participants included in subpopulation; PFS=progression-free survival.
[a]Progression-free survival is defined as the time in months from the date of randomization to progression or death.
[b]Hazard Ratio=Niraparib:Placebo.
Source: [Mirza, 2016]

Secondary endpoints (chemotherapy-free interval [CFI], time to first subsequent therapy [TFST], time to second subsequent therapy [TSST], and time to progression on next-line therapy [PFS2]) demonstrated a persistent treatment effect for participants receiving niraparib in the *gBRCA*mut and overall, non-*gBRCA*mut subpopulations. No detrimental impact of niraparib treatment on OS was observed at the time of the primary analysis. The results were supported by sensitivity analyses that were consistent with the primary efficacy analyses. Importantly, dose reductions had no impact on PFS. Patient-reported outcome (PRO) data measuring quality-of-life (QoL) parameters were similar for participants in the niraparib and placebo treatment arms in both subpopulations. Cumulatively, these data provide compelling evidence that niraparib does not diminish responsiveness to subsequent therapy and that the niraparib treatment effect persists [Mirza, 2016]. Accordingly, in 2017, a recommendation to consider niraparib maintenance therapy for this indication and population was added to the NCCN guidelines.

In a cumulative safety analysis of 1,625 niraparib-treated participants, the most commonly reported treatment-emergent adverse events (TEAEs) (in at least 10%) were primarily gastrointestinal (nausea, vomiting, constipation, and abdominal pain),

constitutional (fatigue and decreased appetite), hematological (anemia, thrombocytopenia, and decreased platelet count), neurological (headache), or psychiatric (insomnia) in nature. While events were generally considered related to study drug, most were mild (Grade 1) to moderate (Grade 2) in severity. Grade 3 or higher TEAEs consisted primarily of hematological events (anemia, neutropenia, and thrombocytopenia) and investigations (platelet count decreased, neutrophil count decreased, and white blood cell count decreased), followed by gastrointestinal events (nausea, vomiting, and abdominal pain). Dose modification has been an important component in the management of adverse events (AEs), and lower doses do not appear to compromise the efficacy of niraparib in terms of PFS. A comprehensive review of the safety profile of niraparib is presented in the current Investigator's Brochure [GSK document Number RPS-CLIN-108400]. Recommendations for dose modification strategies to be used during this study are provided in Section 3.4.1.

1.3.1. Baseline Body Weight and Platelet Count as Predictors of Thrombocytopenia

Additional exploratory analysis of the NOVA study data identified that participants with a baseline body weight <77 kg or with a baseline platelet count <150,000/μL before the initiation of niraparib treatment have a higher incidence of Grade 3 or 4 thrombocytopenia and other AEs from niraparib treatment. A dose-response relationship between AEs and dose was also observed for most of the commonly reported Grade 3 or 4 events, with the highest incidence at the 300 mg dose level. The incidence of these Grade 3 or 4 events was lower at the 200 mg dose level.

The dose modification approach employed in NOVA allowed participants to reach their optimal individual dose after the first 3 cycles. Overall, dose interruptions for any reason were instituted for 80% of participants on niraparib; 72% underwent a dose reduction. Dose reductions tended to occur early, and most participants reached their individual adjusted dose level by Month 4 of treatment.

A PFS analysis from the NOVA study by dose at Month 4 demonstrated that, once the participants reach their optimal individualized dose, the efficacy was not compromised. Therefore, a lower starting dose will assist in reducing the incidence of Grade 3/4 thrombocytopenia in these subgroups of participants without a decrement in efficacy. Further, despite the intent to deliver a starting dose of 300 mg, the median daily dose taken within the first 2 months (where most dose reductions and interruptions occurred) was only 207 mg for participants with baseline body weight <77 kg or baseline platelet count <150,000/μL compared with a median of 295 mg for participants with baseline body weight ≥77 kg and baseline platelet count ≥150,000/μL. Therefore, the efficacy in NOVA was achieved with these participants receiving a true starting dose consistent with a 200-mg starting dose.

The safety data from 2 niraparib studies, QUADRA and TOPACIO, were also evaluated. In the QUADRA study, a lower (13.6%) incidence of Grade 3 or 4 thrombocytopenia during the first cycle was observed in participants with a baseline body weight ≥77 kg and with baseline platelet count ≥150,000/μL as compared to 30.2% incidence in participants with a baseline body weight <77 kg or with a platelet count <150,000/μL.

The Phase 2 portion of the TOPACIO study included 107 participants treated at a starting dose of niraparib of 200 mg in combination with pembrolizumab 200 mg in participants with advanced triple-negative breast cancer or platinum-resistant ovarian cancer. This study represented the largest dataset available with this proactively defined 200 mg starting dose. The lower starting dose in this study led to a lower incidence of Grade 3/4 thrombocytopenia in participants with the baseline characteristics of body weight <77 kg or platelet counts <150,000/µL (14.5%) than in the NOVA (34.6%) or QUADRA (30.2%) studies, which utilized the 300-mg starting dose.

For the NOVA study, participants with a baseline body weight <77 kg or a baseline platelet count <150,000/µL in effect received an average daily dose approximating 200 mg (median=207 mg) due to dose interruption and reduction. It was found the use of a 200-mg niraparib starting dose led to a lower incidence of Grade 3/4 thrombocytopenia events without compromising efficacy. Results from the PRIMA trial confirmed that an individualized starting dose of 200 mg in participants with body weight <77 kg or platelet count <150,000/µL and 300 mg for all other participants does not compromise efficacy. Thereafter, on 29 April 2020, the FDA approved niraparib for first-line maintenance of advanced ovarian cancer with a recommended niraparib dose (200 mg or 300 mg) based on body weight or platelet count. This dosing posology is reflected in the USPI for the frontline setting.

1.4. Background of Dostarlimab

Dostarlimab is a CCI [redacted]

Dostarlimab has been evaluated in 4 ongoing first-in-human (FiH) Phase 1 studies of dostarlimab monotherapy and combination therapies to evaluate the safety and tolerability, PK, pharmacodynamics, and clinical activity of dostarlimab in participants with advanced solid tumors. The clinical experience with dostarlimab is discussed in Section 1.4.2 and in the dostarlimab IB [GSK document Number RPS-CLIN-106356].

1.4.1. Nonclinical Experience

Nonclinical pharmacology and toxicology studies with toxicokinetics have been conducted to support the dostarlimab clinical development. The nonclinical toxicology studies were designed and conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline S6 (R1) Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals, and ICH Guideline S9 Nonclinical Evaluation on Anticancer Pharmaceuticals [ICH S6 (R1), 2011; ICH S7A, 2001; ICH S9, 2009]. The studies are

intended to characterize the potential hazards, identify laboratory markers for any toxicity and to estimate the safety margins that exist to allow the safe progression of human clinical trials with dostarlimab. All studies were conducted to high scientific standards according to the established procedures and standard operating procedures of the performing laboratories.

For in vivo toxicology studies, cynomolgus monkey was selected as the relevant species to evaluate dostarlimab toxicity. The selection was based on DNA homology of PD-1 extracellular domains of different species, cross-species PD-1 receptor binding affinity peripheral blood mononuclear cell binding of dostarlimab, and receptor occupancy of dostarlimab.

Nonclinical toxicology studies comprise a single-dose and a 4-week repeat-dose study with a 4-week recovery period in cynomolgus monkeys. Additional studies consist of tissue cross reactivity studies in both normal human and cynomolgus monkey tissues. All these studies (with the exception of the single-dose study in monkeys and the initial tissue cross reactivity study in normal human tissues) were conducted in compliance with the Organisation for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP) (as revised in 1997) [Organisation for Economic Co-operation and Development, 1998]. In addition, TESARO is conducting a 3-month GLP toxicology study to support further development of dostarlimab and marketing authorization.

Safety pharmacology endpoints assessing major organ system function covering cardiovascular, respiratory and nervous systems were evaluated as part of the 4-week repeat-dose toxicology study in cynomolgus monkeys. The administration of dostarlimab as a weekly IV dose for 4 weeks (5 doses total) to cynomolgus monkeys at dose levels of up to 100 mg/kg did not result in any dostarlimab-related effects on the safety pharmacology parameters evaluated, including electrocardiography, blood pressure (BP), respiration, and neurological examinations.

1.4.2. Clinical Experience

Up-to-date clinical data on niraparib and dostarlimab are discussed in detail in the most current version of the respective Investigator's Brochures, niraparib Investigator's Brochure [GSK document Number RPS-CLIN-108400] and dostarlimab Investigator's Brochure [GSK document Number RPS-CLIN-106356]), including all risks of niraparib and dostarlimab.

As of 20 April 2024, there are 21 ongoing studies with dostarlimab (19 in adults and 2 in pediatrics): 7 Phase 1 studies, 2 Phase 1/2 studies, 7 Phase 2 studies, 1 Phase 2/3 study, and 4 Phase 3 studies. Four Phase 1 studies with dostarlimab monotherapy (Study 213346, GARNET, or Study 4010-01-001) and dostarlimab in combination with other therapies (Study 213348, AMBER or Study 4020-01-001, Study 213351, IOLite or Study 3000-01-002, and Study 213349, CITRINO or Study 4040-01-001; completed) in participants with advanced or metastatic cancer and 3 Phase 2 studies with dostarlimab in combination with other therapies in participants with locally advanced and metastatic squamous NSCLC (Study 213352, JASPER or Study 3000-02-001; completed), with relapsed ovarian cancer (Study 213357, OPAL or Study 3000-02-005; ongoing), or with advanced, relapsed, ovarian cancer (Study 213353, MOONSTONE or Study 3000-02-

006; completed) provided additional safety data. Two double-blind Phase 3 studies with dostarlimab combination therapy are ongoing (this study and Study 213361, RUBY or Study 4010-03-001) and, therefore, were not included in the evaluation of safety in the safety population.

1.4.2.1. Dostarlimab Monotherapy

GARNET (Study 4010-01-001) is an ongoing, FiH Phase 1 study of dostarlimab to evaluate the safety and tolerability, PK, pharmacodynamics, and clinical activity of dostarlimab in participants with recurrent or advanced solid tumors. A total of 21 participants were dosed in the dose escalation phase of the study (Part 1). Dose escalation continued to a maximally administered dose of 10 mg/kg every 2 weeks and a maximum tolerated dose was not identified. No dose limiting toxicities (DLTs) were observed. In Part 2A of the study, the safety and tolerability of dostarlimab was evaluated at 2 fixed dosing schedules: 500 mg Q3W and 1,000 mg every 6 weeks (Q6W). No DLTs were observed in Part 2A. The recommended Phase 2 dose (RP2D) regimen was determined to be 500 mg Q3W for 4 cycles followed by 1,000 mg Q6W for all cycles thereafter, which is being evaluated in expansion cohorts for microsatellite instability-high (MSI-H) and microsatellite stable (MSS) endometrial cancer (EC), non-small cell lung cancer (NSCLC), and non-endometrial MSI H or polymerase ε-mutated cancer in Part 2B of study.

As of 21 January 2020, 535 participants with heavily pretreated advanced solid tumors have been treated with dostarlimab in GARNET. The majority of these participants (98.5%) reported at least 1 TEAE, with events of fatigue, nausea, anemia, and diarrhea being the most frequently reported (>20%). The majority of the Grade ≥3 events occurred in 2% of participants or less each, with the exception of anemia (8.6%), dyspnea (3.7%), abdominal pain (3.4%), fatigue (2.8%), hyponatremia (2.8%), and pulmonary embolism (2.4%). Serious AEs occurred in 38.3% of participants, for which 7.3% of these participants was considered study drug related. Forty-eight participants (9.0%) had an AE leading to study drug discontinuation. Twenty-five participants (4.7%) had a TEAE leading to study drug discontinuation that was considered study drug related. Sixteen participants (3.0%) had a TEAE leading to death. None of the AEs leading to death were considered related to the study drug.

In an updated presentation of the GARNET study at Society of Gynecologic Oncology (SGO) (March 2019), 41 participants with MSI-H EC and 79 participants with MSS EC have had at least 1 tumor assessment. Among the 41 participants with MSI-H EC, the objective response rate (ORR) was 48.8% and consisted of 2 participants with CRs (4.9%) and 18 participants with PRs (43.9). The disease control rate (DCR) among these participants was 63.4%, and at the time of data cutoff, responses were ongoing in 85% of responders. For 79 participants with MSS EC, the ORR was 20.3% including 4 participants with CRs (5.1%) and 12 participants with PRs (15.2%). The DCR among these participants was 46.8%, and responses were ongoing in 81.3% of responders. Dostarlimab demonstrated clinically meaningful response rates regardless of MSI status, with an overall ORR of 30% (49% in the MSI-H cohort and 20% in the MSS cohort).

1.4.2.2. Investigational Therapeutic Combinations with Dostarlimab

In addition to the GARNET dostarlimab monotherapy, 3 additional studies involving dostarlimab and other therapeutic agents are being evaluated.

Study 213348, AMBER or Study 4020-01-001 is an open-label, FiH Phase 1 study of CCI [redacted], that is being conducted in 2 parts in patients with advanced solid tumors. In Part 1C of this study, dostarlimab will be administered in combination with cobolimab. In Part 1D: dostarlimab will be administered in combination with cobolimab and encelimab. In Part 1E dostarlimab will be administered in combination with cobolimab. In Part 1F dostarlimab will be administered in combination with cobolimab and docetaxel.

Study 213351, IOLite or Study 3000-01-002 is an open-label, Phase 1b study of dostarlimab that is being conducted in 9 parts in participants with advanced or metastatic cancer. The study is evaluating DLTs, safety, and tolerability of dostarlimab in combination with niraparib with or without bevacizumab or carboplatin and paclitaxel with or without bevacizumab or carboplatin and pemetrexed with or without cobolimab or carboplatin and nab-paclitaxel with or without cobolimab or cobolimab and carboplatin and paclitaxel.

Study 213349, CITRINO or Study 4040-01-001 was an open-label, FiH Phase 1 study of CCI [redacted], that was conducted in 2 parts in participants with advanced solid tumors. In Part 1C, dostarlimab was administered in combination with encelimab to establish the RP2D regimen for this study drug combination. In Part 2 of the study, the efficacy of encelimab with or without dostarlimab was evaluated in participants with advanced solid tumors.

As of 20 April 2024, an estimated 3657 participants (870 in monotherapy; 2787 in combination with other agents) have been exposed to dostarlimab in sponsored interventional studies. Overall, the safety profile of dostarlimab has been consistent with that of other PD-1 and PD-L1 inhibitors. Given the encouraging clinical activity in heavily pretreated participants with diverse tumor types and the manageable safety profile of dostarlimab, the benefit-risk profile for dostarlimab as a treatment for participants with advanced cancers appears positive.

Please refer to the most current version of the dostarlimab IB [GSK document Number RPS-CLIN-106356] for more information.

1.5. Combination Therapies Proposed in the Current Trial

1.5.1. Addition of PD-1 Inhibitor to Chemotherapy

1.5.1.1. Nonclinical

There is accumulating evidence that in addition to direct cytostatic and cytotoxic effects, the mechanisms of action of conventional chemotherapies may also involve activation of tumor-targeted immune responses, including increasing the immunogenicity of cancer cells and reducing immunosuppression of tumors [Kroemer, 2013; Hato, 2014]. In

nonclinical models, platinum-based agents have been suggested to increase direct cytostatic-mediated activation of T-cells by several mechanisms, including down-regulation of PD-L2, increased adenosine triphosphate, and increased high mobility group protein box-1 release from dying cells [Hato, 2014]. Several immune-stimulatory effects of paclitaxel on the immune system have also been reported; among these are the induction of endoplasmic reticulum stress, which can lead to calreticulin exposure and dendritic cell stimulation [Senovilla, 2012], depletion of myeloid-derived suppressor cells [Liechtenstein, 2014; Sevko, 2013], and boosting of T-cell priming [Pfannenstiel, 2010]. These data suggest that chemotherapy agents may modulate the tumor microenvironment, an effect that could be enhanced by the addition of immune checkpoint inhibitors (ICIs), such as those targeting PD-1 or PD-L1.

1.5.1.2. Clinical

Carboplatin-paclitaxel in combination with anti-PD-1 antibody agents has been studied clinically. In several studies, in participants with advanced NSCLC, the combination has been well tolerated and has shown encouraging antitumor activity. Nivolumab at 5 or 10 mg/kg and carboplatin-paclitaxel combination treatment was evaluated in the CheckMate 012 study, a Phase 1, multicohort study exploring the safety and efficacy of nivolumab monotherapy and nivolumab in combination with current standard therapies in first-line advanced NSCLC. The safety profile of combination treatment was found to be manageable, and the clinical activity of nivolumab 5 mg/kg and carboplatin-paclitaxel combination treatment showed evidence of efficacy [Rizvi, 2016]. Carboplatin-paclitaxel was administered in combination with the anti-PD-1 antibody pembrolizumab in the KEYNOTE-021 study in participants with advanced non-squamous NSCLC. The study concluded that pembrolizumab and carboplatin-paclitaxel combination treatment may be an effective and tolerable first-line treatment option for participants with advanced non-squamous NSCLC [Langer, 2016].

Dostarlimab was evaluated at CCI [redacted] in combination with paclitaxel 175 mg/m^2 and carboplatin AUC 5-6 in advanced cancer participants in Part B of Study 213351, IOLite or Study 3000-01-002. The safety of paclitaxel, carboplatin and dostarlimab in advanced cancer participants was established in Part B of this study.

1.5.2. Addition of anti-PD-1 and PD-L1 Inhibitor to PARP Inhibitor

1.5.2.1. Nonclinical

It has been demonstrated that PARP inhibitor treatment is able to increase lymphocyte infiltration and activation in mouse tumor models, turning “cold” tumors into “hot” tumors, which are more likely to respond to anti-PD-1 therapies [Huang, 2015]. The rationale behind this finding is that PARP inhibition leads to accumulation of DNA damage and cytoplasmic DNA, which stimulates the stimulator of interferon genes (STING)-dependent immune response [Wang, 2019] and results in activation of type I interferon pathway. Indeed, multiple molecular mechanisms have been reported indicating that intrinsic DNA repair deficiency is also able to trigger an innate immune response through the accumulation of cytosolic DNA and activation of the stimulator of interferon gene pathway [Harding, 2017].

Type I interferon has been reported to activate antitumor immunity through multiple mechanisms, including stimulation of innate and adaptive cytotoxic lymphocytes, downregulation of suppressive immune cells such as regulatory T-cells and myeloid-derived suppressor cells, and direct inhibition of tumor cell proliferation. The type I interferon-mediated activation of immune cells is mediated by upregulation of tumor antigen expression; activation of antigen-presenting dendritic cells; and stimulation of the release of secondary mediators such as chemokines, cytokines, and interleukins [Parker, 2016]. Recently, PARP inhibitors have been shown to elevate PD-L1 expression [Jiao, 2017]. This finding suggests that the immunomodulatory effects of PARP inhibitors could be muted by the expression of PD-L1. Thus, blocking anti-PD-1 or PD-L1 may enhance the ability of niraparib to induce durable responses.

The efficacy and tolerability of niraparib in combination with anti-PD-1 therapy was evaluated in several immune-competent nonclinical models and the combination was well tolerated in these studies. The combination was first tested in a HRd ovarian cancer mouse model derived from *BRCA* null genetic background [Xing, 2006], as PARP inhibition was previously shown to increase immune cell infiltration in *BRCA*-deficient models [Huang, 2015]. In a study of an ovarian carcinoma mouse model niraparib (50 mg/kg orally [PO] QD) and anti-mouse anti-PD-1 (anti-mPD-1; 5 mg/kg IP twice weekly) were administered to mice either alone or in combination for 16 days. The combination was tolerated with no treatment-related death. Almost all tumors achieved complete regression upon treatment with niraparib, anti-mPD-1, and the combination. Complete regression was first observed on treatment Day 16 in 2 of 6, 1 of 6, and 4 of 6 mice from the niraparib, anti-mPD-1, and combination groups, respectively [Wang, 2019]. These results suggest that the therapeutic approach of combining niraparib with a PD-1 inhibitor such as dostarlimab may provide additional benefit for participants with HRd tumors.

Niraparib and anti-PD-1 combination treatment has also been evaluated in several syngeneic models representing breast cancer 1 and breast cancer 2 (*BRCA1/2*) wild-type tumors, one of which was the breast cancer mouse model MMTV-LPA1-T22. In a study of a syngeneic transplant breast cancer model, niraparib (50 mg/kg PO QD) and anti-PD-1 antibody (10 mg/kg IV BIW) were administered to mice either alone or in combination for 15 days. While these tumors were moderately responsive to niraparib or anti-PD-1 antibody alone, with average tumor growth inhibition of approximately 45% for niraparib and 30% for PD-1 antibody, synergistic antitumor activity with near-complete tumor growth inhibition (91%) was achieved with the combination. In a similar study using the lung squamous syngeneic model KLN205, stronger tumor growth inhibition was observed for the combination (52%) than for niraparib alone (36%) or anti-PD-1 alone (30.5%). Together, these data support the therapeutic approach of combining niraparib with anti-PD-1 agent in either *BRCA1/2* mutant or wild-type tumors [Wang, 2019].

1.5.2.2. Clinical

The Phase 2 MEDIOLA study enrolled 32 participants with germline *BRCA* mutated platinum-sensitive relapsed ovarian cancer. Participants received olaparib 300 mg PO twice daily for a 4-week run-in, followed by olaparib 300 mg PO twice daily and durvalumab 1.5 g IV every 4 weeks until progressive disease (PD). As of the final interim

data cutoff, the DCR at 12 weeks was 81% and the ORR was 63%. The most common Grace ≥3 AEs were anemia (9%), increased lipase (9%), increased amylase (6%), and neutropenia (3%) [Drew, 2018].

The Phase 1/2 TOPACIO study enrolled 62 participants with recurrent ovarian cancer. Niraparib 200 mg PO and pembrolizumab 200 mg IV were administered on a 21-day cycle to 60 evaluable participants. The ORR was 18% (5% CR, 13% PR); including 47% participants with stable disease (SD), the DCR was 65%. Response rates in biomarker-selected populations were as follows: 18% tumor *BRCA* mutation (t*BRCA*mut), 14% HRDpos, 19% tumor *BRCA* wild type (t*BRCA*wt), and 19% HRDneg. With this combination, the rate of Grade ≥3 thrombocytopenia was 9%; no other safety signals were noted [Konstantinopoulos, 2019].

Part A of Study 213351, referred to as IOLite or formerly referred to as Study 3000-01-002, mentioned in Section 1.5.1.2, evaluated niraparib in combination with dostarlimab. These two agents have non-overlapping safety and metabolic profiles. No participants experienced DLT with niraparib 300 mg and dostarlimab 500 mg/m^2. There were no new safety findings at either dose level.

1.5.3. Combination of PD-1 inhibitor and Bevacizumab

The immunomodulatory activities of vascular endothelial growth factor (VEGF) has been demonstrated nonclinically, including the ability to inhibit dendritic cell maturation [Dikov, 2005], and to promote the accumulation and activation of regulatory T-cells and myeloid-derived suppressor cells (MDSCs) [Gabrilovich, 2012]. VEGF-mediated immunosuppression in cancer was demonstrated in clinical settings, for example, the expression of VEGF in tumor tissue negatively correlates with intra-tumoral T-cell infiltration, and it is associated with poor patient survival in epithelial ovarian cancer. In a renal cell carcinoma xenograft model, niraparib treatment was capable of significantly reducing the numbers of circulating myeloid cells [Kusmartsev, 2008]. Furthermore, in a T-cell receptor transgenic mouse model which mimics the adoptive cell therapy for the treatment of metastatic melanoma in the clinical setting, anti-VEGF antibody significantly increased lymphocyte infiltration into tumors and enhanced the effectiveness of adoptive immunotherapy [Shrimali, 2010].

In a Phase 1 clinical trial including 15 participants with refractory solid tumors, Aflibercept (a recombinant fusion protein consisting of VEGF-binding portions from the extracellular domains of human VEGF receptors 1 and 2) significantly increased the proportion of mature dendritic cells and improved the immune responses in a subset of participants with no increase in the proportion of MDSCs [Fricke, 2007]. In bevacizumab-treated colorectal cancer patients, it has been shown that there is an increase of peripheral T-cell compartments [Manzoni, 2010].

Multiple clinical trials have investigated the effect of combination of the checkpoint inhibitor and bevacizumab in metastatic melanoma and renal cell carcinoma. The combination of anti-PD-L1 and anti-VEGF, atezolizumab and bevacizumab, was recently reported in 10 renal cell carcinoma patients. The combination treatment increased the tumoral CD8+ T-cell infiltration and the antigen-specific T-cell migration, which is associated with durable antitumor activity [Wallin, 2016]. The combination of

atezolizumab and bevacizumab was also reported in 101 metastatic renal cell carcinoma patients in a Phase 2 study [Atkins, 2017]. The combination in PD-L1-positive participants in the first-line setting resulted in antitumor activity, and preliminary activity in the second-line setting was demonstrated in participants who crossed over to atezolizumab and bevacizumab. First-line atezolizumab and bevacizumab versus sunitinib have been evaluated in a Phase 3 study [Motzer, 2018].

Part D of study 3000-01-002 evaluated dostarlimab in combination with paclitaxel, carboplatin and bevacizumab. No DLTs were observed in 6 participants. Part D established the safety of dostarlimab CCI in combination with paclitaxel 175 mg/m^2 and carboplatin AUC.

1.5.4. Combination of Niraparib and Bevacizumab

Tumor cells with a deficiency in homologous recombination are exquisitely sensitive to PARP inhibitors due to synthetic lethality. It has been observed that for tumors without genetic or epigenetic defects in homologous recombination pathway genes, a functional state of HRD may be induced by hypoxia through transcriptional downregulation of homologous recombination-related genes, including *RAD51* and *BRCA1* [Bryant, 2007]. In addition, cyclic (acute) hypoxia and reoxygenation can induce both single-strand and double-strand DNA breaks within tumor cells due to increased levels of reactive oxygen species [Bindra, 2004; Bindra, 2007; Lim, 2014]. These 2 mechanisms working together may lead to heightened sensitivity to PARP inhibitors when cells are under hypoxic stress exerted by angiogenesis inhibitors. It has been observed that PARP inhibitors selectively induce apoptosis in hypoxic tumor regions in vivo, supporting the idea of contextual synthetic lethality between hypoxia-induced functional HRD and PARP inhibition [Mehibel, 2021].

In the clinical setting, preliminary evidence of clinical efficacy has been observed in participants with platinum-sensitive ovarian cancer treated with either niraparib combined with bevacizumab (ENGOT-OV24/AVANOVA trial) or olaparib combined with cediranib (Phase 2), irrespective of their *BRCA* mutation or HRD status [Liu, 2017]. The primary analysis of the AVANOVA trial showed a 6.4-month improvement in median PFS with the combination of niraparib and bevacizumab over niraparib alone with median PFS (ITT) of 11.9 vs 5.5 (adjusted HR: 0.35; p<0.0001). The benefit observed by the combination was in the range for participants with a PFS of 6 to 12 month (11.3 vs 2.2 months, p=0.0006) or >12 months (13.1 vs 6.1 months, p=0.0062) and participants with HRD-positive tumors (11.9 vs 6.1 months, p=0.0019) or HRD-negative tumors (11.3 vs 4.2 months, p=0.0129). The combination showed a median PFS in participants with *BRCA*-mutant tumors of 14.4 vs 9.0 months (p=0.0947) and a statistically significant advantage to participants with *BRCA*-wild type tumors (11.3 vs 4.2 months, p=0.0001). These data provide a strong rationale for combining a PARP inhibitor with an angiogenesis inhibitor [Mirza, 2019].

Niraparib and bevacizumab in combination with dostarlimab is currently being evaluated in Part C of Study 3000-01-002 (IOLite). This open-label, Phase 1b study is being conducted in 9 parts in participants with advanced or metastatic cancer to evaluate DLTs, safety, and tolerability. As of May 2019, 6 participants have been treated with CCI

CCI once daily and dostarlimab in combination with bevacizumab 15 mg/kg Q3W; 1 participant experienced an AE of Grade 3 carotid artery intimal tear attributed to the combination of niraparib and bevacizumab. Seven participants have been treated with niraparib 300 mg once daily and dostarlimab in combination with bevacizumab; 1 participant experienced an AE of Grade 4 neutropenia attributed to niraparib and dostarlimab.

Overall, the combination of niraparib and bevacizumab appears to be safe for administration, with a manageable safety profile. Adverse events observed to date are consistent with those of the individual components and are readily managed through routine laboratory testing (i.e., complete blood count [CBC]), clinical surveillance (i.e., BP monitoring), and adherence to the recommended dose modifications.

1.5.5. Rationale for Combination Therapies Proposed

Based on the totality of available clinical safety data on the combinations of agents under investigation in FIRST as described above, the Sponsor believes the combination of dostarlimab plus platinum-based chemotherapy±bevacizumab and dostarlimab plus niraparib±bevacizumab will be safe and tolerable for participants in FIRST. Furthermore, FIRST will be continuously monitored by an Independent Data Monitoring Committee (IDMC) for any emergent safety issues and appropriate measures will be taken in accordance with the protocol should any issues occur.

1.6. Rationale for Current Study

Availability of better surgical and chemotherapy options has increased the survival of patients with advanced ovarian cancer over the last 2 decades, but treatments remain nonselective, resulting in significant toxicity and short-lived antitumor responses [Grunewald, 2017]. Targeted therapies including the targets of DNA repair, combined with VEGF inhibition and ICIs may provide a better outcome for the treatment of the heterogeneous disease. Preclinical studies report synergistic effect of these drugs when combined [Chan, 2010].

With the PRIMA trial, TESARO intends to improve patient responses in the first-line setting by investigating niraparib maintenance treatment in patients with advanced ovarian cancer following response on first-line platinum-based combination chemotherapy. Topline data from the PRIMA trial are presented in Section 1.2. However, an unmet need still exists to maximize patient response to chemotherapy in the first-line treatment setting, to broaden the eligible maintenance population beyond platinum responders, and to deepen the clinical benefit in first-line maintenance.

Ovarian cancer is a complex disease with significant genetic and molecular heterogeneity [Grunewald, 2017]. The high expression of VEGF receptor, PD-L1 expression, and DNA damage in ovarian tumors provide several targets for treatment and maintenance of disease response.

This study's design will enable Investigators to provide participants with the current SOC for advanced ovarian cancer patients as it has changed during study conduct. Of note, during the study's course, results from pivotal studies have emerged that support the

incorporation of PARP inhibitors as first-line treatment of advanced ovarian cancer. As such, the study is adapted to incorporate evolving treatment paradigms in advanced ovarian cancer patients to ensure that study participants will have access to the most current regimen with or without investigational treatment while maintaining the integrity of the study.

The FIRST study will evaluate the potential to augment the standard carboplatin-paclitaxel regimen with dostarlimab±bevacizumab following diagnosis of late-stage ovarian cancer, followed by maintenance regimen of niraparib as a single agent or in combination with dostarlimab±bevacizumab. There are both manageable safety and non-overlapping metabolic profiles (refer the current versions of the niraparib IB [GSK Document Number RPS-CLIN-108400], the niraparib package insert [ZEJULA (niraparib) capsules for oral use, 2017], the bevacizumab [Genentech/Roche US] package insert [AVASTIN®, 2016], and the dostarlimab IB [GSK Document Number RPS-CLIN-106356] for details) and nonclinical data suggesting possible synergistic interaction between PARP inhibitors and immune checkpoint or anti-angiogenic inhibitors. The PK profile and CCI [redacted] of dostarlimab, during both combination treatments, will be evaluated.

2. TRIAL OBJECTIVES AND PURPOSE

2.1. Primary Objective

The primary objective is to compare the progression free survival (PFS) of platinum-based combination therapy, dostarlimab, and niraparib treatment (Arm 3) to platinum-based combination therapy and niraparib treatment (Arm 2) in participants with Stage III or IV high-grade nonmucinous epithelial ovarian cancer.

CCI [redacted]

2.2. Secondary Objectives

Secondary objectives comparing platinum-based combination therapy, dostarlimab, and niraparib (Arm 3) to platinum-based combination therapy and niraparib (Arm 2) will evaluate:

- Overall survival (OS, CCI [redacted]
- Blinded Independent Central Review (BICR) determined PFS per RECIST v1.1 criteria
- Health related quality of life (HRQoL)
- TFST
- TSST
- Time from randomization to the earliest date of assessment of progression after initiation of subsequent anticancer therapy following study treatment or death by any cause (PFS2)
- ORR CCI [redacted]
- DOR CCI [redacted]
- DCR CCI [redacted]
- PK and immunogenicity of dostarlimab
- PK of niraparib

Secondary objectives for platinum-based combination therapy (Arm 1), platinum-based combination therapy and niraparib (Arm 2) and platinum-based combination therapy, dostarlimab, and niraparib (Arm 3) for all participants will evaluate:

- Safety and tolerability

2.3. Exploratory Objectives

Exploratory objectives include the following:

CCI [redacted]

3. INVESTIGATIONAL PLAN

3.1. Overall Study Design

This is a global, multicenter, randomized, double-blind, controlled, Phase 3 study in participants with newly diagnosed Stage III or IV high-grade nonmucinous epithelial ovarian, fallopian tube, or peritoneal cancer (collectively referred to as "ovarian cancer"). The currently recommended SOC for the first-line treatment of Stage III or IV ovarian cancer is a combination of paclitaxel-carboplatin, with or without concurrent and maintenance bevacizumab. Participants will receive SOC during the Cycle 1 Chemotherapy Run-In Period before randomization at Cycle 2. Concurrent bevacizumab use must be determined prior to randomization at Cycle 2.

Treatment Arm 1 CCI
CCI
CCI
CCI
CCI

CCI

The study is open to participants with inoperable ovarian cancer, participants who have macroscopic residual disease at the end of the PDS and have recovered from PDS, and participants for whom platinum-based combination NACT is planned. Participants with Stage IIIC disease that has been completely resected (also known as complete cytoreduction score of '0' [CC0]) are eligible if they are assessed by the Investigator to have one or more of the high-risk factors defined by the inclusion criteria. Bevacizumab will be allowed where it is part of the SOC according to local treatment guidelines and/or practices.

3.1.1. Adaptation to Study Design

This study's design will enable Investigators to provide participants with the current SOC for advanced ovarian cancer as it has changed during study conduct. Of note, during the study's course, results from pivotal studies have emerged that support the incorporation of PARP inhibitors as first-line treatment of advanced ovarian cancer. As such, the study is adapted to incorporate evolving treatment paradigms in advanced ovarian cancer participants in order to ensure that study participants will have access to the most current regimen or investigational treatment while maintaining the integrity of the study. Full

details on potential adaptations to the study design and participant disposition are located in Appendix 11.

As a result, following Sponsor and Steering Committee discussions, participants were not enrolled into Arm 1 after Amendment 4 was approved at each site. Participants in Arm 1, Chemotherapy Treatment Period who are receiving (±bevacizumab) when Amendment 4 is implemented, may complete the 6 cycles of chemotherapy. After completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants receiving bevacizumab as maintenance therapy may continue at the Investigator's discretion. Participants in Arm 1, Maintenance Treatment Period who are receiving bevacizumab when Amendment 4 is implemented may continue bevacizumab therapy at the Investigator's discretion. Investigators will remain blinded for those participants enrolled in Arm 1 and receiving bevacizumab at the time of implementation of Amendment 4.

Participants in Arm 1 Chemotherapy Treatment Period who are not receiving bevacizumab when Amendment 4 is implemented, may continue the 6 cycles of chemotherapy. After completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants not receiving bevacizumab may start niraparib maintenance therapy as "follow-up anticancer treatment" at the Investigator's discretion. Participants in Arm 1, Maintenance Treatment Period not receiving bevacizumab when Amendment 4 is implemented may start niraparib maintenance therapy as "follow-up anticancer treatment" if the time after Cycle 6 Day 1 of the Chemotherapy Treatment Period is ≤12 weeks. Participants will be permitted to remain on study until withdrawal of consent, sponsor decision to terminate study or death. Participants who do not elect to receive niraparib or bevacizumab maintenance will be discontinued from the study treatment and given the option to stay in the study for follow-up. In order to facilitate this adaptation, Investigators will be unblinded for those participants enrolled in Arm 1 and not receiving bevacizumab at the time of implementation of Amendment 4. The schedule of events for these participants is shown in Table 18.

In total, CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]

Following the analysis conducted at the 31 October 2024 DCO date, no further efficacy analyses will be conducted for the study, as outlined in Section 9.6. Consequently, the scope of data collection is reduced, aligning with the revised schedule of events prior to PACT detailed in Table 16.

Participants may access treatment outside of the study protocol prior to PACT by the DCO date for the final analysis by either a rollover study, Managed Access route, other potential mechanism of access or if the product is commercially available and accessible. Following the DCO date for the final analysis, Study 213350 (FIRST) may move into the Post Analysis Continued Treatment (PACT) phase where the study remains open only to

provide continued access to study treatment for participants who are continuing to derive clinical benefit in the opinion of the Investigator and cannot access the treatment outside of the study protocol by the time of the final analysis DCO date. At that time, the collection of new data for participants who no longer receive study intervention will stop entirely and will be considered to have completed the study. The clinical study database will be closed to new data following the DCO date for the final analysis. Participants still clinically benefiting from study intervention at the time of the PACT phase may continue to receive study treatment and only serious adverse events (SAEs), AEs leading to study intervention discontinuation, overdose, adverse events of special interest (AESIs), and pregnancy cases will be reported directly to the sponsor. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

Figure 1: Study Design

CCI
CCI
CCI
CCI
CCI

[b] All participants previously randomized to placebo and not receiving bevacizumab will be unblinded and provided the option to receive niraparib maintenance if they have received chemotherapy or discontinued chemotherapy ≤12 weeks.

Pre-Screening Period

During the Pre-Screening Period, participants may sign a pre-Screening informed consent form to allow collection of limited tumor and blood samples. The purpose of this period is to ensure that the required tumor tissue sample is submitted, the results from the

CCI blood sample required for randomization are available, and to ensure that the CCI blood sample is collected prior to chemotherapy and if possible, prior to PDS; otherwise, the CCI blood sample may be collected after PDS. The blood sample for CCI is required.

The Pre-Screening Period can take place within the 14 days prior to the Screening Period, defined as the date of signing the main informed consent, but does not have to encompass the full period. A participant can move to the Screening Period once deemed able.

Screening Period

During the Screening Period, participants will sign the main consent form and complete all assessments required to determine eligibility into the study. The Screening Period is within 28 days prior to Cycle 1 Day 1 (C1D1) of the Chemotherapy Run-In Period.

Chemotherapy Run-In Period (Cycle 1)

Prior to randomization, all participants will receive 1 cycle of paclitaxel-carboplatin during a Chemotherapy Run-In Period (Section 3.3.1). Participants may also receive bevacizumab with paclitaxel-carboplatin as part of SOC per local practice. However, bevacizumab must not be administered less than 28 days before or 28 days following major surgery, and post-operative incisions must be fully healed. The determination to use bevacizumab must be made prior to randomization. Participants will be randomized following Cycle 1, prior to treatment in Cycle 2 during the Chemotherapy Treatment Period. Randomization may occur up to one week prior to Cycle 2 Day 1.

IP chemotherapy and weekly paclitaxel will not be allowed.

Chemotherapy Treatment Period (Cycles 2 to 6)

Prior to chemotherapy administration of Cycle 2, all of the following criteria must be met:

- Absolute neutrophil count (ANC) ≥1,500 cells/µL, or ≥1,000 cells µL if granulocyte-colony stimulating factor (G-CSF) is to be administered.
- Platelet count ≥100,000 /µL
- Hemoglobin ≥8 g/dL

Thereafter, re-treatment criteria for remaining chemotherapy Cycles 3 to 6 should be in accordance with treatment guidelines per local practice.

Following randomization, participants who have inoperable disease or who have undergone PDS will receive cycles 2 to 6 of paclitaxel-carboplatin, for a total of 6 cycles of chemotherapy inclusive of Cycle 1. Participants will also receive dostarlimab/placebo in combination with paclitaxel-carboplatin started with Cycle 2 of chemotherapy, for a total of 5 cycles (Section 3.3.1). Participants may also receive bevacizumab with paclitaxel-carboplatin as part of SOC per local practice. However, bevacizumab must not be administered less than 28 days before or 28 days following major surgery, and post-operative incisions must be fully healed.

Participants for whom NACT is planned will receive 3 to 4 cycles of paclitaxel-carboplatin prior to interval debulking surgery (inclusive of Cycle 1) and 2 to 3 additional cycles of paclitaxel-carboplatin following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor. These participants will also receive dostarlimab/placebo, which will be started with Cycle 2 of chemotherapy, for a total of 5 cycles. Chemotherapy and dostarlimab/placebo will resume upon recovery of surgery. Participants for whom NACT is planned may receive bevacizumab with paclitaxel-carboplatin per local practice; however, bevacizumab must not be administered less than 28 days before or 28 days following major surgery, and post-operative incisions must be fully healed.

IP chemotherapy and weekly paclitaxel will not be allowed.

Maintenance Treatment Period

Participants who complete the Chemotherapy Treatment Period without PD will start the Maintenance Treatment Period 3 weeks after Cycle 6 Day 1 (Section 3.3.2). Dostarlimab/placebo ± bevacizumab will continue in the Maintenance Treatment Period in combination with oral niraparib maintenance treatment, per study schedule. However, the start of niraparib will be delayed at least 6 weeks after Cycle 6 Day 1 and up to 9 weeks after to allow for adequate recovery of hematologic toxicity.

Prior to receiving first dose of oral niraparib maintenance treatment, participants must have a CBC that demonstrates adequate recovery from hematologic toxicity from chemotherapy.

- Absolute neutrophil count (ANC) ≥1,500 cells/µL
- Platelet count ≥100,000 /µL
- Hemoglobin ≥9 g/dL
- BP <150/100 mmHg

Weekly CBC is to be performed for the first 4 weeks from the start of niraparib in the Maintenance Treatment Period as follows:

1. Week 1 (Day of first dose): Cycle X Maintenance Day 1 (-3 day window)
2. Week 2: Cycle X Day 8 (no window, 7 days from First Dose)
3. Week 3: Unscheduled Visit (no window, 14 days from First Dose)
4. Week 4: Cycle X+1 Maintenance Day 1 (-3 day window)

During the Maintenance Treatment Period, participants will receive oral niraparib daily and IV dostarlimab/placebo on Day 1 of every other Cycle (every 6 weeks) for up to 3 years in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator's decision. Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor. After completing 1 year of maintenance treatment (=17

cycles [±1] of niraparib) and 9 cycles [±1] of dostarlimab/placebo), and if not receiving bevacizumab, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration (beginning with C19M and continuing with odd cycles only). Participants will be dispensed CCI of niraparib beginning with cycle C17M and continuing with odd cycles until the end of treatment.

Participants on any of the 3 Arms may continue bevacizumab Q3W for up to 15 months or a total of 22 consecutive or non-consecutive cycles (inclusive of bevacizumab administered during the Chemotherapy Treatment Period) as per local practice. At completion of bevacizumab treatment, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration.

It is recommended that drugs be administered CCI CCI The recommended order of administration is provided below, unless local clinical practice or institutional policies differ:

- During the Chemotherapy Treatment Period, CCI CCI CCI
- During the Maintenance Treatment Period, CCI CCI

3.2. Number of Participants

In total, CCI have been randomized into the study. The study started with a CCI CCI Arm 1 *BCRAwt* participant enrollment was stopped after implementation of Amendment 4. CCI CCI

3.3. Treatment Assignment

3.3.1. Chemotherapy Run-In and Treatment Period

During the Chemotherapy Treatment Period, participants who have inoperable ovarian cancer, who have undergone PDS, or who are planned to undergo IDS, and who are considered as candidates for systemic platinum-based combination chemotherapy, will receive paclitaxel followed by carboplatin on Day 1 of a 21-day treatment cycle. All participants for whom NACT is planned will receive 3 to 4 cycles of chemotherapy prior to IDS (inclusive of Cycle 1) and 2 to 3 additional cycles following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor. Initiation of the subsequent cycles post-IDS will be upon post-operative recovery of the participant. Bevacizumab may be administered every 21 days (Q21D) per local practice SOC but should not be administered less than 28 days before or 28 days following major surgery. Bevacizumab use must be determined prior to randomization at Cycle 2. Participants will also receive CCI dostarlimab/placebo after completion of each carboplatin infusion on Day 1 of a 21-day cycle starting with Cycle 2.

IP chemotherapy and weekly paclitaxel will not be allowed.

3.3.2. Maintenance Treatment Period

After completion of the sixth cycle of chemotherapy, niraparib will not be administered until bone marrow recovery is confirmed and will be delayed at least 6 weeks after Cycle 6 Day 1. All participants who received dostarlimab/placebo and/or bevacizumab during the Chemotherapy Treatment Period will continue to receive those agents during the bone marrow recovery period starting 3 weeks after Cycle 6 Day 1.

Participants who do not have PD on first-line chemotherapy and have recovery to baseline of any hematologic toxicities (see Section 3.1) will enter the Maintenance Treatment Period. Oral niraparib (all arms) will be dispensed to participants on Day 1 of Q21D cycle beginning with Cycle 2 or Cycle 3 of the Maintenance Treatment Period for up to 3 years in the absence of PD, unacceptable toxicity, participant withdrawal, or Investigator's decision.

Participants will receive dostarlimab/placebo at CCI on Day 1 of every other maintenance cycle (i.e., every 6 weeks) beginning with Maintenance Cycle 1 for up to 3 years in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator's decision. Participants on any arm may continue bevacizumab on Day 1 of each 21-day cycle beginning with Maintenance Cycle 1 for up to 15 months (inclusive of bevacizumab administered during the Chemotherapy Treatment Period) per local practice.

Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor.

The starting dose of niraparib will be based on the participant's actual body weight and platelet count, as measured prior to dosing in the Maintenance Treatment Period. Participants with an actual body weight of ≥77 kg and a platelet count of ≥150,000/µL will take CCI at each dose administration. Participants with an actual body weight of <77 kg, a platelet count of <150,000/µL, or both will take CCI Dose modifications will not be based upon changes in the participant's actual body weight during study participation (see Section 3.4).

Additionally, BP and heart rate will be performed weekly for the first 8 weeks from the first dose of niraparib in the Maintenance Treatment Period.

After completing 1 year of maintenance treatment (=17 cycles [±1] of niraparib) and 9 cycles [±1] of dostarlimab/placebo, and if not receiving bevacizumab, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration. If receiving bevacizumab treatment, and following completion, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration.

Treatment details are provided in Table 7 (Arm 1), and Table 8 (Arm 2 and Arm 3). It is recommended that drugs be administered CCI [redacted] CCI [redacted] The recommended order of administration is provided below, unless local clinical practice or institutional policies differ:

- During the Chemotherapy Treatment Period, CCI [redacted] CCI [redacted] CCI [redacted]
- During the Maintenance Treatment Period, CCI [redacted] CCI [redacted]

Table 7: Study Treatment (Standard of Care and Investigational Therapy) Dosage and Mode of Administration: Arm 1 (Post-Amendment 4)

Treatment Combination	Dosage and Frequency	Mode of Administration
Chemotherapy Run-In Period (Cycle 1)		
Paclitaxel	175 mg/m^2 on Day 1 Q21D	180-minute IV infusion
Carboplatin	AUC of 5 to 6 mg/mL/min on Day 1 Q21D	60-minute IV infusion
Bevacizumab	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15 min) IV infusion[a]
Chemotherapy Treatment Period (Cycles 2 to 6)		
Dostarlimab Placebo[b]	CCI [redacted]	CCI [redacted] CCI [redacted]
Paclitaxel[e]	175 mg/m^2 on Day 1 Q21D	180-minute IV infusion
Carboplatin[e]	AUC of 5 to 6 mg/mL/min on Day 1 Q21D	60-minute IV infusion
Bevacizumab	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15 min) IV infusion[a]
Maintenance Treatment Period[d, h]		
Dostarlimab Placebo[b]	CCI [redacted] on Day 1 every 6 weeks to continue up to 3 years[f] in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator decision	CCI [redacted] CCI [redacted]
Bevacizumab	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15 min) IV infusion[a]

Treatment Combination	Dosage and Frequency	Mode of Administration
Niraparib/Placebo[c]	CCI [redacted] to continue up to 3 years[g] in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator decision	Oral

Abbreviations: AE=adverse event; AUC=area under the curve; IV=intravenous.

[a] The initial dose of bevacizumab will be delivered over 90 (±15) minutes. If the first infusion is tolerated without infusion-associated AEs (fever and/or chills), the second infusion may be delivered over 60 (±10) minutes. If the 60-minute infusion is well-tolerated, all subsequent infusions may be delivered over 30 (±10) minutes. Sites can defer to local practice for administration of bevacizumab if different from the process described here.

[b] Dostarlimab placebo will be administered using a CCI [redacted] for those participants in Arm 1 who remain blinded and receiving bevacizumab only. For participants who are unblinded, dostarlimab placebo will not be administered.

[c] All participants previously randomized to placebo and not receiving bevacizumab will be unblinded and provided the option to receive niraparib. Participants should be dosed according to the criteria specified in Section 3.4.1. The first dose will be administered at the study site. Participants will be instructed to take their study medication dose at the same time each day. Participants must swallow and not chew all CCI [redacted]. The consumption of water and food is permissible.

[d] After completing 1 year of maintenance treatment (=17 cycles [±1] of niraparib), and if not receiving bevacizumab, participants may return for clinic visits and assessments every 6 weeks. If receiving bevacizumab treatment, following its completion, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab placebo IV administration.

[e] Sites can refer to local practice guidelines for any dose modifications/delays associated with chemotherapy (carboplatin and paclitaxel).

[f] Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive dostarlimab placebo beyond 3 years following consultation with the investigator and the Sponsor.

[g] Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib/placebo beyond 3 years following consultation with the investigator and the Sponsor.

[h] For participant management following analysis (DCO 31 October 2024), prior to PACT, ongoing participants not previously unblinded according to Amendment 4 are to be centrally unblinded, followed by discontinuation of placebo treatment and the study.

Table 8: Study Treatment (Standard of Care and Investigational Therapy) Dosage and Mode of Administration: Arms 2 and 3

Treatment Combination	Dosage and Frequency	Mode of Administration
Chemotherapy Run-In Period (Cycle 1)		
Paclitaxel	175 mg/m^2 on Day 1 Q21D	180-minute IV infusion
Carboplatin	AUC of 5 to 6 mg/mL/min on Day 1 Q21D	60-minute IV infusion
Bevacizumab (optional)	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15min) IV infusion[a]
Chemotherapy Treatment Period (Cycles 2 to 6)		
Dostarlimab placebo (Arm 2) or dostarlimab (Arm 3)[b]	CCI [redacted]	CCI [redacted] CCI [redacted]
Paclitaxel[e]	175 mg/m^2 on Day 1 Q21D	180-minute IV infusion
Carboplatin[e]	AUC of 5 to 6 mg/mL/min on Day 1 Q21D	60-minute IV infusion
Bevacizumab (optional)	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15min) IV infusion[a]
Maintenance Treatment Period[d, f]		
Dostarlimab placebo (Arm 2) or dostarlimab (Arm 3)[b]	CCI [redacted] on Day 1 every 6 weeks to continue up to 3 years[f] in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator decision	CCI [redacted] CCI [redacted]
Bevacizumab (optional)	7.5 mg/kg Q21D or 15 mg/kg Q21D for a total of 15 months	90-minute (±15 min) IV infusion[a]
Niraparib[c]	CCI [redacted] CCI [redacted] CCI [redacted] CCI [redacted] to continue up to 3 years[g] in the absence of disease progression, unacceptable toxicity, participant withdrawal, or Investigator decision	Oral

Abbreviations: AE=adverse event; AUC=area under the curve; IV=intravenous; Q21D=every 21 days.

[a] The initial dose of bevacizumab will be delivered over 90 (±15) minutes. If the first infusion is tolerated without infusion-associated AEs (fever and/or chills), the second infusion may be delivered over 60 (±10) minutes. If the 60-minute infusion is well tolerated, all subsequent infusions may be delivered over 30 (±10) minutes. Sites can defer to local practice for administration of bevacizumab if different from the process described here.

[b] Dostarlimab placebo (Arm 2) or dostarlimab (Arm 3) will be administered using a CCI [redacted]

[c] Participants should be dosed according to the criteria specified in Section 3.4.1. The first dose will be administered at the study site. Participants will be instructed to take their niraparib dose at the same time each day. Participants must swallow and not chew all CCI [redacted]. The consumption of water and food is permissible.

[d] After completing 1 year of maintenance treatment (=17 cycles [±1] of niraparib) and 9 cycles [±1] of dostarlimab placebo [Arm 2] or dostarlimab [Arm 3]), and if not receiving bevacizumab, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration. If receiving bevacizumab treatment, following its completion, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab placebo (Arm 2) or dostarlimab (Arm 3) IV administration.

[e] Sites may refer to local practice guidelines for any dose modifications/delays associated with chemotherapy (carboplatin and paclitaxel).

[f] Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor. For participant management following analysis (DCO 31 October 2024), prior to PACT, participants ongoing on study drugs are to be centrally unblinded and administration of dostarlimab placebo will be discontinued. Niraparib study drug may be continued, if applicable.

[g] Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib beyond 3 years following consultation with the investigator and the Sponsor.

For PACT phase, niraparib (capsule/tablet) and dostarlimab will be open-label.

3.3.3. Duration of Treatment

3.3.3.1. Planned Study Conduct Duration

This study will last approximately 94 months (time from first participant enrolled until last patient last visit).

3.3.3.2. Planned Study Treatment Duration

Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor. Participants may continue bevacizumab maintenance (administered during the chemotherapy portion and maintenance portion) for up to 15 months or a total of 22 consecutive or non-consecutive cycles (inclusive of bevacizumab administered during the Chemotherapy Treatment Period) as per local practice and in the absence of PD, unacceptable toxicity, or participant withdrawal, or based on Investigator's decision.

For participant management following analysis (DCO 31 October 2024), prior to PACT, participants ongoing on study drugs are to be centrally unblinded and dostarlimab placebo administration is to be discontinued (i.e., Arm 1 niraparib placebo and/or dostarlimab placebo [not previously unblinded according to Amendment 4] and Arm 2 dostarlimab placebo). Arm 1 participants will be discontinued from the study following niraparib placebo and/or dostarlimab placebo discontinuation. Arm 2 participants may continue niraparib study drug, if applicable.

Following unblinding, prior to PACT, participants who are deriving clinical benefit from study treatment as assessed by the Investigator may transition to continue receiving treatment outside of the study, as it becomes available and accessible. Refer to Section 5.5 for further details.

For PACT, Study treatment will continue for up to 3 years from the final DCO date (Section 4.3.1), or until transition to an alternative method of continued treatment access outside of the study (Section 5.5), or until manufacturing of the product ceases, or until a study intervention discontinuation criterion (Section 4.3.1), as assessed by the Investigator, has been met, whichever occurs first. Alternative continued treatment access outside of this study may be implemented, as it becomes available. Refer to Sections 5.5 and 5.6 for further details.

3.4. Dose Adjustment Criteria

3.4.1. Niraparib

To manage adverse reactions, consider interruption of treatment, dose reduction, or dose discontinuation. The recommended dose modifications for adverse reactions are listed in Table 9, Table 10, and Table 11.

For participants whose initial dose is CCI [redacted], dose reductions to CCI [redacted] and subsequently to CCI [redacted] CCI [redacted] will be allowed. No further dose reduction will be allowed.

For participants whose initial dose is CCI [redacted], dose reduction to CCI [redacted] will be allowed. No further dose reduction will be allowed.

Table 9: Niraparib Dose Reduction for Adverse Reactions

Dose level	Initial Dose: CCI [redacted] CCI [redacted]	Initial Dose: CCI [redacted] CCI [redacted]
Starting dose	CCI [redacted]	CCI [redacted]
First dose reduction		
Second dose reduction		N/A

Abbreviations: AE=adverse event; N/A=not applicable.
[a] If further dose reduction is required due to AE management, discussion with the Sponsor is required.

For PACT, niraparib (capsule/tablet) and dostarlimab will be open-label.

Table 10: Dose Modifications for Non Hematologic Adverse Reactions

Non-hematologic NCI-CTCAE Grade ≥3 adverse reaction where prophylaxis is not considered feasible or adverse reaction event persists despite treatment	Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. Resume niraparib at a reduced dose per Table 9. Up to 1 dose reduction is permitted.
NCI-CTCAE Grade ≥3 treatment related adverse reaction event lasting more than 28 days while the participant is administered niraparib CCI [redacted]	Discontinue medication.
PRES: There have been reports of PRES in participants receiving niraparib	Discontinue niraparib and treat specific symptoms including hypertension.

Abbreviations: NCI-CTCAE=National Cancer Institute - Common Terminology Criteria for Adverse Events; PRES= Posterior Reversible Encephalopathy Syndrome.

Table 11: Dose Modifications for Hematologic Adverse Reactions

Weekly blood draws for CBC will be monitored until the adverse reaction resolves, and to ensure safety of the new dose, weekly blood draws for CBC will also be required for an additional 4 weeks after the adverse reaction has been resolved to the specified levels, after which monitoring every 4 weeks may resume.	
Platelet count <100,000/µL	First occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100,000 /µL. • Resume niraparib at the same or reduced dose per Table 9 • If nadir platelet count was <75,000/µL, resume at a reduced dose after recovery.
	Second occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100,000/µL. • Resume niraparib at a reduced dose per Table 9. • Discontinue niraparib if the platelet count has not returned to acceptable levels within 28 days of the dose interruption period or if the participant has already undergone dose reduction to CCI [redacted]

Neutrophil <1,000/µL or Hemoglobin <8 g/dL	• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until neutrophil counts return to ≥1,500/µL or hemoglobin returns to ≥9 g/dL. • Resume niraparib at a reduced dose per Table 9 • Discontinue niraparib if neutrophil or hemoglobin level has not returned to acceptable levels within 28 days of the dose interruption period, or if the participant has already undergone dose reduction to CCI [redacted]
Hematologic adverse reaction requiring red blood cell and/or platelet transfusion	• For participants with platelet count ≤10,000/µL, platelet transfusion should be considered. If there are other risk factors such as co-administration of anticoagulation or antiplatelet drugs, consider interrupting these drugs and/or transfusion at a higher platelet count. • RBC transfusion is at the discretion of the Investigator. • Resume niraparib at a reduced dose.
MDS/AML	Any suspected case of MDS/AML reported while a participant is receiving treatment or followed for post-treatment assessments must be referred for evaluation to a local hematologist to perform bone marrow aspirate and biopsy as per local practice. The study site must receive a copy of the hematologist's report of aspirate/biopsy findings, which must include a classification according to WHO, and other sample testing reports related to MDS/AML. If a diagnosis of MDS/AML is confirmed by a hematologist, the participant must permanently discontinue study treatment.

Abbreviations: AML=acute myeloid leukemia; CBC=complete blood count; MDS=myelodysplastic syndrome; QD=once daily; RBC=red blood cell.

3.4.2. Dostarlimab

Adverse events (both non-serious and serious) associated with dostarlimab exposure may represent an immunologic etiology. These AEs may occur shortly after the first dose or several months after the last dose of treatment.

In general, dostarlimab must be withheld for drug-related Grade 3 toxicities, as well as for certain immune-related adverse events of interest (irAEIs) but may be resumed upon recovery to Grade ≤1 and until the next scheduled cycle; dostarlimab will be permanently discontinued for any drug-related Grade 4 AE. Dostarlimab must be permanently discontinued for certain drug-related irAEIs as described in Table 12. If dostarlimab dose interruption is longer than 1 month, the Sponsor should be contacted to discuss the disposition of the participant.

Refer to the American Society of Clinical Oncology-NCCN guidelines for the overall management of immune-related AEs (irAEs). The specific irAEs typically observed with PD-1 antibodies will be managed according to the guidelines summarized below [Brahmer, 2018]

Immune-Related Adverse Events of Interest and Guidelines for Management

Given the mechanism of action of dostarlimab, it is anticipated that activation of cellular immune system can be manifested as irAEs. The fundamental principles of managing drug-related irAEs are discontinuation of the ICI, a course of corticosteroids and routine supportive measures based upon the severity of the irAE. Supportive measures may include hormone replacement and/or sub-specialist consultation. Guidelines for irAE management are available through the American Society of Clinical Oncology or the European Society of Medical Oncology [Brahmer, 2018; Haanen, 2017]. Based on available safety data from checkpoint inhibitors, TEAEs with the specific grades listed in Table 12 were selected as irAEs. The irAEs may be updated upon emerging data.

For all drug-related irAEs listed in Table 12, dostarlimab should be withheld until the participant is clinically and metabolically stable and AEs are resolved to Grade 1. If systemic steroids are used as part of irAEI management, the total dose of daily steroids should be equal to or less than prednisone 10 mg at the time of resuming dostarlimab. Please refer to Table 12 for details on the management of dostarlimab dose delays and discontinuation for specific events.

All treatment delays (including any missed doses) as well as discontinuations and the reason for delays, interruptions, or discontinuation of dostarlimab should be recorded in the electronic case report form (eCRF).

Table 12: Dostarlimab Guidelines for Immune-Related Adverse Events

Toxicity	Withhold Treatment for AE Grade	Restarting Treatment/Discontinuation
Diarrhea/colitis	2 to 3	Restart dosing when toxicity resolves to Grade 1.
	4 or recurrent Grade 3	Permanently discontinue.
AST, ALT, or increased bilirubin	2 (AST or ALT >3 and ≤5×ULN or total bilirubin >1.5 and ≤3×ULN)	Restart dosing when toxicity resolves to Grade 1.
	3 to 4 (AST or ALT >5×ULN or total bilirubin >3×ULN)	Permanently discontinue.[a]
T1DM or hyperglycemia	3 to 4 hyperglycemia or T1DM (associated with metabolic acidosis or ketonuria)	Restart dosing in appropriately managed, clinically and metabolically stable participants. Insulin replacement therapy is required.
Immune-related encephalitis	Any grade	Permanently discontinue.
Uveitis	≥Grade 2	Restart the treatment when toxicity resolves to Grade 1. For any recurrent uveitis or uveitis resistant to topical steroids, permanently discontinue treatment.
Myositis	2 to 3	Restart the treatment when toxicity resolves to Grade 1
Hypophysitis	2 to 4	For Grade 2 to 3, hold until hormonal therapy results in return to adequate levels by laboratory values and restart dosing when toxicity resolves to Grade 1. For recurrence or worsening of ≥Grade 2 hypophysitis after steroid taper has been completed and participant is on adequate hormone replacement therapy, permanently discontinue. For Grade 4, permanently discontinue.
Adrenal insufficiency	2 to 4	Hold until hormonal therapy results in return to adequate levels by laboratory values and restart dosing when toxicity resolves to Grade 1. For recurrent or worsening ≥Grade 2 adrenal insufficiency while adequate hormonal replacement is continuing, permanently discontinue study drug.

Toxicity	Withhold Treatment for AE Grade	Restarting Treatment/Discontinuation
Hypo- and hyperthyroidism	3 or 4	Hold until hormonal therapy results in return to adequate levels by laboratory values and restart dosing when toxicity resolves to Grade 1.
Infusion-related reaction	2[b]	Restart dosing when toxicity resolves to Grade 1.
	3 to 4	Permanently discontinue.
Pneumonitis	2	Restart dosing when toxicity resolves to Grade1. If Grade 2 recurs, permanently discontinue.
	3 to 4 or recurrent Grade 2	Permanently discontinue.
Severe exfoliative dermatologic events	Grade 3 or Suspected DRESS, SJS or TEN	Withhold.
	Grade 4 or Confirmed DRESS, SJS or TEN	Permanently discontinue.
Renal failure or nephritis	2 with creatinine >1.5 to ≤3×ULN	Restart dosing when toxicity resolves to Grade 1.
	>3 with creatinine >3×ULN	Permanently discontinue.
Myocarditis	Grade 2, 3 or 4	Permanently discontinue.
Severe neurologic events (myasthenic syndrome/myasthenia gravis, Guillain Barré Syndrome, transverse myelitis)	Grade 2, 3 or 4	Permanently discontinue.
Hemophagocytic lymphohistiocytosis	Any grade	Permanently discontinue.
Recurrence of AEs after resolution to Grade ≤1	3 to 4	Permanently discontinue.
Other irARs	Based on severity and type of reaction (Grade 2 or 3)	Restart dosing when toxicity resolves to Grade 1.
	Grade 4 or recurrent Grade 3	Permanently discontinue.

Abbreviations: AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; PO=per oral; T1DM=type 1 diabetes mellitus; ULN=upper limit of normal. DRESS=drug reaction with eosinophilia and systemic symptom; irAR=immune related adverse reaction; SJS=Stevens Johnson Syndrome; TEN=toxic epidermal necrolysis

[a] For participants with liver metastasis who begin treatment with Grade 2 AST or ALT, if AST or ALT increases by ≥50% relative to baseline and lasts for at least 1 week, then study drug should be discontinued.

[b] Upon resolution within 1 hour of stopping drug infusion, the infusion may be restarted at CCI [redacted]. Otherwise, study drug will be withheld until symptoms resolve, and the participant should be premedicated with diphenhydramine 50 mg PO (or equivalent dose of antihistamine) and acetaminophen 500-1,000 mg PO (or equivalent dose of antipyretic) for the next scheduled dose. Participants who develop Grade 2 toxicity despite adequate premedication should be permanently discontinued from further study treatment administration.

3.4.3. Bevacizumab

Dose reductions of bevacizumab are not permitted in this study. Please refer to the local bevacizumab package insert.

Bevacizumab treatment should be withheld no less than 28 days before and 28 days following major surgery. In participants who experience wound healing complications during the study, treatment with bevacizumab should be withheld until the wound is fully healed.

3.4.4. Carboplatin and Paclitaxel

Dose adjustments should be made per local practice guidelines. There are no dose escalations planned (including dose re-escalation after a dose reduction).

Toxicities related to carboplatin and paclitaxel will be managed per local guidelines. If a participant has a suspected hypersensitivity reaction to either chemotherapy, the Sponsor should be consulted prior to discontinuation of either therapy. If a participant experiences hypersensitivity to carboplatin, then cisplatin may be used in place of carboplatin. Desensitization to carboplatin will not be allowed on study. If a participant experiences hypersensitivity or clinically significant neuropathy on paclitaxel treatment, docetaxel can be substituted per the Investigator's discretion.

Carboplatin (or cisplatin) and paclitaxel (or docetaxel) must be given on the same day; hence, delays in 1 study treatment should result in delay of all study treatments until they can all safely be given, except in the situation when a participant experiences toxicity related to bevacizumab. In this case, the bevacizumab should be omitted, and treatment can proceed with carboplatin (or cisplatin) and paclitaxel (or docetaxel). Bevacizumab can be administered at a later date, after the toxicities related to bevacizumab have resolved.

For all participants, if the causality of an AE cannot be determined to 1 investigational agent, consider discontinuing both and speak to the Sponsor prior to any dose modification, including dose interruption, reduction, or withdrawal.

3.5. Criteria for Study Termination

The Sponsor may terminate this study at any time. The Sponsor will notify the Investigators when the study is to be placed on hold, completed, or terminated.

3.6. Study Conduct

3.6.1. Schedule of Events

The schedule of events for the study is provided in Table 16.

3.6.2. Procedures and Assessments

Treatment Cycles

Treatment cycles are 21 days long.

Visits should occur within ±3 days of the scheduled visit. This window also applies to study procedures, with all procedures allowed to be performed up to ±3 days of the scheduled visit. All times should be recorded using the 24-hour clock (e.g., 23:20, not 11:20 PM).

Interval Debulking Surgery (IDS)

Participants for whom NACT is planned will receive 3 to 4 cycles of chemotherapy treatment prior to IDS (inclusive of Cycle 1) and an additional 2 to 3 cycles following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor. Initiation of the subsequent cycles post-IDS will be upon post-operative recovery of the participant. Bevacizumab should not be administered less than 28 days before or 28 days following major surgery. Additionally, participants indicated for IDS will also have a pre-operative scan during the chemotherapy period.

Radiographic Evaluation for Primary Outcome

All participants are required to undergo radiographic evaluation throughout the study as described in the schedule of events and Appendix 6. RECIST v1.1 tumor assessment via computed tomography (CT) or magnetic resonance imaging (MRI) scan of the chest/abdomen/pelvis and clinically indicated areas is required at Screening, prior to IDS (if applicable), prior to the start of the maintenance period, and at regular intervals throughout the maintenance. If participant had CT/MRI of the chest/abdomen/pelvis and clinically indicated areas within the 28-day Screening window before C1D1 but prior to signing the informed consent form (ICF), the participant is not required to complete an additional CT/MRI scan for study Screening. CT/MRI scans completed during Screening prior to signing ICF must have been performed and available for submission per the image acquisition guidelines. If there are lesions in the chest and/or clinically indicated areas at Screening, then these areas should be screened at each subsequent timepoint. Otherwise, only abdomen/pelvis are required after Screening.

During the Maintenance Treatment Period, imaging to assess disease status must occur at C1D1 (±14 days) of the Maintenance Treatment Period, and then every 4 months (±7 days) for 24 months, followed by every 6 months (±7 days) during the third year and every year thereafter until PD or initiation of follow-up anticancer therapy. CCI [redacted] Following completion of 3 years of maintenance therapy, participants will be evaluated clinically with annual scans and additional unscheduled scans for suspicion of disease progression based on increases in CA 125 or

other suspicious symptoms. Participants may be considered for treatment beyond 3 years in consultation with the Sponsor. Prior to PACT (included in Amendment 10), RECIST v1.1. scans may occur at the time of clinical suspicion of disease progression or at an annual interval, whichever occurs first according to the PI discretion and local practice guidelines.

CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted] Clinically stable participants are those with no signs or symptoms of clinically significant or rapid progression of disease, including worsening of laboratory values or decline in performance status (ECOG) and no progressive tumor at critical anatomical sites (e.g., cord compression, intracranial tumor hemorrhage) requiring urgent medical intervention. CCI [redacted]
CCI [redacted]

Assessment of Response by RECIST

CCI [redacted]
CCI [redacted]
CCI [redacted] Details on RECIST v1.1, including evaluation of target and non-target lesions and definitions of response are provided in Appendix 4. PET/CT may be used to evaluate disease progression if an equivocal new lesion is seen on CT or MRI.

Treatment and Assessment After Progression

Investigator's decision to continue treatment beyond the initial assessment of progression should be based on the participant's overall clinical condition, including performance status, clinical symptoms, and laboratory data. A participant may receive dostarlimab/placebo treatment while waiting for confirmatory imaging if he/she is clinically stable per the following criteria:

- Absence of signs and symptoms indicating clinically significant progression of disease, including worsening of laboratory parameters.
- No decline in performance status.
- Does not have rapid progression of disease.
- Treatment beyond progression will not delay an imminent intervention to prevent serious complications of disease progression (e.g., central nervous system metastases and cord compression).

Patient-Reported Outcomes and Health-related Quality of Life

The following HRQoL assessments will be obtained: the European Quality of Life 5-Dimension 5-Level Scale (EQ-5D-5L), the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30), and the EORTC-QLQ Ovarian Module OV28 (EORTC-QLQ-OV28). These will be collected at the following time points:

- Chemotherapy Run-In (21-day cycle): C1D1.
- Chemotherapy Treatment (21-day cycles): Cycle 2/Day 1, and every 2 cycles thereafter (Cycle 4/Day 1, ending Cycle 6/Day 1).
- Maintenance Treatment (21-day cycles): Day 1 of every cycle (i.e., Q21D±7 days) for the first 3 cycles, Day 1 of every 3 cycles (i.e., every 9 weeks±7 days) through 15 cycles, Cycle 17 and every 6 cycles thereafter until PD or end of study treatment. Not applicable prior to PACT (included in Amendment 10).
- Post-treatment: For participants who discontinue treatment, HRQoL assessments should be collected at the end of treatment (EOT) Visit, 30-day post EOT (±7 days) Safety Follow-up Visit, 90-day post EOT (±14 days) Long-Term Follow-up Visit, and every 180 days (±14 days) after the Long-Term Follow-up Visit (every other post-treatment assessment beginning on post-treatment assessment), which will continue until death or the end of study data collection. Not applicable prior to PACT (included in Amendment 10).

All HRQoL assessments during the Chemotherapy Treatment and Maintenance Periods should be collected in clinic, on the day of study drug administration, prior to dosing or clinical procedures. They may be completed remotely if the participant is no longer actively returning to the site.

Biomarker Assessment

CCI [redacted]

Pharmacokinetic/Immunogenicity Assessment

PK blood samples will be collected for dostarlimab and niraparib (Table 19 and Table 20, respectively) for evaluation from all sites. Serum and plasma samples generated for dostarlimab and niraparib PK evaluation will be based on a CCI [redacted]
CCI [redacted]

Niraparib PK will be collected in the Maintenance Treatment Period only. To allow for hematologic toxicity recovery (approximately 6 to 9 weeks), participants will begin niraparib dosing at Cycle 2 or Cycle 3 of the Maintenance Treatment Period, and niraparib PK sampling will start accordingly on Day 1 as follows:

Cycle 2 niraparib start: Niraparib PK samples drawn on Cycle 2, Cycle 3, Cycle 7, and Cycle 9.

Cycle 3 niraparib start: Niraparib PK samples drawn on Cycle 3, Cycle 7, and Cycle 9.

CCI samples are the aliquots of PK sample collections and will be collected for CCI only (Table 19). CCI will be evaluated through CCI CCI (Screening, confirmatory, and titer), as well as CCI CCI (Not applicable per Amendment 10).

PACT Phase

Following the final analysis DCO date, the study may move into the PACT phase (see Section 5.6 for details). Participants who continue to receive study treatment during the PACT phase will be monitored for safety (see Section 8.2) and will receive follow-up care in accordance with standard local clinical practice. Assessments will revert to the standard of care at a participant's particular study site. Study treatment will continue for up to 3 years from the final DCO date, or until transition to an alternative method of continued treatment access (outside of the study), or manufacturing of the product ceases, or the study intervention discontinuation criteria are met (Section 4.3.1), whichever occurs first. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

End of Treatment Visit and Safety Follow-up Visit

All participants will undergo an EOT visit within 7 days after the last dose of study treatment or at the time of disease progression, whichever occurs first. A safety follow-up visit will be conducted 30 days (±7 days) after the last dose of the last study treatment or before the initiation of follow-up anticancer therapy. Safety follow-up visits are required only for those participants who have not started follow-up anticancer therapy. After the 30-day (±7 days) safety follow-up visit, all participants will enter the post-treatment follow-up period of telephone assessment for survival status, documentation and management of any AEs/SAEs, adverse events of special interest (AESIs), and follow-up anticancer therapy every 90 (±14 days) until participant discontinuation of study, withdrawal of consent, or death. CCI CCI CCI If a participant discontinues treatment within 28 days of the scan that indicates PD, then the EOT scan will not be performed.

Refer to schedule of events (Table 16) for adjustments to End of Treatment Visit and Safety Follow-up visits prior to PACT.

Following the local implementation of Amendment 10, the study will conclude all post-treatment long-term follow-up data collection beyond 90 days (±14 days) after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy or no follow-up data collection is required for the study if the participant transitions to continue the treatment outside of the study). After the 30-day (±7 days) safety follow-up visit, there will be only one post-treatment follow-up assessment for SAE and AESIs at 90 days following the last dose of study treatment.

A safety follow-up visit is not carried out for a participant who transitions to continue treatment outside of the study prior to PACT (see Section 5.5).

For a participant discontinuing treatment in the PACT phase, no end of treatment or safety follow-up visit is required.

Safety Assessments

Safety assessments conducted throughout the Chemotherapy Treatment Period and Maintenance Treatment Period include collection of TEAEs, serious adverse events (SAEs), treatment discontinuations or dose delays or reductions due to AEs, ECOG performance, clinical laboratory results (hematology and chemistry), vital sign measurements, observations during physical examination, and use of concomitant medications.

AEs are required to be captured through 30 days after cessation of study treatment; SAEs are required to be captured through 90 days after cessation of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy); and any pregnancies that occur within 180 days post-treatment discontinuation are to be captured. Once the specified safety reporting period has elapsed , if the Investigator learns of an AESI or an SAE that is considered reasonably related to the study intervention or study participation, the Investigator must promptly notify the Sponsor. All AEs and SAEs experienced by a participant, regardless of the suspected causality, will be monitored until the AE or SAE has resolved, until any abnormal laboratory values have returned to baseline or normalized, until there is a satisfactory explanation for the change(s) observed, until the participant is lost to follow-up or withdraws consent, or until the participant has died.

The niraparib AESIs for this study are myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), secondary cancers (new malignancies other than MDS/AML). There are no AESIs for dostarlimab. AESIs must be reported to the Sponsor as soon as the Investigator becomes aware of them.

For PACT, SAEs, AEs leading to study intervention discontinuation, AESI, pregnancy, and overdose cases will be reported, as outlined in Section 8.2.

3.7. End-of-Study Definition

A final DCO representing the end of data collection, prior to EOS, is defined as the DCO date for the final analysis. Following the final DCO date, the study may move into the PACT phase and the clinical study database will be closed to new data. Participants who have not transitioned to continue treatment access outside of the study at the time at final DCO who are receiving study treatment may continue, as described in Section 5.5, to receive niraparib and/or dostarlimab if they are deriving clinical benefit as assessed by the Investigator. Although the clinical study database will be closed to new data, the study will remain open until all participants discontinue study treatment and the EOS definition is reached.

The EOS is defined as the date of the Last Subject Last Visit (LSLV; defined as the date of the last subject to complete the study [i.e., assessments as defined in the Schedule of Events or last dose plus, if applicable, 90 day AE reporting period]).

4. SELECTION AND WITHDRAWAL OF PARTICIPANTS

4.1. Participant Inclusion Criteria

To be considered eligible to participate in this study the following requirements must be met:

1. Participants must be female, ≥18 years of age, able to understand the study procedures, and agree to participate in the study by providing written informed consent.
2. Participants with a histologically confirmed diagnosis of high-grade nonmucinous epithelial ovarian (serous, endometrioid, clear cell, carcinosarcoma, and mixed pathologies), fallopian tube, or peritoneal cancer that is Stage III or IV according to the FIGO or tumor, node and metastasis staging criteria [i.e., American Joint Committee on Cancer].
3. All participants with Stage IV disease are eligible. This includes those with inoperable disease, those who undergo PDS (R0 or macroscopic disease), or those for whom NACT is planned.
4. Participants with Stage III are eligible if they meet one or more of the following criteria:
    a. Stage IIIC participants with CC0 resection if they meet the following criteria: Aggregate ≥5 cm extra-pelvic disease during PDS as assessed by the Investigator.
    b. All participants with inoperable Stage III disease.
    c. All Stage III participants with macroscopic residual tumor (per Investigator judgment) following PDS.
    d. All Stage III participants for whom NACT is planned.
5. Participants must provide a blood sample for CCI testing at Pre-Screening or Screening.
6. Participant must provide CCI CCI
7. Participants of childbearing potential must have a negative serum or urine pregnancy test (beta human chorionic gonadotropin) within 3 days prior to receiving the first dose of study treatment.
8. Participants must be postmenopausal, free from menses for >1 year, surgically sterilized, or willing to use highly effective contraception to prevent pregnancy (see Appendix 3) or must agree to abstain from activities that could result in pregnancy throughout the study, starting with enrollment through 180 days after the last dose of study treatment.
9. Participants must have adequate organ function, defined as follows (Note: CBC test should be obtained without transfusion or receipt of stimulating factors within 2 weeks before obtaining Screening blood sample):

a. ANC ≥1,500/µL
b. Platelet count ≥100,000/µL
c. Hemoglobin ≥9 g/dL
d. Serum creatinine ≤1.5×upper limit of normal (ULN) or calculated creatinine clearance ≥60 mL/min using the Cockcroft-Gault equation
e. Total bilirubin ≤1.5×ULN or direct bilirubin ≤1.5×ULN
f. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5×ULN unless liver metastases are present, in which case they must be ≤5×ULN

10. Participants must have an ECOG score of 0 or 1.
11. Participants must have normal BP or adequately treated and controlled hypertension (systolic BP ≤140 mmHg and/or diastolic BP ≤90 mmHg).
12. Participants must agree to complete HRQoL questionnaires throughout the study.
13. Participants must be able to take oral medication.

4.2. Participant Exclusion Criteria

Participants will not be eligible for study entry if any of the following criteria are met:

1. Participant has mucinous, germ cell, transitional cell, or undifferentiated tumor.
2. Participant has low-grade or Grade 1 epithelial ovarian cancer.
3. Stage III participant with CC0 resection after PDS (i.e., no macroscopic residual disease, unless inclusion criterion #4a is met).
4. Participant has not adequately recovered from prior major surgery.
5. Participant has a known condition, therapy, or laboratory abnormality that might confound the study results or interfere with the participant's participation for the full duration of the study treatment in the opinion of the Investigator.
6. Participant is pregnant or is expecting to conceive children while receiving study drug or for up to 180 days after the last dose of study drug. Participant is breastfeeding or is expecting to breastfeed within 30 days of receiving the final dose of study drug (women should not breastfeed or store breastmilk for use, during niraparib treatment and for 30 days after receiving the final dose of study treatment).
7. Participant has known active central nervous system metastases, carcinomatous meningitis, or both.
8. Participant has clinically significant cardiovascular disease (e.g., significant cardiac conduction abnormalities, uncontrolled hypertension, myocardial infarction, uncontrolled cardiac arrhythmia or unstable angina <6 months to enrollment, New York Heart Association Grade 2 or greater congestive heart failure, serious cardiac arrhythmia requiring medication, Grade 2 or greater

peripheral vascular disease, and history of cerebrovascular accident within 6 months).

9. Participant has a bowel obstruction by clinical symptoms or CT scan, subocclusive mesenteric disease, abdominal or gastrointestinal fistula, gastrointestinal perforation, or intra-abdominal abscess.
10. Participant initiating bevacizumab as SOC has proteinuria as demonstrated by urine protein:creatinine ratio ≥1.0 at Screening or urine dipstick for proteinuria ≥2 (participants discovered to have ≥2 proteinuria on dipstick at baseline should undergo a 24-hour urine collection and must demonstrate <2 g of protein in 24 hours to be eligible).
11. Participant has any known history or current diagnosis of MDS or AML.
12. Participant has been diagnosed and/or treated with any therapy for invasive cancer <5 years from study enrollment, completed adjuvant chemotherapy and/or targeted therapy (e.g., trastuzumab) less than 3 years from enrollment, or completed adjuvant hormonal therapy less than 4 weeks from enrollment. Participants with definitively treated non-invasive malignancies such as cervical carcinoma in situ, ductal carcinoma in situ, Grade 1 or 2, Stage I endometrial cancer, or non-melanomatous skin cancer are allowed.
13. Participant is at increased bleeding risk due to concurrent conditions (e.g., major injuries or major surgery within the past 28 days prior to start of study treatment and/or history of hemorrhagic stroke, transient ischemic attack, subarachnoid hemorrhage, or clinically significant hemorrhage within the past 3 months).
14. Participant is immunocompromised. Participants with splenectomy are allowed. Participants with known human immunodeficiency virus (HIV) are allowed if they meet all of the following criteria:
    a. Cluster of differentiation 4 ≥350/µL and viral load <400 copies/mL
    b. No history of acquired immunodeficiency syndrome–defining opportunistic infections within 12 months prior to enrollment
    c. No history of HIV-associated malignancy for the past 5 years
    d. Concurrent anti-retroviral therapy as per the most current National Institutes of Health (NIH) Guidelines for the Use of Anti-retroviral Agents in Adults and Adolescents Living with HIV started >4 weeks prior to study enrollment [US Department of Health and Human Services, 2017].
15. Participant has known active hepatitis B (e.g., hepatitis B surface antigen reactive) or hepatitis C (e.g., hepatitis C virus ribonucleic acid [qualitative] is detected).
16. Participant is considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease, or uncontrolled infection. Specific examples include, but are not limited to, history of non-infectious pneumonitis that required steroids, current pneumonitis, uncontrolled autoimmune disease, uncontrolled ventricular arrhythmia, recent myocardial infarction within 90 days of consent, 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).

17. Participant has had investigational therapy administered within 4 weeks or within a time interval less than at least 5 half-lives of the investigational agent, whichever is longer, prior to the first scheduled day of dosing in this study.
18. Participant has received a live vaccine within 14 days of planned start of study therapy. Seasonal influenza vaccines that do not contain live viruses are allowed.
19. Participant has a known contraindication or uncontrolled hypersensitivity to the components of paclitaxel, carboplatin, niraparib, bevacizumab, dostarlimab, or their excipients.
20. Prior treatment for high-grade nonmucinous epithelial ovarian, fallopian tube, or peritoneal cancer (immunotherapy, anticancer therapy, radiation therapy).
21. Participant 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 (e.g., thyroid hormone or insulin).
22. Participant 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.

4.3. Participant Withdrawal Criteria

4.3.1. Discontinuation from Treatment

Participants may be discontinued from study treatment at any time. Participants who discontinue from study treatment will not be replaced. Participants who discontinue from the final study treatment will attend the EOT visit within 7 days after the last dose of study treatment, followed by the 30-day (±7 days) Safety Follow-up Visit. End of treatment is described as within 7 days after discontinuation of the last study treatment. Safety Follow-up Visit and the post-treatment, long-term follow-up period include OS assessment.

Following the local implementation of Amendment 10, the study will conclude all post-treatment long-term follow-up data collection beyond 90 days (±14 days) after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy, or no follow-up data collection is required for the study if the participant transitions to continue the treatment outside of the study). A participant's most recent long-term follow-up visit, which is greater than or equal to 90 days (±14 days) post-treatment (if applicable), before Amendment 10 becomes effective, will be recognized as the participant's final follow-up visit.

Specific reasons for discontinuing treatment include the following, in addition to those indicated in Section 3.4:

- AE
  - If a participant has any treatment-related National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE) v4.03 Grade 3 or 4 AEs (see Table 11 separate guidelines for platelet count) that have not reverted to NCI-CTCAE v4.03 Grade 1 or better within 28 days.
  - If upon re-challenge with study treatment at the lowest allowable dose any NCI-CTCAE v4.03 Grade 3 or 4 AEs recur, the participant must be discontinued from niraparib treatment.
  - AEs as defined per protocol (Table 10 and Table 11).
- In the case of thrombocytopenia, if the platelet count has not returned to ≥100,000/µL within 28 days of dose interruption.
- If the participant has disease progression according to RECIST v1.1 criteria by Investigator.
- If the participant has disease progression according to clinical criteria of histology/cytology confirmed PD in the absence of radiographic progression
- If there is risk to the participant as judged by the Investigator, Sponsor, or both.
- If the participant has had severe non-compliance with protocol as judged by the Investigator, Sponsor, or both.
- If the participant becomes pregnant.
- If the participant decides to discontinue study treatment. Note: Participant should continue in long term study follow up. For a participant discontinuing treatment in the PACT phase, no end of treatment or follow-up visits are required.
- If the participant is lost to follow-up.
- If the participant dies.
- PACT phase: 3 years of study treatment administration have been completed following final DCO date.

4.3.2. Withdrawal of Consent

If a participant considers withdrawal of consent, the Investigator is to determine whether the participant is willing to be followed up for subsequent procedures in the long-term follow-up period and for OS. Such participants will be required to indicate whether they agree to continue these procedures and to use of the blood and tumor samples they provided for the study for research purposes; the latter information will be recorded on the appropriate eCRF page. Survival status will be collected for participants who withdraw consent using acceptable means, including public records where allowed, per local regulations. The post-treatment, long-term follow-up period will continue until Amendment 10 is locally effective; the study will be closed for further post-treatment long-term follow-up data collection (refer to Section 4.3.1 for further details).

4.3.2.1. Further Research Maintaining Confidential Participant Information

The Sponsor may conduct further research on specimens collected during this study. CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]

In an effort to optimize the research that can be conducted with further research specimens, it is essential to link study participant clinical study data with further research test results. The clinical study data allow specific analyses to be conducted. Knowing participant characteristics like gender, age, medical history, treatment type, and treatment outcomes are critical to understanding the clinical context of further research analytical results.

To maintain privacy of information collected from specimens obtained for further research, the Sponsor has developed secure policies and procedures. All specimens will be single coded per ICH E15 guidelines, "Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories" [ICH Harmonised Tripartite E15, 2007].

At the clinical study site, unique codes will be placed on further research specimens for transfer to the storage facility. This first code is a random number that does not contain any personally identifying information embedded within it in order to maintain participant privacy. The link (or key) between participant identifiers and this first unique code will be held at the study site. No personal identifiers will appear on the specimen tube.

Documentation of participant life-time consent for further research will be captured in the eCRFs. Any specimens for which such an informed consent cannot be verified will be destroyed, as will those requested to be destroyed at time of consent withdrawal.

Participants may withdraw their consent for further research and have their specimens and all derivatives destroyed. Participants may withdraw their consent at any time by contacting the Investigator.

4.3.3. Discontinuation from the Study

Participants may be discontinued from the study for any of the following reasons:

- Withdrawal of consent by the participant, who is at any time free to discontinue participation in the study, without prejudice to further treatment
- Lost to follow up
- Death from any cause
- Sponsor decision to terminate study

If a participant is thought to be lost to follow-up or discontinues the study, attempts should be made to contact the participant to determine the reason for discontinuation. For participants who are thought to be lost to follow-up, at least 3 documented attempts over 6 months, including 1 attempt via certified mail or local equivalent methods, should be made to contact the participant before the participant is deemed lost to follow-up. These contact attempts should be documented in the participant's medical record.

Site personnel, or a trusted independent third party, should attempt to collect the vital status of the participant within legal and ethical boundaries for all participants randomized. Public sources may be searched for vital status information. If vital status is determined as deceased, this will be documented. Sponsor personnel will not be involved in any attempts to collect vital status information.

The Sponsor will notify the Investigators when the study is to be placed on hold, completed, or terminated. Per Investigator discretion and in consultation with the Sponsor, participants who are still receiving and benefiting from study treatment may have an option to continue to receive study treatment.

5. TREATMENT OF PARTICIPANTS

5.1. Description of Study Drug

Details about the investigational products are provided in Table 13. Following the analysis (DCO 31 October 2024), prior to PACT, participants ongoing on study drugs are to be centrally unblinded and placebo administration discontinued (i.e., Arm 1 niraparib placebo and/or dostarlimab placebo [not previously unblinded according to Amendment 4] and Arm 2 dostarlimab placebo). Arm 1 participants will be discontinued from the study following niraparib placebo and/or dostarlimab placebo discontinuation.

Table 13: Investigational Products

	Investigational Products		
Product name	Niraparib/placebo[a]	Niraparib[a]	Dostarlimab/placebo
Dosage form	CCI [redacted]		
Unit dose			
Route of administration	Oral	Oral	Intravenous
Physical description	CCI [redacted]		

[a] All participants in Arm 1 only who were previously randomized to placebo and are not receiving bevacizumab will be unblinded and provided the option to receive niraparib maintenance if they have received chemotherapy or discontinued chemotherapy ≤12 weeks.

[b] Transition from CCI [redacted] form anticipated during the PACT phase of the study.

For PACT, niraparib (capsule/tablet) and dostarlimab will be open-label.

5.2. Concomitant Medications

Any medication the participant takes other than the study treatment, including herbal and other non-traditional remedies, is considered a concomitant medication. All concomitant medications must be recorded in the eCRF. The following information must be recorded in the eCRF for each concomitant medication: generic name, route of administration, start date, stop date, dosage, and indication. Any changes in the dosage or regimen of a concomitant medication must be recorded in the eCRF.

At Screening, participants will be asked what medications they have taken during the last 30 days. At each subsequent study visit, participants will be asked what concomitant medications they are currently taking.

5.2.1. Prohibited Medications

Known prior medications that exclude a participant from participating in the study are described in the exclusion criteria (Section 4.2).

Participants are prohibited from receiving the following therapies during the Screening and treatment phase of this study:

- Systemic anticancer or biological therapy
- Immunotherapy not specified in this protocol
- Chemotherapy not specified in this protocol
- Investigational agents other than niraparib and dostarlimab
- Live vaccines within 14 days prior to the first dose of study treatment. Seasonal flu vaccines that do not contain live viruses are allowed.
- COVID-19 vaccine within 14 days prior to the first dose of dostarlimab.

An increased risk of infection by the administration of live virus and bacterial vaccines has been observed with conventional chemotherapy drugs. Effects with niraparib are unknown; therefore, live virus and bacterial vaccines should not be administered to participants in the study.

No other anticancer therapy is permitted during the course of the study treatment for any participant. Palliative radiotherapy (excluding the pelvic region and/or palliative radiotherapy encompassing >20% of the bone marrow within 1 week of the first dose of study treatment) is allowed for pre-existing small areas of painful metastases that cannot be managed with local or systemic analgesics, as long as no evidence of disease progression is present.

Systemic glucocorticoids for any purpose other than to manage symptoms of suspected irAEs. (Note: Use of inhaled steroids, local steroid injection, topical steroids, and steroid eye drops are allowed). If medically deemed necessary (e.g., acute asthma, or chronic obstructive pulmonary disease exacerbation, prophylaxis for IV contrast if indicated), Investigators are allowed to use their judgment to treat participants with systemic steroids. In such cases, systemic steroids should be stopped at least 24 hours prior to the next dose of study treatment. Note: corticosteroids used for premedication for chemotherapeutic agents specified in the protocol are allowed.

The niraparib safety profile includes risk for thrombocytopenia, and bevacizumab may increase the potential for bleeding (hemorrhage); therefore, participants should be advised to use caution when taking anticoagulants (e.g., warfarin) and antiplatelet drugs (e.g., aspirin).

Niraparib has the potential to weakly induce cytochrome P450 (CYP) 1A2. Therefore, participants and Investigators are advised to use caution with drugs that are substrates of CYP1A2 with narrow therapeutic range, such as theophylline and tizanidine.

Physicians should follow the current versions of the niraparib IB, local practice guidelines and package inserts for carboplatin, paclitaxel, and bevacizumab, and the dostarlimab IB for information on the general management of the participants receiving these therapies.

5.3. Treatment Compliance

Compliance with inclusion and exclusion criteria will be assessed as outlined in Section 4.1 and Section 4.2, respectively.

Study treatment (paclitaxel-carboplatin, niraparib, bevacizumab, and dostarlimab) will be administered by site personnel at study sites as detailed in Section 6.5.

Study drug accountability will be monitored as detailed in Section 6.6.

5.4. Randomization and Blinding

5.4.1. Participant Identification

All participants who enter into the Pre-Screening period of the study (defined as the point at which the participant signs the Pre-Screening ICF) will receive a unique participant identification number. This number will be used to identify the participant throughout the study and must be used on all study documentation related to that participant. A participant will be considered enrolled when the participant has consented and been screened, and when all eligibility criteria have been confirmed in the eCRF. The participant identification number must remain constant throughout the entire study; it must not be changed at the time of enrollment.

5.4.2. Randomization Scheme

CCI [redacted]

5.4.3. Blinding and Breaking the Blind

The participant, Investigator, Blinded Study Staff, the Blinded Sponsor study team and its representatives will be blinded to the CCI [redacted] and assigned treatment. An unblinded study team consisting of, at a minimum, a site Pharmacist, back-up Pharmacist, and Sponsor Monitor will keep confidential the treatment assignment of each participant and will dispense the study medication, retain and monitor the drug accountability records for the trial.

If an individual's role on the trial requires information about treatment assignment (e.g., an individual is involved in emergency unblinding), procedures will be used to ensure all other personnel remain blinded.

The identity of the treatments will be concealed by the use of study treatments that are all identical in appearance, packaging, labeling, and schedule of administration. CCI [redacted] CCI [redacted] CCI [redacted] For PACT, niraparib CCI [redacted] and dostarlimab will be open-label.

Treatment assignment may be unblinded for urgent or non-urgent clinical reasons as determined by the Investigator. The Sponsor's guidance regarding unblinding is as follows: the participant has confirmed disease progression as defined by the protocol (Section 7.1) and knowledge of experimental therapy may guide future treatment or treatment decisions for the participant in the case of an emergency medical event (as assessed by the treating physician). Participants who require unblinding of treatment assignment will be permanently discontinued from study treatment but will continue to be followed unless the participant withdraws consent.

The primary source for unblinding is the RaveX RTSM (formerly known as iMedidata Balance). Unblinding through RaveX RTSM can only be performed by individuals with the role of "Investigator blinded - can unblind," typically the Investigator and/or other limited medically qualified personnel deemed appropriate by the Investigator. The Help Desk is the secondary source for unblinding when RaveX RTSM is either not accessible by the primary Investigator or when an alternate qualified medical representative needs immediate access to treatment information. Additional information on the process for unblinding the identity of the assigned treatment is outlined in the Pharmacy Manual.

Following implementation of Amendment 4, Arm 1 participants receiving bevacizumab will remain blinded. Arm 1 participants not receiving bevacizumab will be unblinded centrally by the Sponsor and a communication will be sent to the investigative site unblinding the participants and indicating the treatment groups as outlined in Appendix 11.

5.4.3.1. Unblinding Post Analysis (31 October 2024, Prior to PACT)

The Sponsor may choose to initiate unblinding of Investigators to participants' study treatment assignment prior to PACT, or if the study is concluding or closure is initiated. Participants receiving niraparib and/or dostarlimab might continue with their treatment until a post-trial treatment outside of the study is in place, or continue into the PACT phase if treatment is not available and accessible, as outlined in Sections 5.5 and 5.6. The investigator may contact the medical monitor to discuss the participant's decision on their study treatment. Investigators may also request a participant's HRD status (if available) to determine post-trial niraparib treatment access in the participant's country, if relevant.

The study may be centrally unblinded prior to PACT, at which point randomization codes and treatment assignments will be provided to the investigators. Following the analysis (DCO 31 October 2024), the study Sponsor team was unblinded to the participants' HRD status (if available) and their assigned treatments, encompassing both placebo and active

drug groups. This unblinding was necessary to effectively manage ongoing participant care and plan for post-trial continued treatment access.

For participant management following the analysis (DCO 31 October 2024), prior to PACT, participants ongoing on study drugs are to be centrally unblinded and dostarlimab placebo administration is to be discontinued (i.e., Arm 1 niraparib placebo and/or dostarlimab placebo [not previously unblinded according to Amendment 4] and Arm 2 dostarlimab placebo). Arm 1 participants will be discontinued from the study following niraparib placebo and/or dostarlimab placebo discontinuation. Participants in Arm 2 and Arm 3 receiving active treatments, such as niraparib and/or dostarlimab, and centrally unblinded will not be discontinued from study treatment. These participants will be allowed to either continue with the study drug during the PACT phase or transition out of the study once treatment access becomes available and accessible, either before or during PACT, if applicable.

5.5. Continued Access to Study Intervention After the End of the Study

The investigator is responsible for ensuring that consideration has been given to the post-trial care of the participants' medical condition, whether or not GSK is providing specific post-trial provision.

The study remains open until all participants discontinue study treatment and the EOS definition is reached (see Section 3.7). Prior to PACT, participants who would continue to benefit and who have an acceptable tolerability profile to access niraparib and/or dostarlimab, if eligible, at the discretion of the treating physician and patient, excluding if there are safety concerns, may transition by the final DCO to continue treatment outside of the study protocol (if available). If the product(s) is/are not commercially available and accessible, participants may transition to either a rollover study, Managed Access route, or other potential mechanism of access. The selection of continued treatment access route will be according to availability in the participant's country and as permitted by local regulations. During the PACT phase, alternative continued treatment access route outside of this study may be implemented, as it becomes available.

For a Managed Access mechanism, if applicable, access will be given to eligible participants if the treating physician confirms that criteria are met (such as, a positive benefit-risk ratio and that there is no comparable or suitable alternative therapy available) and submits an explicit request to GSK for assessment. Niraparib and/or dostarlimab may be provided for a minimum of 3 years, or until the intervention becomes commercially available and accessible in the participant's country, or until manufacturing of the product ceases, whichever occurs first.

In a rollover study, if applicable, participants will be followed for safety and continue until treatment discontinuation criteria are met or according to the duration of the rollover study remaining at the time of transition, whichever occurs first.

Safety follow-up visits should be conducted (see Section 8.2) if the participant discontinues study treatment and does not continue niraparib and/or dostarlimab by a post-trial access route. Following such visits, the participant will have completed the study.

5.6. Continued Access to Study Intervention After Data Cut-off Prior to EoS

Following the DCO date for the final analysis, Study 213350 (FIRST) may move into the PACT phase. Participants receiving dostarlimab and/or niraparib at the time of the final analysis DCO date may continue to receive dostarlimab and/or niraparib if, in the opinion of their treating physician, they are clinically benefiting from continued treatment, they do not meet any protocol-defined treatment discontinuation criteria (Section 4.3.1) and the Sponsor is notified. Study treatment will continue for up to 3 years from the final DCO date (Section 4.3.1), or until transition to an alternative method of continued treatment access outside of the study (Section 5.5), or until manufacturing of the product ceases, or until a study intervention discontinuation criterion (Section 4.3.1), as assessed by the Investigator, has been met, whichever occurs first. Alternative continued treatment access outside of this study may be implemented, as it becomes available.

Participants who continue niraparib and/or dostarlimab in the PACT phase will be cared for in accordance with local standard clinical practice. Additional guidance on treatment with the study intervention and participant management is provided in the Pharmacy manual and Section 6.

Participants will continue to be monitored for all SAEs, AEs leading to study intervention discontinuation, overdoses, AESIs, and pregnancy while receiving niraparib and/or dostarlimab and these events must continue to be reported to the sponsor in accordance with Section 8.2. Information relating to participant care will be recorded on participant medical records but will not be reported for the purposes of this study.

For dispensing of study intervention and maintaining study intervention accountability in the PACT phase, please refer to the Pharmacy Manual. All other assessments will revert to standard of care at their site.

6. STUDY DRUG MATERIALS AND MANAGEMENT

Study drugs and their product family roles are defined below.

Study Drug	Product Family Role
Bevacizumab	AxMP
Carboplatin	AxMP
Paclitaxel	AxMP
Dostarlimab	IMP
Niraparib	IMP

6.1. Study Drug

6.1.1. Niraparib

CCI [redacted] CCI [redacted] is an orally available, potent, and highly selective PARP1 and PARP2 inhibitor. CCI [redacted] CCI [redacted] CCI [redacted] CCI [redacted] CCI [redacted].

6.1.2. Dostarlimab

Dostarlimab is an CCI [redacted] CCI [redacted]

6.2. Study Drug Packaging and Labeling

The label text of the study treatments will comply with Good Manufacturing Practice. The niraparib study treatment will be labeled in a blinded fashion. The site will be provided open-label dostarlimab, and the unblinded pharmacist will prepare the appropriate drug or placebo for administration. Carboplatin [Carboplatin Injection, 2023; CARBOplatin Injection BP, 2022], paclitaxel [Paclitaxel Injection Multidose Vial, 2023; Paclitaxel Powder for Injectable Suspension Nanoparticle, 2021], and bevacizumab [AVASTIN®, 2016; ZIRABEV- bevacizumab injection, 2023] are described in their respective prescribing information.

For PACT, niraparib (capsule/tablet) and dostarlimab will be open-label.

6.3. Study Drug Storage

All study treatment supplies must be stored in accordance with the Pharmacy Manual instructions and package labeling. Until dispensed or administered to the participants, the study treatment will be stored in a securely locked area that is accessible only to authorized personnel.

6.4. Study Drug Preparation

The Pharmacy Manual contains specific instructions for the preparation of each dose of the dostarlimab infusion solution.

6.5. Order of Study Drug Administration

It is recommended that drugs be administered starting with CCI CCI The recommended order of administration is provided below, unless local clinical practice or institutional policies differ:

- During the Chemotherapy Treatment Period, CCI CCI CCI
- During the Maintenance Treatment Period, CCI CCI

6.5.1. Investigational Medicinal Products

6.5.1.1. Niraparib

Participants who do not have PD on chemotherapy and with recovery to baseline (pre-randomization) of hematologic toxicities will enter the Maintenance Treatment Period. Oral niraparib placebo (Arm 1) or niraparib (Arms 2 and 3) will be dispensed to participants on Day 1 of Q21D cycle beginning with Cycle 2 or Cycle 3 of the Maintenance Treatment Period for up to 3 years, in the absence of PD, unacceptable toxicity, or participant withdrawal, or based on Investigator's decision. Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor.

On Day 1 of each applicable cycle, niraparib will be administered upon completion of bevacizumab or dostarlimab infusion; the first dose will be administered at the study site.

The starting dose of niraparib will be based on the participant's actual body weight and platelet count (Table 14) as measured prior to dosing in the Maintenance Treatment Period. Participants with an actual body weight of ≥77 kg and a platelet count of ≥150,000/µL will CCI at each dose administration. Participants with an actual body weight of <77 kg, a platelet count of <150,000/µL, or both will take CCI at each dose administration. Dose modifications will not be based upon changes in the participant's actual body weight during study participation (see Section 3.4).

For participants whose starting dose is CCI, escalation to CCI is permitted if no treatment interruptions or discontinuations were required during the first 2 cycles of therapy. This escalation will occur at the discretion of the Investigator, following discussion with the Sponsor.

Table 14: Recommended Initial Starting Dose

Baseline Criteria	Starting Dose
≥77 kg and ≥150,000/µL	CCI [redacted]
<77 kg OR <150,000/µL OR both	

Participants will be instructed to take their niraparib dose CCI at approximately the same time each day. Participants must swallow and not chew all CCI. The consumption of water and food with CCI is permissible. If a participant vomits or misses a dose of niraparib, a replacement dose should not be taken.

Details on the administration of niraparib can be found in the Pharmacy Manual.

6.5.1.2. Dostarlimab

During the Chemotherapy Treatment Period, dostarlimab/placebo CCI will be administered at the study site via a CCI on Day 1 of Q21D cycle. Dostarlimab/placebo will be started with Cycle 2 of chemotherapy and does not need to be held prior to or following major surgery.
Dostarlimab/placebo±bevacizumab will continue from the Chemotherapy Treatment Period through the Maintenance Treatment Period.

During the Maintenance Treatment Period, dostarlimab/placebo CCI will be administered via a CCI on Day 1 of every other cycle (every 6 weeks). At the time of disease progression, dostarlimab treatment will be unblinded and treatment with IV dostarlimab/placebo will be discontinued.

Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor.

Details on the administration of dostarlimab/placebo can be found in the Pharmacy Manual.

6.5.2. Non-Investigational Medicinal Products

6.5.2.1. Bevacizumab

For participants in all 3 Arms, during the Chemotherapy Treatment Period, optional bevacizumab 7.5 mg/kg or 15 mg/kg may be administered at the study site via a 90-minute IV infusion on Day 1 of Q21D cycle. The initial dose of bevacizumab will be delivered over 90 (±15) minutes. If the first infusion is tolerated without infusion-associated AEs (fever and/or chills), the second infusion may be delivered over 60 (±10) minutes. If the 60-minute infusion is well tolerated, all subsequent infusions may be delivered over 30 (±10) minutes.

Participants undergoing PDS or IDS may be administered bevacizumab as SOC (per local practice) during Cycles 1 to 6. After PDS or IDS, bevacizumab must not be administered less than 28 days before or 28 days following major surgery, and the post-operative incision must be fully healed.

During the Maintenance Treatment Period, participants in all 3 Arms may continue bevacizumab for up to 15 months (inclusive of bevacizumab administered during the Chemotherapy Treatment Period) [AVASTIN®, 2016].

Details on the administration of bevacizumab can be found in the local package insert; local practice guidelines for administration of bevacizumab should be followed.

6.5.2.2. Paclitaxel-Carboplatin (Cycles 1 to 6)

Paclitaxel and carboplatin may be administered per local practice guidelines if those guidelines differ from the description below. If a participant experiences a hypersensitivity to carboplatin, then cisplatin may be used in place of carboplatin. Desensitization to carboplatin will not be allowed on study. If a participant experiences hypersensitivity or clinically significant neuropathy on paclitaxel treatment, docetaxel can be substituted per the Investigator's discretion.

For participants in all 3 Arms, paclitaxel will be administered at 175 mg/m^2 via a 180-minute IV infusion on Day 1 of Q21D cycle during the Chemotherapy Run-In and Treatment Periods.

For participants in all 3 Arms, paclitaxel will be followed by carboplatin administered at an AUC of 5 to 6 mg/mL/min via a 60-minute IV infusion on Day 1 of Q21D cycle during the Chemotherapy Treatment Period.

Participants who have inoperable disease or who have undergone PDS will receive 6 cycles of paclitaxel-carboplatin.

Those participants who are to undergo IDS will receive 3 to 4 additional cycles of paclitaxel-carboplatin prior to surgery and an additional 2 to 3 cycles of paclitaxel-carboplatin in combination with dostarlimab/placebo following surgery, for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor.

6.6. Study Drug Accountability

The Investigator or designee is responsible for maintaining accurate dispensing records of the study treatments throughout the clinical study.

Details of maintaining drug accountability, including information on the accountability log, will be provided in the Pharmacy Manual.

All dispensation and accountability records for dostarlimab/placebo will be available for review by the Unblinded Study Monitor, who will assume the responsibility to reconcile the dostarlimab/placebo study treatment accountability log. The Unblinded Pharmacist will dispense study dostarlimab/placebo treatment for each participant according to the

protocol and Pharmacy Manual. The Study Monitor (blinded or unblinded) will assume the responsibility to reconcile the niraparib study treatment accountability log. The pharmacist (blinded or unblinded) will dispense niraparib study treatment for each participant according to the protocol and Pharmacy Manual.

6.7. Study Drug Handling and Disposal

At the end of study, when all participants have stopped protocol treatment, complete drug reconciliation per batch should be available at the site for verification in order to allow drug destruction or return procedure. After receiving Sponsor approval in writing, the investigational site is responsible for destruction of study drug according to local regulations. If a site does not have the capability for onsite destruction, the Sponsor will provide a return for destruction service through a third party. Both the unused and expired study treatment must be destroyed, upon authorization of the Sponsor, according to local regulations and procedures, and a copy of the destruction form must be filed in the study binder.

The medication provided for this study is to be used only as indicated in this protocol and only for the participants entered in this study.

7. ASSESSMENT OF EFFICACY

7.1. Primary Efficacy Endpoint

The primary efficacy endpoint is PFS, CCI [redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted] The same imaging modality (CT or MRI) should be used throughout the study. Positron emission tomography/CT may be used according to clinical guidelines, but its use is not a study requirement.

CCI [redacted]

CCI [redacted]

CCI [redacted]

The central review process will be as follows:

1. All imaging and supportive clinical data will be submitted for central review, as specified in the Imaging Charter.
2. Blinded Independent Central Review (BICR) CCI [redacted] will be conducted by 2 independent radiologists (along with an arbiter, as necessary).

A central blinded clinician will review clinical information.

Cycle timing will be delayed for treatment interruptions. Tumor assessment should occur according to Study Day schedule regardless of whether study treatment is interrupted (i.e., counting from C1D1 of the Chemotherapy or Maintenance Treatment Period as appropriate). If a participant discontinues treatment for a reason other than progression by RECIST v1.1, death, withdrawal of consent, or loss to follow-up, scans must continue at the specified intervals CCI [redacted]

CCI [redacted] Following completion of 3 years of maintenance therapy, in the absence of progression, participants will be evaluated clinically with annual scans and additional unscheduled scans for suspicion of disease progression based on increases in CA 125 or other suspicious symptoms. Participants may be considered for treatment beyond 3 years in consultation with the Sponsor.

7.2. Secondary Efficacy Endpoints

7.2.1. Overall Survival

OS is defined as the date of randomization to the date of death by any cause. Following the EOT visit, survival status will be collected for all participants using acceptable means, including telephone contact. New malignancy information will also be collected as part of the telephone contact survival status assessment.

GSK may request that updated survival data be collected on randomized participants outside the protocol window noted in the Schedule of Events (Table 17). At the time of the request, the site will determine survival status for each participant by the method agreed with the participant (unless the participant has withdrawn consent for survival follow-up) or allowed per local regulations (i.e., public sources).

Following the local implementation of Amendment 10, the study will conclude all post-treatment, long-term follow-up data collection beyond 90 days (±14 days) after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy, or no follow-up data collection is required for the study if the participant transitions to continue the treatment outside of the study). A participant's most recent long-term follow-up visit, which is greater than or equal to 90 days (±14 days) post-treatment (if applicable), before Amendment 10 becomes effective, will be recognized as the participant's final follow-up visit.

Updated survival data is no longer required following study discontinuation.

7.2.2. BICR determined PFS per RECIST v1.1

The BICR determined PFS [redacted]

7.2.3. Health-Related Quality of Life

Please see Section 3.6.2 for details on HRQoL.

The HRQoL assessments should be conducted in clinic, on the day of study drug administration, prior to dosing or clinical procedures during the Chemotherapy Treatment and Maintenance Periods. They may be completed remotely if the participant is no longer actively returning to the site. It is estimated that HRQoL assessments will take less than 20 minutes at each time point. Since these are questionnaires, their completion will not interfere with or prevent future treatment or clinical studies. HRQoL assessments should be administered prior to conducting any other procedures at each assessment.

European Quality of Life 5-Dimension 5-Level Scale

The EQ-5D-5L (Appendix 8) questionnaire is one of the most widely used instruments to measure HRQoL across oncology and non-oncology indications. It consists of a descriptive system and the European Quality (EQ) Visual Analogue Scale. The descriptive system comprises 5 questions, 1 for each of 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each is rated according to 5 response levels ("no problems," "slight problems," "moderate problems," "severe problems," "unable"/"extreme problems"). Responses to the questionnaire can be converted to a single utility index value. The EQ Visual Analogue Scale records the respondent's self-rated health on a 100-point scale between "Best imaginable health state" and "Worst imaginable health state." The absolute scores and change from baseline in the EQ-5D-5L VAS will be evaluated.

EORTC-QLQ-C30 and EORTC-QLQ-OV28

The EORTC-QLQ-C30 (Appendix 9) is a 30-item questionnaire used to measure HRQoL in participants with cancer; it has been translated and validated in over 100 languages and has been used in more than 3,000 studies worldwide (https://qol.eortc.org/questionnaires/core/eortc-qlq-c30/). The EORTC-QLQ-C30 is composed of both multi-item scales and single-item measures. These include 5 functional scales (Physical functioning, Role functioning, Emotional functioning, Cognitive functioning, and Social functioning), 3 symptom scales (Fatigue, Nausea and vomiting, and Pain), 6 single items (Dyspnea, Insomnia, Appetite loss, Constipation, Diarrhea, and Financial difficulties) and a global health status/health-related quality of life scale. The EORTC-QLQ-C30 employs a week recall period for all items and a 4-point scale for the functional and symptom scales/items with response categories "Not at all," "A little," "Quite a bit," and "Very much." The 2 items assessing global health status/quality of life utilize a 7-point scale ranging from 1 ("Very Poor") to 7 ("Excellent") [Aaronson, 1993].

The EORTC-QLQ-C30 is often used with other disease-specific instruments such as the ovarian-specific EORTC-QLQ-OV28 (Appendix 10), which assesses ovarian cancer participants' abdominal/gastrointestinal symptoms, other chemotherapy side effects, hormonal/menopausal symptoms, body image, attitude to disease/treatment, and sexual functioning.

The absolute scores and change from baseline in the EORTC-QLQ-C30, and EORTC-QLQ-OV28 HRQoL assessments will be evaluated.

7.2.4. Time to First Subsequent Therapy

TFST is defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy or death of any cause, whichever occurs first.

7.2.5. Time to Second Subsequent Therapy

TSST is defined as the time from the date of randomization to the start date of the second subsequent anticancer therapy or death of any cause, whichever occurs first.

7.2.6. Progression-Free Survival 2

PFS2 is defined as the time from the date of randomization to the date of first PD per Investigator's assessment after initiation of subsequent anticancer therapy or death due to any cause, whichever occurs first.

7.2.7. Objective Response Rate

ORR is defined as the proportion of participants with CR or PR CCI [redacted] CCI [redacted] (Appendix 4), for participants with measurable disease at baseline.

7.2.8. Duration of Response

DOR is defined as the time from first documentation of CR or PR [redacted] (Appendix 4) or death by any cause, whichever occurs first for participants with measurable disease at baseline.

7.2.9. Disease Control Rate

DCR is defined as the proportion of participants with a best overall response of CR, PR, or SD [redacted] (Appendix 4), for participants with measurable disease at baseline.

7.3. Biomarker Endpoints

[redacted]

7.4. Immunogenicity Endpoints

[redacted]

7.5. Pharmacokinetic Endpoints

Blood samples for the PK measurement of dostarlimab (Table 19) and niraparib (Table 20) will be obtained for all participants at all sites. [redacted]

Complete instructions for collection, processing, shipping, and handling of biomarker and PK/[redacted] samples are detailed in the study-specific Laboratory Manual.

8. ASSESSMENT OF SAFETY

8.1. Safety Parameters

CCI [redacted]

8.1.1. Demographic/Medical History

CCI [redacted]
CCI [redacted]
CCI [redacted]

8.1.1.1. Disease History

For disease history, the following will be documented:

- Date of diagnosis
- Tumor type
- Stage at time of initial diagnosis
- Histology and grade of disease at diagnosis
- Genotyping, CCI [redacted]
  CCI [redacted]

8.1.1.2. Medical and Surgical History

Major medical and surgical history (including medication history and history of thrombocytopenia, neutropenia, leukopenia, or anemia) will be collected. Details of any prior invasive malignancy will be collected. Medical and surgical history will be obtained by interviewing the participant or by reviewing the participant's medical records.

8.1.1.3. Previous and Concomitant Medications

Previous and concomitant medications will be documented as described in Section 5.2. Medications will be coded using World Health Organization (WHO) Anatomical Therapeutic Chemical classification.

8.1.2. Vital Signs

Blood pressure, temperature and heart rate (pulse) will be measured at Screening and at every visit. Additionally, BP and heart rate will be performed weekly for the first 8 weeks from the first dose of niraparib in the Maintenance Treatment Period (Table 17).

8.1.3. Weight and Height

Weight and height will be measured in accordance with the schedule of events (Table 17).

Height will be measured at Screening only. Weight will be measured at Screening and at every visit.

8.1.4. Physical Examination

Physical examinations and symptom-directed physical examinations will be performed in accordance with the schedule of events (Table 17).

Any physical examination or vital sign abnormalities assessed as clinically significant should be recorded as an AE or SAE. If SAE criteria are met, the finding should be recorded and reported according to the SAE reporting process (see Section 8.2.5).

8.1.5. Laboratory Assessments

The following laboratory variables will be determined in accordance with the schedule of events (Table 17).

These tests will be performed by the local laboratory at the clinical site. All labs in the Chemotherapy Treatment Period and the Maintenance Period may be performed up to -3 days from Day 1 dosing.

Any abnormal laboratory value assessed as clinically significant should be recorded as an AE. If SAE criteria are met or if the laboratory abnormality is an AESI (see Section 8.2.7), the event should be recorded and reported according to the SAE reporting process (see Section 8.2.5).

Hematologic, blood chemistry and coagulation factor testing may occur more frequently than is specified in the Schedule of Events in Table 18, if medically indicated per Investigator judgment or if the event meets the criteria for study treatment dose modification (see Section 3.4). Additional tests may be performed at a laboratory facility other than the study site, but the test results must be reported to the study site, the study site must keep a copy of test results with the participant's study file, and the results must be entered into the eCRF.

Any suspected case of MDS/AML or secondary cancer (new malignancy other than MDS/AML) reported while a participant is receiving treatment or followed for post-treatment assessments must be referred for evaluation to a local hematologist to perform bone marrow aspirate and biopsy as per local practice. The study site must receive a copy of the hematologist's report of aspirate/biopsy findings, which must include a classification according to WHO, and other sample testing reports related to MDS/AML. Report data will be entered in the appropriate eCRF pages, and the site must keep a copy of all reports with the participant's study file.

8.1.5.1. Hematology

The following hematologic parameters will be measured:

- **CBC:**
  - Hemoglobin
  - Platelet count
  - White blood cell count
  - Differential white blood cell count
- **Coagulation factors:**
  - International normalized ratio
  - Activated partial thromboplastin time

8.1.5.2. Blood Chemistry

The following blood chemistry parameters will be measured:

- **Blood chemistry:**
  - Sodium
  - Potassium
  - Chloride
  - Calcium
  - Magnesium
  - Glucose
  - Total bilirubin
  - AST
  - ALT
  - Total protein
  - Albumin
  - Creatinine
  - Urea or blood urea nitrogen
  - Thyroid function (thyroid stimulating hormone [TSH])
  - Amylase

8.1.5.3. Tumor Marker

CA 125 will be obtained at Screening and at Day 1 of each cycle during the Chemotherapy Treatment Period and at Day 1 of each cycle during the Maintenance Treatment Period. After 1 year of maintenance (i.e., after cycle 17), CA 125 will be obtained Q6W until end of treatment.

8.1.5.4. Urine Protein

For participants receiving bevacizumab, urine dipstick for protein determination will be performed at Screening. Participants discovered to have ≥2 proteinuria on dipstick should not be administered bevacizumab, should undergo a 24-hour urine collection, and must demonstrate <2 g of protein in 24 hours to be eligible for bevacizumab treatment.

8.1.5.5. Drug Screen

Not applicable.

8.1.5.6. Pregnancy Screen

Niraparib and dostarlimab are known to have properties that require the participant to use contraception and may have adverse effects on a fetus in utero. A negative serum or urine pregnancy test is required within 3 days prior to C1D1 for females of childbearing potential. Urine pregnancy testing will be performed on Day 1 of each subsequent cycle and at the Safety Follow-Up Visit. Participants should start using birth control from Screening throughout the study period up to 180 days after the last dose of study treatment. If there is any question that a participant will not reliably comply with the contraception requirements, they should not be enrolled in the study, and any participant who becomes pregnant should be withdrawn from the study. Any pregnancies that occur within 180 days post-treatment discontinuation are to be reported as described in Section 8.2.11.

8.1.6. Hepatitis B and Hepatitis C Testing

Hepatitis B virus/Hepatitis C virus (HBV/HCV) testing will be done at Screening.

8.1.7. ECOG Performance Status

Performance status will be assessed using the ECOG scale (see Appendix 6) in accordance with the schedule of events (Table 17). The same observer should assess performance status each time.

8.1.8. Electrocardiogram

Standard 12-lead electrocardiograms (ECGs) will be performed at Screening.

8.2. Adverse and Serious Adverse Events

8.2.1. Definitions

8.2.1.1. Adverse Event

Any untoward medical occurrence that occurs in a participant or clinical investigation subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An AE can, therefore, be any unfavorable and unintended sign (including clinically significant laboratory findings), symptom, or disease temporally associated with the use of an investigational product or other study treatment, whether or not considered related to the product.

Adverse events may include the onset of new illness and the exacerbation of pre-existing medical conditions. An AE can include an undesirable medical condition occurring at any time after the signing of the informed consent, including baseline or washout periods, even if no study treatment has been administered (See Section 8.2.3 for information about AE collecting and reporting.).

8.2.1.2. Serious Adverse Event

Any untoward medical occurrence, that, at any dose:

- Results in death;
- Is life threatening (i.e., an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe);
- Requires inpatient hospitalization* or prolongation of existing hospitalization;
- Results in persistent or significant disability or incapacity;
- Is a congenital abnormality or birth defect;
- Is an important medical event†

*Exception: Hospitalization for elective procedures, for protocol compliance, or for observation will not be considered criteria for an SAE. Adverse events due to disease progression do not need to be reported as SAEs because they are part of the natural history of advanced cancer. The reason for the planned hospitalization should be captured in medical history section in the eCRF. Complications experienced during these hospitalizations must be reported as AEs (or SAEs, if hospitalization is prolonged due to the AE).

†Medical and scientific judgment should be exercised in determining whether situations or events should be considered SAEs: an important medical event may not be immediately life-threatening or result in death or require hospitalization but may jeopardize the participant or require intervention to prevent one of the above outcomes. Examples of such events are allergic bronchospasm, blood dyscrasias, or convulsions that may require intensive treatment in an emergency room or at home but do not result in hospitalization, development of drug dependency or drug abuse, and transmission of

disease associated with the administration of the study drug. (See Section 8.2.5 for information about SAE reporting.)

8.2.1.3. Treatment-Emergent Adverse Event

Any event that was not present prior to the initiation of study treatment or any event already present that worsens in either intensity or frequency following exposure to study treatment.

8.2.1.4. Adverse Event of Special Interest

Any AE (serious or non-serious) that is of scientific and medical concern specific to the study treatment, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor is appropriate.

8.2.1.5. Overdose

An overdose is a deliberate or accidental administration of study treatment to a study participant, at a dose greater than that which was assigned to that participant per the study protocol and under the direction of the Investigator. If an overdose occurs, the Investigator and the Sponsor should be notified immediately, and the participant should be observed closely for AEs. Associated AEs should be treated and monitored by the Investigator. The dosage of study drug administered, any associated AEs, and/or treatment provided to the participant because of the overdose, should be documented on the applicable sections within the eCRF.

8.2.2. Assessment of Adverse Events

8.2.2.1. Severity Assessment

All AEs will be assessed by the Investigator for severity according to Common Terminology Criteria for Adverse Events (CTCAE) v4.03: 14 June 2010; NIH, National Cancer Institute (NCI). The CTCAE severity grades 1 through 5 provide unique clinical descriptions of severity of each AE. The CTCAE v4.03 is available on the NCI/NIH website.

Please note that there is a distinction between serious and severe AEs: Severity is a measure of intensity whereas seriousness is defined by the criteria in Section 8.2.1.2. For example, a mild degree of gastrointestinal bleeding requiring an overnight hospitalization for monitoring purposes may be considered an SAE but is not necessarily severe.

8.2.2.2. Relationship to Study Intervention

The Investigator must provide a causality assessment regarding the relationship of the event with the study drug and/or study procedure for all AEs. One of the following categories should be selected based on medical judgment, considering all contributing factors:

- Related: A causal relationship between the medicinal product (or study procedures or both) and AE is a reasonable possibility. For example, the occurrence of the AE cannot be explained by other causative factors. The AE,

however, can be explained by pharmacological effect of the medicinal product such as a similar event having been reported previously, alteration of the dose effect, or the timing or seriousness of the AE, etc. Positive rechallenge/dechallenge is supportive.

- Not Related: A causal relationship between the medicinal product (or study procedures or both) and AE is not a reasonable possibility: there is no temporal relationship between the medicinal product and event, or an alternative etiology is more reasonable.

8.2.2.3. Expectedness

The Sponsor will be responsible for determining whether an AE is 'expected' or 'unexpected'. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information provided in the Reference Safety Information in the niraparib or dostarlimab IB.

8.2.3. Collection and Recording Adverse Events

Adverse events may be volunteered spontaneously by the study participant, or discovered by the study staff during physical examinations or by asking an open, non-leading question such as, "How have you been feeling since your last study visit?" The Investigator will document the nature of AE, date of onset of the AE (and time, if known), date of outcome of the AE (and time, if known), severity of the AE, action taken with study drug as a result of the AE, assessment of the seriousness of the AE, and assessment of the causal relationship of the AE to study drug and/or study procedure.

Adverse events, including laboratory abnormalities that are assessed as clinically significant or require intervention, should be described using a diagnosis whenever possible, rather than individual underlying signs and symptoms. When a clear diagnosis cannot be identified, each sign or symptom should be recorded as a separate AE.

All SAEs will be collected from the signing of the ICF for this study up to 90 days (±14 days) after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy) and recorded in the eCRF. Serious AEs will also be reported on an SAE form as described in Section 8.2.5 of this protocol. Once the specified post-treatment safety reporting period has elapsed, if the Investigator learns of an SAE that is considered reasonably related to the study intervention or study participation, the Investigator must promptly notify the Sponsor.

All AEs, regardless of the source of identification (e.g., physical examination, laboratory assessment, ECG, or reported by participant), will be collected and recorded in the eCRF for each participant from the signing of the ICF for this study up to 30 days after the last dose of study treatment.

Concomitant illnesses that existed before entry into the study will not be considered AEs unless the illness worsens during the Treatment Period. Pre-existing conditions will be recorded as Medical History in the eCRF and on the SAE Report Form.

Disease progression is an efficacy criterion and is therefore not considered an AE or SAE (even if fatal). Disease progression should be reported within the eCRF. If AEs/SAEs occur in relation to disease progression that are not consistent with the natural progression of the participant's disease, these AEs/SAEs must be reported per AE/SAE reporting requirements described in Section 8.2.5.

8.2.3.1. Safety Reporting During PACT

For participants in the PACT phase of the study, the Sponsor will continue to collect safety information. Investigators must report directly to the Sponsor all SAEs, AEs leading to study treatment discontinuation, overdose, AESIs, and pregnancy cases via paper forms. SAEs, AEs leading to study intervention discontinuation, AESI, and overdose cases will be reported during the PACT study intervention period and for up to 90 days (±14 days) after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy). Any pregnancies that occur within 180 days post-treatment discontinuation will be captured for all participants (not only participants in PACT Phase), in accordance with Section 8.2.11.

For all PACT phase participants who transition to continue treatment outside of the study (for example through Managed Access route or commercial access), the day of their last dose of study intervention during the PACT phase is the end date for safety collection and reporting for this study. Once the specified post-treatment safety reporting period has elapsed, investigators are not obliged to actively seek information on AEs, SAEs or AESIs, however if the Investigator learns of an AESI or an SAE that is considered reasonably related to the study intervention or study participation, the Investigator must promptly notify the Sponsor. The Sponsor retains the right to request additional information for any participant with ongoing AEs/SAEs/AESIs at EOS, if judged necessary.

Additionally, any SAEs that are ongoing at the time of the final DCO (prior to PACT) must be followed up to resolution unless the event is considered by the Investigator unlikely to resolve, or the participant is lost to follow-up. Updates to these events will also occur via paper forms directly to the Sponsor. The Sponsor retains the right to request additional information for any participant with ongoing AEs/SAEs/AESIs at final DCO, if judged necessary.

8.2.4. Follow-Up of Adverse Events

All AEs experienced by a participant, regardless of the suspected causality, will be monitored until the AE or SAE has resolved, until any abnormal laboratory values have returned to baseline or normal levels, until stabilized with a satisfactory explanation for the changes observed, until the participant is lost to follow-up, or until the participant has died.

If an Investigator becomes aware of an SAE after the specified follow-up period and considers the SAE related to the study drug, the Investigator should report the SAE to the Sponsor according to timelines for reporting SAEs described in Section 8.2.3.

8.2.5. Reporting

The Investigator must report all SAEs, and all follow-up information to the Sponsor on an SAE Report Form within 24 hours of becoming aware of the initial event or follow-up information. The Investigator must provide a causality assessment and must sign and date all SAE Report Forms.

It is the responsibility of the Investigator to review source documentation and describe pertinent information on the SAE Report Form. If supporting documentation is requested (e.g., hospital reports, consultant reports, death certificates, autopsy reports, etc.), the Investigator should highlight all relevant and pertinent information within such documents, ensure that any participant's personal identifiers (including Medical Record number) are removed, and submit the documents with the SAE Form to the Sponsor. The Sponsor (or designee) will return a confirmation of receipt for all email reports (if received from other than a "no reply" domain) within 1 business day.

After receipt of the initial report, the Sponsor (or designee) will review the information and, if necessary, contact the Investigator to obtain further information. The Investigator must promptly respond to queries from the Sponsor.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting (including Suspected Unexpected Serious Adverse Reaction [SUSAR reporting]) to the regulatory authority, institutional review boards (IRBs)/independent ethics committees (IECs), and investigators.

In the PACT phase, all completed paper safety reports must be sent to the Sponsor by email or fax within the timeframes shown in Table 15.

Table 15: Timeframes for Submitting SAE, Pregnancy and Other Event Reports to GSK in the PACT Phase

Type of event	Initial reports		Follow-up of relevant information on a previous report	
	Timeframe	**Documents**	**Timeframe**	**Documents**
SAEs	24 hours*‡	paper SAE report form	24 hours*	paper SAE report form
Pregnancies	24 hours*	paper pregnancy notification form	24 hours*	paper pregnancy follow-up form
AESIs	24 hours**‡	paper AE or SAE (as applicable) report form	24 hours*	paper AE or SAE (as applicable) report form
Overdose	24 hours*	paper AE or SAE (as applicable) report form	24 hours*	paper AE or SAE (as applicable) report form
AE leading to discontinuation	24 hours*	paper AE or SAE (as applicable) report form	24 hours*	paper AE or SAE (as applicable) report form

AE = Adverse event; AESIs = Adverse event of special interest; SAE = Serious adverse event.
* Timeframe allowed after receipt or awareness of the information by the investigator/site staff.
** Timeframe allowed once the investigator determines that the event meets the protocol definition of an AESI.
‡ Paper Reports will be dated and signed by the investigator (or designee). For each SAE/AESI, the investigator(s) must document in the medical notes that they have reviewed the SAE/AESI and have provided an assessment of causality.

8.2.6. Submission and Distribution of Serious Adverse Event Reports

Per regulatory requirements, if an event is assessed by the Sponsor as a SUSAR, it is the responsibility of the Sponsor to submit the SUSAR to Regulatory Authorities according to applicable regulations and in accordance with regional reporting requirements. For example, in the EU/EEA, the Sponsor will assess expectedness of all serious adverse

reactions (SARs) and report SUSARs in an expedited manner to the EudraVigilance database in accordance with CTR 536/2014 Annex I D20(c). Sponsor policy and applicable provision to Investigators as necessary should also apply.

In addition, the SUSAR will be distributed to the Investigators/sites, utilizing a Council for International Organizations of Medical Sciences report form, or the MedWatch 3500A form. Urgent safety measures and/or other events that are not SUSARs that are determined to potentially affect the benefit-risk balance of the clinical trial will also be submitted by the Sponsor to Regulatory Authorities according to applicable local regulations.

The timelines for reporting SUSARs by the sponsor are:

- In the case of fatal or life-threatening SUSARs, within 7 calendar days after the sponsor became aware of the reaction;
- In the case of non-fatal or non-life-threatening SUSARs, within 15 calendar days after the sponsor became aware of the reaction;
- In the case of a SUSAR which was initially considered to be non-fatal or non-life threatening, but which turns out to be fatal or life-threatening, within 7 calendar days after the sponsor became aware of the reaction being fatal or life-threatening.

8.2.7. Adverse Events of Special Interest

AESIs for niraparib are the following:

- MDS and AML
- Secondary cancers (new malignancies other than MDS or AML)

There are no AESIs for dostarlimab.

Reporting AESIs: All occurrences of AESIs must be reported. If the AESI is serious, it should be reported in EDC; if the AESI is nonserious, it should be reported on a designated AESI paper form. The completed electronic SAE custom report from EDC or the AESI paper form must be sent to the Sponsor by email or fax within 24 hours of awareness of the event.

AESI should be collected and reported as follows:

- MDS and AML and secondary cancers (new malignancies other than MDS/AML) should be reported to the Sponsor until death or loss to follow-up.
- During the PACT phase, investigators must continue to directly report AESIs during treatment with niraparib and for 90 days after the last dose of niraparib. If the Investigator learns of an AESI after the last dose of niraparib, the Investigator must promptly notify the Sponsor.

8.2.8. Myelodysplastic Syndrome/Acute Myeloid Leukemia

MDS and AML including cases with fatal outcome, have been reported with the use of niraparib. In clinical trials, the duration of niraparib treatment in participants prior to developing MDS/AML varied from 1 month to >4 years. The cases were typical of secondary, cancer therapy-related MDS/AML. All participants had received platinum-containing chemotherapy regimens, and many had also received other DNA-damaging agents and radiotherapy. Some of the participants had a history of bone marrow suppression. For suspected MDS/AML or prolonged hematological toxicities, the participant should be referred to a hematologist for further evaluation. If MDS and/or AML is confirmed, then niraparib should be permanently discontinued and the participant should be treated appropriately.

8.2.9. Hypertension, Including Hypertensive Crisis

Hypertension, including hypertensive crisis, has been reported with the use of niraparib. Pre-existing hypertension should be adequately controlled before starting niraparib treatment. While receiving treatment, hypertension should be medically managed with antihypertensive medicinal products with or without niraparib dose adjustment.

Blood pressure and heart rate should be monitored at least weekly for the first 2 months of niraparib treatment in the maintenance setting, then monthly for the first year and periodically thereafter during treatment with niraparib. Niraparib should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.

8.2.10. Posterior Reversible Encephalopathy Syndrome

There have been rare reports of niraparib-treated patients developing signs and symptoms that are consistent with posterior reversible encephalopathy syndrome (PRES). PRES is a rare neurologic disorder that can present with the following signs and symptoms including seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended, along with discontinuation of niraparib. The safety of reinitiating niraparib therapy in patients previously experiencing PRES is not known.

8.2.11. Pregnancy

The Investigator must report all pregnancies and the outcomes to the Sponsor. The Sponsor has the responsibility to monitor the outcome of all pregnancies reported during the clinical study.

Each pregnancy must be reported by the Investigator to the Sponsor on an Initial Pregnancy Report Form within 24 hours of becoming aware of the pregnancy. Pregnancy is not an AE, and therefore does not need to be reported as an AE in the eCRF unless there is a suspicion that the study drug may have interfered with the effectiveness of a contraceptive medication. The Investigator must follow-up all pregnancies, document the course and the outcome, and report this information to the Sponsor on a Pregnancy

Outcome Report Form within 24 hours of becoming aware - even if the participant was withdrawn from the study or the study has finished.

An elective abortion without complications should not be regarded as an AE, however, it should be reported as the outcome to the pregnancy on the Pregnancy Outcome Report Form. Therapeutic abortions should be reported as a treatment procedure; the reason for the therapeutic abortion should be reported on the Pregnancy Outcome Report Form and as an AE in the eCRF. Hospitalization for normal delivery of a healthy newborn should not be considered an SAE.

Any SAE that occurs during pregnancy must be recorded on the Pregnancy Outcome Report Form, reported as an SAE on the SAE Report Form (e.g., maternal serious complications, therapeutic abortion, ectopic pregnancy, stillbirth, neonatal death, congenital anomaly, birth defect) and reported to the Sponsor within 24 hours. Hospitalization for normal delivery of a healthy newborn should not be considered an SAE.

After the study transitions to the PACT phase, investigators must continue to directly report pregnancies for up to 180 days following the last dose of study treatment for all participants. This includes those who discontinued study treatment prior to the PACT phase, as well as participants continuing in the PACT phase.

9. STATISTICS

Full details of the statistical analyses will be provided in the study's statistical analysis plan (SAP). The SAP will be finalized prior to database lock. Any changes to the methods described in the plan will be described and justified in the final clinical study report.

All analyses will include summary statistics, including the number and percentage for categorical variables and the number of participants, mean, standard deviation, median, minimum, and maximum for continuous variables. Time-to-event analyses will be performed using the Kaplan Meier method. Two-sided 95% CIs will be provided where appropriate.

9.1. Sample Size Determination

CCI

[redacted]

9.2. Analysis Populations

- The ITT population consists of all randomized participants. Any deceased participants randomized in error with death prior to randomization will be excluded from the population. Participants will be analyzed as randomized.
- The Safety Analysis Population includes all randomized participants who received at least 1 dose of study treatment after randomization. Participants will be analyzed according to the treatment that they actually received.
- The PK Analysis Population is defined as all participants in Arm 2 (niraparib only) and Arm 3 (both niraparib and dostarlimab) who received at least 1 dose of either drug and have at least 1 measurable postdose PK result. PK populations are defined separately for niraparib and dostarlimab.

CCI [redacted]

9.3. Demographics, Medical History, Baseline Characteristics, and Concomitant Medications

CCI [redacted]

9.4. Efficacy Analyses

CCI [redacted]

CCI [redacted]

9.4.1. Primary Efficacy Analysis

CCI [redacted]

9.4.2. Secondary Efficacy Analyses

CCI [redacted]

9.5. Safety Analyses

CCI [redacted]

9.6. Interim Analyses

Planned periodic safety analyses will be conducted by the IDMC after 24 randomized

CCI [redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted]

9.7. Final Analyses

A final safety analysis at the time of final DCO will be performed.

9.8. Biomarker Analysis

CCI [redacted]

9.9. Immunogenicity Analysis

CCI [redacted]

9.10. Pharmacokinetic Analysis

CCI [redacted]

9.10.1. Statistical Analysis of PK Data

CCI [redacted]

9.10.2. Exploratory Biomarker Analyses

If deemed appropriate and if data permit, CCI [redacted]
CCI [redacted]
CCI [redacted]
CCI [redacted]

10. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

10.1. Study Monitoring

Before an investigational site can enter a participant into the study, a representative of the Sponsor will visit the investigational study site to:

- Determine the adequacy of the facilities to support the clinical trial, including, but not limited to, clinical sample collection and management as per the laboratory manual.
- Discuss with the Investigator(s) and other personnel their responsibilities with regard to protocol adherence, and the responsibilities of the Sponsor or its representatives. This will be documented in a Clinical Study Agreement between the Sponsor and the Investigator.

During the study, a monitor from the Sponsor or representative will have regular contacts with the investigational site, for the following:

- Provide information and support to the Investigator(s).
- Confirm that facilities remain acceptable and that clinical samples are being appropriately managed.
- Confirm that the investigational team is adhering to the protocol, that data are being accurately recorded in the case report forms, and that investigational product and other study treatment accountability checks are being performed.
- Perform source data verification. This includes a comparison of the data in the case report forms with the participant's medical records at the hospital or practice, and other records relevant to the study. This will require direct access to all original records for each participant (e.g., clinic charts).
- Record and report any protocol deviations not previously sent to the Sponsor.
- Confirm AEs and SAEs have been properly documented on eCRFs, and confirm any SAEs have been forwarded to the Sponsor and those SAEs that met criteria for reporting have been forwarded to the IRB.

The monitor will be available between visits if the Investigator(s) or other staff needs information or advice.

10.2. Audits and Inspections

Authorized representatives of the Sponsor, a regulatory authority, an IEC, or an IRB may visit the site to perform audits or inspections, including source data verification. The purpose of a Sponsor audit or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, Good Clinical Practice (GCP) guidelines of the ICH, and any applicable regulatory requirements. The Investigator should contact the Sponsor immediately if contacted by a regulatory agency about an inspection.

10.3. Institutional Review Board (IRB)/Institutional Ethics Committee (IEC)

The Principal Investigator must obtain IRB or IEC approval, as appropriate, for the investigation. Initial IRB/IEC approval, and all materials approved by the IRB/IEC for this study including the participant consent form and recruitment materials must be maintained by the Investigator and made available for inspection.

11. QUALITY CONTROL AND QUALITY ASSURANCE

To ensure compliance with GCPs and all applicable regulatory requirements, the Sponsor may conduct a quality assurance audit. The Sponsor will be responsible for notifying Regulatory Authorities of serious breaches of GCP per applicable local regulations.

Please see Section 10.2 for more details regarding the audit process.

12. ETHICS

12.1. Ethics Review

The final study protocol, including the final version of the ICF, must be approved or given a favorable opinion in writing by an IRB or IEC, as appropriate. The Investigator must submit written approval to the Sponsor before he or she can enroll any participant into the study.

The Principal Investigator is responsible for informing the IRB or IEC of any amendment to the protocol in accordance with local requirements. In addition, the IRB or IEC must approve all advertising used to recruit participants for the study. The protocol must be re-approved by the IRB or IEC upon receipt of amendments and annually, as local regulations require.

The Principal Investigator is also responsible for providing the IRB with reports of any reportable serious adverse drug reactions (ADR) from any other study conducted with the investigational product. The Sponsor will provide this information to the Principal Investigator.

Progress reports and notifications of serious ADR will be provided to the IRB or IEC according to local regulations and guidelines.

12.2. Ethical Conduct of the Study

The study will be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki (please see Appendix 7) and are consistent with ICH/GCP guidelines, applicable regulatory requirements, and the Sponsor's policy on Bioethics.

12.3. Written Informed Consent

The Principal Investigator(s) at each center will ensure that the participant is given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study. Participants must also be notified that they are free to discontinue from the study at any time. The participant should be given the opportunity to ask questions and allowed time to consider the information provided.

The participant's signed and dated informed consent must be obtained before conducting any study procedures.

The Principal Investigator(s) must maintain the original, signed ICF. A copy of the signed ICF must be given to the participant.

13. DATA HANDLING AND RECORDKEEPING

13.1. Inspection of Records

The Sponsor will be allowed to conduct site visits to the investigation facilities for the purpose of monitoring any aspect of the study. The Investigator agrees to allow the monitor to inspect the drug storage area, study drug stocks, drug accountability records, participant charts and study source documents, and other records relative to study conduct.

13.2. Retention of Records

The Sponsor and the Investigator will ensure the clinical trial master file is archived for at least 25 years after the end of the clinical trial. Medical files of participants will be archived in accordance with national law.

The clinical trial master file will be archived in a manner that guarantees its easy availability and accessibility for competent authorities upon their request. Any change in ownership of the clinical trial master file will be properly documented. The new owner will be required to uphold the responsibilities outlined in this protocol. As the sponsor, TESARO (GSK) will designate specific individuals within the organization to manage the archives. Access to these archives will be limited to these designated individuals. The media chosen for archiving the clinical trial master file will ensure the content remains intact and readable throughout the specified archiving period.

The Principal Investigator must maintain all documentation relating to the study for a period of 2 years after the last marketing application approval or, if not approved, 2 years following the discontinuance of the test article for investigation. If it becomes necessary for the Sponsor or the Regulatory Authority to review any documentation relating to the study, the Investigator must permit access to such records.

14. PUBLICATION POLICY

GSK seeks to publish medically or scientifically significant results in searchable peer-reviewed scientific literature within 18 months from Last Subject Last Visit (LSLV). The publication policy is based on the guidelines described in the Joint ENGOT and GOG-Foundation Requirements for Trials with Industry Partners [Vergote, 2019] and agreed upon by the FIRST Publication Steering Committee Charter which outlines the conditions for authorship, decision-making, data analysis, and publication guidelines. Information regarding publication of study results is contained in the Clinical Trial Agreement for this study. GSK follows the International Committee of Medical Journal Editors standards for authorship and implements the Good Publication Practices to guide its publications.

15. LIST OF REFERENCES

Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365-376.

ACS. Ovarian CancerFacts and Figures 2016. Available at: http://www.cancer.org/cancer/ovariancancer/index. Accessed: 16 August 2016.

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012;30(17):2039-2045.

Atkins MB, McDermott DF, Powles T, et al. IMmotion150: A phase II trial in untreated metastatic renal cell carcinoma (mRCC) patients (pts) of atezolizumab (atezo) and bevacizumab (bev) vs and following atezo or sunitinib (sun). J Clin Oncol. 2017;35:15_suppl:4505-4505.

AVASTIN® (bevacizumab) solution for intravenous infusion Prescribing Information. San Francisco, CA: Genentech Inc. 2016. Available at: https://www.gene.com/download/pdf/avastin_prescribing.pdf.

Bindra RS, Crosby ME, Glazer PM. Regulation of DNA repair in hypoxic cancer cells. Cancer Metastasis Rev. 2007;26(2):249-60.

Bindra RS, Schaffer PJ, Meng A, et al. Down-regulation of Rad51 and decreased homologous recombination in hypoxic cancer cells. Mol Cell Biol. 2004;24(19):8504-18.

Brahmer JR, Lacchetti C, Schneider BJ, et al. Management of Immune-Related Adverse Events in Patients Treated with Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2018;36(17):1714-1768.

Bryant HE, Schultz N, Thomas HD, et al. Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase. Nature. 2005;434(7035):913-7. Erratum in: Nature. 2007;447(7142):346.

Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med. 2011;365(26):2473-2483.

Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. Nature. 2011;474(7353):609-15.

CARBOplatin Injection BP, Prescribing information. Accord Healthcare Inc. December 2022.

Carboplatin Injection, Prescribing information. Eugia Pharma INC. February 2023.

Chan JK, Brady MF, Penson RT, et al. Weekly vs. Every-3-Week Paclitaxel and Carboplatin for Ovarian Cancer. N Engl J Med. 2016;374(8):738-748.

Chan N, Pires IM, Bencokova Z, et al. Contextual synthetic lethality of cancer cell kill based on the tumor microenvironment. Cancer Res. 2010;70(20):8045-8054.

Chi DS, Eisenhauer EL, Zivanovic O, et al. Improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical paradigm. Gynecologic oncology. 2009;114:26-31.

Coleman RL, Oza AM, Lorusso D, et al. Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a randomised, double-blind, placebo-controlled, phase 3 trial [published correction appears in Lancet. 2017;390(10106):1948]. Lancet. 2017;390(10106):1949-1961.

Dikov MM, Ohm JE, Ray N, et al. Differential roles of vascular endothelial growth factor receptors 1 and 2 in dendritic cell differentiation. J Immunol. 2005;174(1):215-222.

Disis ML, Patel MR, Pant S, et al. Avelumab (MSB0010718C; anti-PD-L1) in patients with recurrent/refractory ovarian cancer from the JAVELIN Solid Tumor phase Ib trial: Safety and clinical activity. J Clin Oncol. 2016;34(15_suppl):5533.

Drew Y, de Jonge M, Hong SH, et al. An open-label, phase II basket study of olaparib and durvalumab (MEDIOLA): Results in germline BRCA-mutated (gBRCAm) platinum-sensitive relapsed (PSR) ovarian cancer (OC). Gynecol Oncol. 2018;149 Suppl:246-247.

du Bois A, Luck HJ, Meier W, et al. A randomized clinical trial of cisplatin/paclitaxel versus carboplatin/paclitaxel as first-line treatment of ovarian cancer. J Natl Cancer Inst. 2003;95(17):1320-1329.

Fricke I, Mirza N, Dupont J, et al. Vascular endothelial growth factor-trap overcomes defects in dendritic cell differentiation but does not improve antigen-specific immune responses. Clin Cancer Res. 2007;13(16):4840-4848.

Gabrilovich DI, Ostrand-Rosenberg S, Bronte V. Coordinated regulation of myeloid cells by tumours. Nat Rev Immunol. 2012;12(4):253-268.

González-Martín A, Pothuri B, Vergote I, et al. Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2019;381(25):2391-2402.

Grunewald T, Ledermann JA. Targeted Therapies for Ovarian Cancer. Best Pract Res Clin Obstet Gynaecol. 2017;41:139-152.

GSK Document Number RPS-CLIN-106356. Dostarlimab Investigator's Brochure. Version 9. 16 Aug 2024 (or the most current available version).

GSK Document Number RPS-CLIN-108400. Niraparib Investigator's Brochure. Version 16. 19 Jun 2024 (or the most current available version).

Haanen JBAG, Carbonnel F, Robert C, et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up [published correction appears in Ann Oncol. 2018;29(Suppl 4):iv264-iv266]. Ann Oncol. 2017;28(suppl_4):iv119-iv142.

Hamanishi J, Mandai M, Ikeda T, et al. Safety and Antitumor Activity of Anti-PD-1 Antibody, Nivolumab, in Patients With Platinum-Resistant Ovarian Cancer. J Clin Oncol. 2015;33(34):4015-4022.

Hamanishi J, Mandai M, Iwasaki M, et al. Programmed cell death 1 ligand 1 and tumor-infiltrating CD8+ T lymphocytes are prognostic factors of human ovarian cancer. Proc Natl Acad Sci USA. 2007;104(9):3360-3365.

Harding SM, Benci JL, Irianto J, et al. Mitotic progression following DNA damage enables pattern recognition within micronuclei. Nature. 2017;548(7668):466-470.

Hato SV, Khong A, de Vries IJ, Lesterhuis WJ. Molecular pathways: the immunogenic effects of platinum-based chemotherapeutics. Clin Cancer Res. 2014;20(11):2831-2837.

Hollis RL, Gourley C. Genetic and molecular changes in ovarian cancer [published correction appears in Cancer Biol Med. 2017 May;14 (2):196-201]. Cancer Biol Med. 2016;13(2):236-247.

Huang J, Wang L, Cong Z, et al. The PARP1 inhibitor BMN 673 exhibits immunoregulatory effects in a Brca1(-/-) murine model of ovarian cancer. Biochem Biophys Res Commun. 2015;463(4):551-556.

ICH Harmonised Tripartite E15. Definitions for genomic biomarkers, pharmacogenomics, pharmacogentics, genomic data and sample coding categories - Scientific guideline; 2007. EMEA/CHMP/ICH/437986/2006.

ICH S6 (R1). Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals - Scientific guideline; 2011. EMA/CHMP/ICH/731268/1998.

ICH S7A. Safety Pharmacology Studies for Human Pharmaceuticals - Scientific guideline; 2001. EMA/CPMP/ICH/539/2000.

ICH S9. Non-clinical Evaluation for Anticancer Pharmaceuticals - Scientific guideline; 2009. EMEA/CHMP/ICH/646107/2008.

Infante JR, Braiteh F, Emens LA, et al. Safety, clinical activity and biomarkers of atezolizumab (atezo) in advanced ovarian cancer (OC). Ann Oncol. 2016;27(suppl 6):vi296–vi312:871P.

Jiao S, Xia W, Yamaguchi H, et al. PARP Inhibitor Upregulates PD-L1 Expression and Enhances Cancer-Associated Immunosuppression. Clin Cancer Res. 2017;23(14):3711-3720.

Katsumata N, Yasuda M, Isonishi S, et al. Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): a randomised, controlled, open-label trial. Lancet Oncol. 2013;14(10):1020-1026.

Kawahara N, Ogawa K, Nagayasu M, et al. Candidate synthetic lethality partners to PARP inhibitors in the treatment of ovarian clear cell cancer. Biomed Rep. 2017;7(5):391-399.

Konstantinopoulos PA, Waggoner S, Vidal GA, et al. Single-Arm Phases 1 and 2 Trial of Niraparib in Combination With Pembrolizumab in Patients With Recurrent Platinum-Resistant Ovarian Carcinoma. JAMA Oncol. 2019;5(8):1141-1149.

Kroemer G, Galluzzi L, Kepp O, et al. Immunogenic cell death in cancer therapy. Annu Rev Immunol. 2013;31:51-72.

Kusmartsev S, Eruslanov E, Kubler H, et al. Oxidative stress regulates expression of VEGFR1 in myeloid cells: link to tumor-induced immune suppression in renal cell carcinoma. J Immunol. 2008;181(1):346-353.

Laken H, Kehry M, McNeeley P, et al. Identification and characterization of TSR-042, a novel anti-human PD-1 therapeutic antibody. European Journal of Cancer. 2016;69 (Suppl. 1):S102.

Langer CJ, Gadgeel SM, Borghaei H, et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. Lancet Oncol. 2016;17(11):1497-1508.

Ledermann JA, Raja FA, Fotopoulou C, et al. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi24-32.

Liechtenstein T, Perez-Janices N, Gato M, et al. A highly efficient tumor-infiltrating MDSC differentiation system for discovery of anti-neoplastic targets, which circumvents the need for tumor establishment in mice. Oncotarget. 2014;5(17):7843-7857.

Lim JJ, Yang K, Taylor-Harding B, et al. VEGFR3 inhibition chemosensitizes ovarian cancer stemlike cells through down-regulation of BRCA1 and BRCA2. Neoplasia. 2014;16(4):343-53.e1-2.

Liu JF, Barry WT, Birrer MJ, et al. Overall survival and updated progression-free survival results from a randomized phase 2 trial comparing the combination of olaparib and cediranib against olaparib alone in recurrent platinum-sensitive ovarian cancer. J Clin Oncol. 2017;35(15_suppl):5535.

Manzoni M, Rovati B, Ronzoni M, et al. Immunological effects of bevacizumab-based treatment in metastatic colorectal cancer. Oncology. 2010;79(3-4):187-196.

Mehibel M, Xu Y, Li CG, et al. Eliminating hypoxic tumor cells improves response to PARP inhibitors in homologous recombination-deficient cancer models. J Clin Invest. 2021;131(11):e146256

Mirza MR, Lundqvist EÅ, Birrer MJ, et al. Niraparib plus bevacizumab versus niraparib alone for platinum-sensitive recurrent ovarian cancer (NSGO-AVANOVA2/ENGOT-ov24): a randomised, phase 2, superiority trial. The Lancet Oncology. 2019;20(10):1409-19.

Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016;375(22):2154-64.

Moore K, Colombo N, Scambia G, et al. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2018;379(26):2495-2505.

Motzer RJ, Powles T, Atkins MB, et al. IMmotion151: a randomized phase III study of atezolizumab plus bevacizumab vs sunitinib in untreated metastatic renal cell carcinoma (mRCC). J Clin Oncol. 2018;36(6_suppl):578-578.

National Cancer Institute. The Surveillance Epidemiology, and End Results (SEER) Program. Cancer Stat Facts: Ovarian Cancer. 2016. Accessed 2016. Available at: https://seer.cancer.gov/statfacts/html/ovary.html.

Organisation for Economic Co-operation and Development. OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring. Number 22: Advisory Document of the Working Party on Good Laboratory Practice on GLP Data Integrity. OECD Principles on Good Laboratory Practice (as revised in 1997). ENV/MC/CHEM(98)17. 26-Jan-1998. Accessed 2018. Available at: https://doi.org/10.1787/9789264078536-en.

Ozols RF, Bundy BN, Greer BE, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2003;21(17):3194-3200.

Paclitaxel Injection Multidose Vial, Prescribing information. Eugia Pharma INC. March 2023.

Paclitaxel Powder for Injectable Suspension Nanoparticle, Albumin-bound Paclitaxel, Prescribing information. Panacea Biotec Pharma Limited. November 2021.

Parker BS, Rautela J, Hertzog PJ. Antitumour actions of interferons: implications for cancer therapy. Nat Rev Cancer. 2016;16(3):131-144.

Perren TJ, Swart AM, Pfisterer J, et al. A phase 3 trial of bevacizumab in ovarian cancer. N Engl J Med. 2011;365(26):2484-2496.

Pfannenstiel LW, Lam SS, Emens LA, et al. Paclitaxel enhances early dendritic cell maturation and function through TLR4 signaling in mice. Cell Immunol. 2010;263(1):79-87.

Pignata S, Scambia G, Katsaros D, et al. Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol. 2014;15(4):396-405.

Pujade-Lauraine E, Hilpert F, Weber B, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014;32(13):1302-1308.

Pujade-Lauraine E, Ledermann JA, Selle F, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2017;18(9):1274-1284.

Ray-Coquard IL, Pautier P, Pignata S, et al. Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer. N Engl J Med. 2019a;381(25):2416-2428.

Ray-Coquard IL, Pautier P, Pignata S, et al. Phase III PAOLA-1/ENGOT-ov25 trial: Olaparib plus bevacizumab (bev) as maintenance therapy in patients (pts) with newly diagnosed, advanced ovarian cancer (OC) treated with platinum-based chemotherapy (PCh) plus bev. Ann Oncol. 2019b;30 (Suppl 5):v894-5.

Rizvi NA, Hellmann MD, Brahmer JR, et al. Nivolumab in Combination With Platinum-Based Doublet Chemotherapy for First-Line Treatment of Advanced Non-Small-Cell Lung Cancer. J Clin Oncol. 2016;34(25):2969-2979.

Schwartz LH, Litière S, de Vries E, et al. RECIST 1.1-Update and clarification: From the RECIST committee. Eur J Cancer. 2016;62:132-137.

Senovilla L, Vitale I, Martins I, et al. An immunosurveillance mechanism controls cancer cell ploidy. Science. 2012;337(6102):1678-1684.

Sevko A, Michels T, Vrohlings M, et al. Antitumor effect of paclitaxel is mediated by inhibition of myeloid-derived suppressor cells and chronic inflammation in the spontaneous melanoma model. J Immunol. 2013;190(5):2464-2471.

Shrimali RK, Yu Z, Theoret MR, et al. Antiangiogenic agents can increase lymphocyte infiltration into tumor and enhance the effectiveness of adoptive immunotherapy of cancer. Cancer Res. 2010;70(15):6171-6180.

Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68(4):284-296.

US Department of Health and Human Services, Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV; 2017. Accessed 2017. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines.

Varga A, Piha-Paul SA, Ott PA, et al. Antitumor activity and safety of pembrolizumab in patients (pts) with PD-L1 positive advanced ovarian cancer: Interim results from a phase Ib study. J Clin Oncol. 2015;33(15_suppl):5510.

Vergote I, Coleman RL, Pignata S, et al. Joint ENGOT and GOG Foundation requirements for trials with industry partners. Gynecol Oncol. 2019;154(2):255-258.

Vergote I, Trope CG, Amant F, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med. 2010;363(10):943-953.

Walker JL, Brady MF, DiSilvestro PA, et al. A phase III trial of bevacizumab with IV versus IP chemotherapy in ovarian, fallopian tube, and peritoneal carcinoma: An NRG oncology study. Gynecologic Oncology. 2016;1(141):208-208.

Wallin JJ, Bendell JC, Funke R, et al. Atezolizumab in combination with bevacizumab enhances antigen-specific T-cell migration in metastatic renal cell carcinoma. Nat Commun. 2016;7:12624.

Wang Z, Sun K, Xiao Y, et al. Niraparib activates interferon signaling and potentiates anti-PD-1 antibody efficacy in tumor models. Sci Rep. 2019;9(1):1853.

WHO. International Agency for Research on Cancer: ovarian cancer estimated incidence, mortality and prevalence. Accessed 2018. Available at: https://gco.iarc.fr/today/data/factsheets/cancers/25-Ovary-fact-sheet.pdf.

Xing D, Orsulic S. A mouse model for the molecular characterization of BRCA1-associated ovarian carcinoma. Cancer Res. 2006;66(18):8949-8953.

Yang Y, Yang Y, Yang J, et al. Tumor Microenvironment in Ovarian Cancer: Function and Therapeutic Strategy. Front. Cell Dev. Biol. 2020;8:758.

ZEJULA (niraparib) capsules for oral use, Prescribing Information. TESARO.; 2017.

Zhang L, Conejo-Garcia JR, Katsaros D, et al. Intratumoral T-cells, recurrence, and survival in epithelial ovarian cancer. N Engl J Med. 2003;348(3):203-213.

ZIRABEV- bevacizumab injection, Prescribing information. Pfizer Laboratories Division, Pfizer Inc. February 2023.

16. APPENDICES

APPENDIX 1. SCHEDULE OF EVENTS

Post Analysis Continuation of Treatment (PACT)_ Phase:

Following the DCO date for final analysis, the study may move into the PACT phase (see Section 5.6 for details). Participants who continue to receive study intervention during the PACT phase will be monitored and will receive follow-up care in accordance with standard local clinical practice. Assessments will revert to the standard of care at a participant's particular study site and only SAEs, AEs leading to discontinuation of study intervention, overdoses, AESIs, and pregnancy cases will be reported directly to the sponsor via paper forms (Section 8.2.5).

Prior to PACT Phase (All Ongoing Patients):

Following the analysis conducted at the 31 October 2024, DCO date, no further efficacy analyses will be conducted for the study, as outlined in Section 9.6. Consequently, the scope of data collection is reduced, aligning with the revised schedule of events detailed in Table 16.

Table 16: Schedule of Events: Prior to PACT (All Ongoing Participants)

Visit **Procedure**[j]	**Maintenance Treatment Period**[a, b, i]	**EOT**	**Safety Follow-Up**[k]	**Post-Treatment Assessment** [c, h]
	C(n)			
Day	**1**	**Within 7 days of last dose**	**30 (±7) days**	**90 (±14) days (applicable to SAE and AESI reporting only)**
Physical examination		X	X	
Vital signs	X	X		
AE/SAE/AESI reporting[c]	X	X	X	X
ECOG performance status	X	X		
CBC with differential[d]	X	X	X	
Blood chemistry[f]	X	X	X	
TSH[e]	Q6W			
Amylase[e]	Q6W			
Pregnancy reporting[c]		Any pregnancies that occur		

Visit **Procedure**[j]	**Maintenance Treatment Period**[a, b, i]	**EOT**	**Safety Follow-Up**[k]	**Post-Treatment Assessment** [c, h]
		within 180 days post-treatment discontinuation are to be reported as described in Section 8.2.11.		
Oral niraparib dispensed or collected	X			
IV dostarlimab infusions[g]	Q6W			
Concomitant medications	X	X	X	X
Anticancer therapies assessment [c, h, k]			X	X
RECIST v1.1 assessment Chest/Abdomen/Pelvis CT or MRI[l]	X			
Bone marrow aspirate and biopsy	For any suspected MDS/AML case reported while on study, a bone marrow aspirate/biopsy must be performed by a local hematologist to confirm MDS/AML.			

Abbreviations: AE=adverse event; AESI=AE of special interest; AML=acute myeloid leukemia; C=cycle 125; CBC=complete blood count; ECOG=Eastern Cooperative Oncology Group; EOT=end of treatment; IV=intravenous; MDS=myelodysplastic syndrome; Q6W=every 6 weeks; SAE=serious adverse event, TSH=thyroid stimulating hormone; wks=weeks.

[a] All labs in the Maintenance Period may be performed up to -3 days from Day 1 dosing.

[b] In the Maintenance Treatment Period: Prior to dosing of study drug, the PI must review a CBC, blood chemistry, TSH, and amylase assessment.

[c] All AEs are required to be captured through 30 days after cessation of study treatment. SAEs are required to be captured through 90 days after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy). Investigators must continue to directly

report AESIs during treatment with niraparib and for 90 days after the last dose of niraparib. If the Investigator learns of an AESI after the last dose of niraparib, the Investigator must promptly notify the Sponsor. Any pregnancies that occur within 180 days post-treatment discontinuation will be captured for all participants (not only participants in PACT Phase). If applicable, when a patient transitions off study to continue treatment prior to PACT, safety reporting should be via the reporting mechanism applicable to the access route outside the study. Once the specified safety reporting period has elapsed, investigators are not obliged to actively seek information on AEs, SAEs or AESIs, however if the Investigator learns of an AESI or an SAE that is considered reasonably related to the study, it should be reported directly to GSK Global Safety through the standard specified reporting routes.

[d] If dose interruption or modification is required at any point on study because of hematologic toxicity, weekly (±3 days) blood draws for CBC will be monitored until the AE resolves, and to ensure safety of the new dose, weekly (±3 days) blood draws for CBC will also be required for an additional 4 weeks after the AE has been resolved to the specified levels (week 1 - first dose after re-start [CXM day 1], week 2 – 7 days after re-start [CXM day 8], week 3 – 14 days after re-start [CXM day 15], week 4 – 21 days after re-start [CX+1M day 1], after which monitoring every 4 weeks may resume. After 1 year of maintenance (after cycle 17), CBC will be done every 6 weeks.

[e] TSH and amylase will only be collected for patients on Arm 3 (for patients either actively receiving dostarlimab with Niraparib or dostarlimab alone or discontinued dostarlimab but continue to receive Niraparib on Arm 3). TSH and amylase will not be collected for patients receiving Niraparib alone (applicable to participants in Arm 2 or Arm 1 (previously unblinded according to amendment 4).

[f] The following blood chemistry parameters will be measured: sodium, potassium, chloride, calcium, magnesium, glucose, total bilirubin, AST, ALT, total protein, albumin, creatinine, and urea or blood urea nitrogen. Blood chemistry will be done every 6 weeks.

[g] In the Maintenance Treatment Period, IV dostarlimab will be administered every 42 days (6 weeks). On days that participants receive oral niraparib and or IV dostarlimab, dostarlimab will be administered first, and then niraparib (only applicable to participants on Arm 3).

[h] After the 30-day (±7 days) safety follow-up visit, participants will undergo one post-treatment follow-up assessment for serious adverse events (SAEs) and adverse events of special interest (AESIs) at 90 days after their last dose of study treatment. If a participant transitions to treatment outside of the study prior to PACT or if an Arm 1 participant (not previously unblinded discontinues placebo), post-treatment follow-up assessments will not be conducted. Following the local implementation of Amendment 10, the study will conclude all post-treatment follow-up data collection after 90 days (±14 days) from the last dose of study treatment, or after a minimum of 30 days if the participant begins alternative anticancer therapy. No follow-up data collection is required for participants who transitions to continue the treatment outside of the study. A participant's latest long-term follow-up visit which greater or equal to 90 days (±14 days) post-treatment (if applicable), before Amendment 10 becomes effective, will be recognized as the participant's final follow-up visit.

[i] During the maintenance treatment period, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab IV administration. Participants will be dispensed 2 bottles of niraparib every 6 weeks to coincide with dostarlimab IV administration.

[j]. All tests and procedures are required to be performed, and results evaluated prior to dosing

[k]. Safety follow-up visit is only needed for participants who have not begun a follow-up anticancer therapy. Participants transitioning to treatment outside the study before PACT or Arm 1 participants discontinuing placebo study drugs, as per amendment 4, do not require this visit.

[l] RECIST v1.1 tumor assessment via CT or MRI scan of chest/abdomen/pelvis and clinically indicated areas during the Maintenance Treatment Period, is optional and participants may be evaluated clinically with annual scans until PD or up to maintenance therapy discontinuation, whichever is earliest. Additional unscheduled scans (of any anatomical region that may be clinically indicated) for suspicion of disease progression based on increases in CA 125 or other suspicious symptoms are allowed. Imaging modality must be consistent with previous assessments whenever feasible. Alternate imaging modalities are allowed for identification of new lesions in anatomical regions that have not been previously scanned. EOT scan will not be performed. Participants who discontinue study treatment in the absence of

PD per RECIST v1.1 are not to continue radiographic imaging. If a participant discontinues treatment within 28 days of the scan that indicates PD, then the EOT scan will not be performed.

Table 17: Schedule of Events: All Study Arms

Visit[a] **Procedure**[b]	**Pre-Screening**[c]	**Screening**	**Chemo. Run-In Period**	**Chemo. Treatment Period**[d]		**Maintenance Treatment Period**[d, e, aa]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[y]
			C1	**C2**	**C(n)**	**C1**			**C2**		**C(n)**			
Day	**-42 to -29**	**-28 to -1**	**1**	**1**	**1**	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Pre-Screening Consent	X													
Informed consent		X												
Demographics		X												
Medical, surgical, cancer (including genotyping), and medication history		X												
Physical examination		X[ab]										X	X	
Vital signs, height, and weight[f]		X[ab]	X	X	X	X			X	X	X	X		
12-lead ECG		X[ab]												

Visit[a] **Procedure**[b]	**Pre-Screening**[c]	**Screening**	**Chemo. Run-In Period**	**Chemo. Treatment Period**[d]		**Maintenance Treatment Period**[d, e, aa]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[y]
			C1	**C2**	**C(n)**	**C1**			**C2**		**C(n)**			
Day	**-42 to -29**	**-28 to -1**	**1**	**1**	**1**	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Adverse event monitoring[g]		X	X	X	X	X			X		X	X	X	X
ECOG performance status		X[ab]	X	X	X	X			X		X	X		
Required tumor tissue samples[h]	X[h]	X[i]			X[z]									
Blood sample for [redacted]	X[j]	X[i]												
CBC with differential[k]		X[ab]	X[l]	X	X	X	X	X	X	X	X	X	X	
Coagulation		X [ab]		As clinically indicated[m]										
Blood chemistry[n]		X[ab]	X[l]	X	X	X			X		X	X	X	
TSH		X [ab]				X					Q6W			
Amylase				X		X					Q6W			
Serum or urine pregnancy test[o]		X[ab]	X[l]	X	X	X			X		X		X	

Visit[a] **Procedure**[b]	**Pre-Screening**[c]	**Screening**	**Chemo. Run-In Period**	**Chemo. Treatment Period**[d]		**Maintenance Treatment Period**[d, e, aa]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[y]
			C1	**C2**	**C(n)**	**C1**			**C2**		**C(n)**			
Day	**-42 to -29**	**-28 to -1**	**1**	**1**	**1**	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
HBV/HCV test		X[ab]												
Serum-based tumor markers (eg, CA 125)[p]		X[ab]	X[l]	X	X	X			X		X			
[redacted]	X[q]	X[i]		X (before IDS)		X						X		
Blood sample for PK/[redacted]				Refer to Table 19 and Table 20. PK sample should be collected at EOT if the participant discontinues before completing the final on-treatment PK blood sample collection.										
Urine sample for protein[r]		X[ab]												
HRQoL: EQ-5D-5L EORTC-QLQ-C30, and EORTC-QLQ-OV28[s]			X	X	X	X			X		X	X	X	X[s]
Symptom-directed PE			X	X	X	X			X		X			

Visit[a] **Procedure**[b]	**Pre-Screening**[c]	**Screening**	**Chemo. Run-In Period**	**Chemo. Treatment Period**[d]		**Maintenance Treatment Period**[d, e, aa]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[y]
			C1	**C2**	**C(n)**	**C1**			**C2**		**C(n)**			
Day	**-42 to -29**	**-28 to -1**	**1**	**1**	**1**	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Randomization[t]				X										
Concomitant medications		X	X	X	X	X	X	X	X		X	X	X	
Oral niraparib/placebo dispensed or collected									X		X	X		
IV dostarlimab (Arm 3) or placebo (Arms 1 and 2) infusions[u]				X	X	X					Q6W			
Paclitaxel-carboplatin infusion (all Arms)[v]			X	X	X									
Anticancer therapies assessment														X
Survival assessment														X

Visit[a] **Procedure**[b]	**Pre-Screening**[c]	**Screening**	**Chemo. Run-In Period**	**Chemo. Treatment Period**[d]		**Maintenance Treatment Period**[d, e, aa]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[y]
			C1	**C2**	**C(n)**	**C1**			**C2**		**C(n)**			
Day	**-42 to -29**	**-28 to -1**	**1**	**1**	**1**	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Bone marrow aspirate and biopsy				For any suspected MDS/AML case reported while on study, a bone marrow aspirate/biopsy must be performed by a local hematologist to confirm MDS/AML.										
RECIST v1.1 assessment Chest/Abdomen/Pelvis CT or MRI[w, x]		X[ab]			X[z]	X					X	X		

Abbreviations: CCI [redacted]; AE=adverse event; AESI=AE of special interest; AML=acute myeloid leukemia; C=cycle; C1D1=Cycle 1 Day1; CA 125=cancer antigen 125; CBC=complete blood count; chemo.=chemotherapy; CT=computed tomography; CCI [redacted] ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; EORTC-QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; EORTC-QLQ-OV28=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Ovarian Cancer Module OV28; EOT=end of treatment; EQ-5D-5L=European Quality of Life 5-Dimension 5-Level Scale; CCI [redacted] CCI [redacted]; HBV/HCV=hepatitis B virus/hepatitis C virus; HRQoL=health-related quality of life; HRR=homologous recombinant repair; ICF=informed consent; IDS=interval debulking surgery; IV=intravenous; MDS=myelodysplastic syndrome; MRI=magnetic resonance imaging; n=number of participants; PD=progressive disease; PE=physical examination; PK=pharmacokinetics; Q6W=every 6 weeks; RECIST=Response Evaluation Criteria in Solid Tumors; SAE=serious adverse event, TSH=thyroid stimulating hormone; wks=weeks.

[a] Treatment cycles are 21 days long; visits and all assessment should occur within ±3 days of the scheduled visit.

[b] All tests and procedures are required to be performed, and results evaluated prior to dosing.

[c] The Pre-Screening Period can take place within the 14 days prior to the Screening Period but does not have to encompass the full period. A participant can move to the Screening Period once deemed able.

[d] All labs in the Chemotherapy Treatment Period and the Maintenance Period may be performed up to -3 days from Day 1 dosing.

[e] In the Maintenance Treatment Period, dostarlimab/placebo IV infusion will start 3 weeks after chemotherapy Cycle 6 Day 1 and will be administered every 6 weeks thereafter. Hematologic recovery is not required to start dostarlimab/placebo therapy. The start of niraparib will be delayed at least 6 weeks after Cycle 6 Day 1 and up to 9 weeks after to allow for adequate recovery of hematologic toxicity. Principal Investigators at Maintenance, C1D1 sites should confirm that laboratory values remain within the protocol-specified criteria. The Sponsor and CCI will not review these data prospectively. Prior to dosing of study drug, the PI must review a CBC, blood chemistry, TSH, and amylase assessment. Review of CA125 prior to dosing is not required.

[f] Height will be measured only at Screening. Weight will be measured at Screening and at every visit. Blood pressure, temperature, and heart rate (pulse) will be measured at Screening and at every visit. Additionally, BP and heart rate will be performed weekly (±3 days) for the first 8 weeks from the first dose of niraparib in the Maintenance Treatment Period (week 1 – first dose [CXM day 1], week 2 – 7 days after first dose [CXM day 8], weekly – weeks 3 to 7], week 8 – 49 days after first dose [CX+7M day 1].

[g] All AEs are required to be captured through 30 days after cessation of study treatment. SAEs are required to be captured through 90 days after the last dose of study treatment (or for a minimum of 30 days post-treatment discontinuation if the participant starts alternative anticancer therapy). Any pregnancies that occur within 180 days post-treatment discontinuation are to be captured. Study drug-related SAEs and AESIs will be collected every 90 (±14) days after the last dose of study drug until study closeout, or as otherwise indicated in AESI Section 8.2.7.

[h] All the participants are required to provide sufficient tumor tissue sample CCI . Tumor samples must be collected from participants before C1D1. Participants who undergo IDS will be required to provide tumor tissue sample collected from IDS in addition to the tumor sample provided at Pre-Screening or Screening.

[i] If sample was collected during Pre-Screening, it does not need to be collected again during Screening.

[j] Participants must provide blood samples for CCI at Pre-Screening or Screening for randomization. For those participants who did not provide a CCI at the pre-Screening/Screening stage, a sample may be provided at a later time following Investigator's consultation with the Sponsor.

[k] If dose interruption or modification is required at any point on study because of hematologic toxicity, weekly (±3 days) blood draws for CBC will be monitored until the AE resolves, and to ensure safety of the new dose, weekly (±3 days) blood draws for CBC will also be required for an additional 4 weeks after the AE has been resolved to the specified levels (week 1 - first dose after re-start [CXM day 1], week 2 – 7 days after re-start [CXM day 8], week 3 – 14 days after re-start [CXM day 15], week 4 – 21 days after re-start [CX+1M day 1], after which monitoring every 4 weeks may resume. Weekly CBC is required for 4 weeks from the initial dose of niraparib (week 1 - first dose [CXM day 1], week 2 – 7 days after first dose [CXM day 8], week 3 – 14 days after first dose [CXM day 15], week 4 – 21 days after first dose [CX+1M day 1]. After 1 year of maintenance (after cycle 17), CBC will be done every other cycle.

[l] Screening assessments completed within 7 days of the first dose do not need to be repeated. Pregnancy tests completed within 3 days of the first dose do not need to be repeated.

[m] Coagulation will be collected if required due to an AE.

[n] The following blood chemistry parameters will be measured: sodium, potassium, chloride, calcium, magnesium, glucose, total bilirubin, AST, ALT, total protein, albumin, creatinine, and urea or blood urea nitrogen. After 1 year of maintenance (after Cycle 17), blood chemistry will be done every other cycle starting with Cycle 19.

[o] For participants of childbearing potential only.

[p] After 1 year of maintenance (after cycle 17), CA 125 will be done every other cycle.

[q] Samples will be collected at Pre-Screening or Screening, (same time with sample for CCI , before IDS, C1D1 of the Maintenance Treatment Period, and at the EOT visit.

[r] For participants receiving bevacizumab only: urine dipstick for protein determination should be performed prior to Screening. Participants discovered to have ≥2 proteinuria on dipstick should not be administered bevacizumab, should undergo a 24-hour urine collection, and must demonstrate <2 g of protein in 24 hours to be eligible for bevacizumab treatment.

[s] HRQoL assessments will be collected on site on the day of study treatment administration, prior to dosing and clinical procedures, during the treatment period on the day of dose administration, prior to dosing and clinical procedures at C1D1, Cycle 2/Day 1, and every 2 cycles thereafter (Cycle 4/Day 1, Cycle 6 Day 1) and during the Maintenance Treatment Period at Day 1 of every cycle (i.e., Q21D±7 days) for the first 3 cycles, Day 1 of every 3 cycles (i.e., every 9 weeks±7 days) through 15 cycles, Cycle 17 and every 6 cycles thereafter until PD or end of study treatment. For participants who discontinue treatment, HRQoL assessments should be collected at the EOT Visit, 30 days post EOT (±7 days) Safety Follow-up Visit, 90-days post EOT (±14 days) Long-Term Follow-up Visit, and every 180 days (±14 days) after the 90-day Long-Term Follow-up Visit, which will continue until death or the end of study data collection. HRQoL assessments may occur remotely if the participant is no longer actively returning to the clinic.

[t] 21 ±7 days after Screening, i.e., during the Chemotherapy Run-In Period but before treatment in Cycle 2. Randomization may occur up to one week prior to Cycle 2 Day 1.

[u] IV dostarlimab/placebo will be administered Q21D (3 weeks) during the Chemotherapy Treatment Period. In the Maintenance Treatment Period, IV dostarlimab/placebo will be administered 21 (±3) days (three weeks) after Cycle 6 Day 1 and every 42 days (6 weeks) thereafter. On days that participants receive CCI [redacted] Participants who continue to derive benefit from study treatment based on continuation of best overall response indicated by imaging, remain clinically stable, and are willing to continue study visits and assessments may continue to receive niraparib and/or dostarlimab/placebo beyond 3 years following consultation with the investigator and the Sponsor.

[v] Those participants who are to undergo IDS will receive 3 to 4 cycles of chemotherapy treatment prior to IDS (inclusive of Cycle 1) and an additional 2 to 3 cycles following surgery for a maximum of 6 cycles of chemotherapy that cannot be extended. Interval debulking surgery planned after 6 cycles of chemotherapy should be discussed with the Sponsor; however, bevacizumab may not be administered less than 28 days before or 28 days following major surgery.

[w] RECIST v1.1 tumor assessment via CT or MRI scan of chest/abdomen/pelvis and clinically indicated areas is required at Screening and prior to IDS (if applicable) during the Chemotherapy Treatment Period. If there are lesions noted in the chest and/or other clinically indicated areas at Screening, then repeat scans of these areas at each follow-up; otherwise, only scans of the abdomen and pelvis are required at each follow-up. During the Maintenance Treatment Period, imaging to assess disease status must occur at C1D1 (±14 days) of the Maintenance Treatment Period, and then every 4 months (±7 days) for 24 months, followed by every 6 months (±7 days) during the third year and every year thereafter until PD or the initiation of follow-up anticancer therapy. Additional unscheduled scans (of any anatomical region that may be clinically indicated) must be performed if participant has increasing CA 125 values or other suspicious symptoms. Imaging modality must be consistent with previous assessments whenever feasible. Alternate imaging modalities are allowed for identification of new lesions in anatomical regions that have not been previously scanned. CCI [redacted] CCI [redacted] If a participant discontinues treatment within 28 days of the scan that indicates PD, then the EOT scan will not be performed. Following completion of 3 years of maintenance therapy, participants will be evaluated clinically with annual scans and additional unscheduled scans for suspicion of disease progression based on increases in CA 125 or other suspicious symptoms. Alternatively, participants may be considered for treatment beyond 3 years in consultation with the Sponsor.

[x] If participant had CT/MRI of the chest/abdomen/pelvis and clinically indicated areas within the 28-day Screening window before C1D1 but prior to signing the main ICF, the participant is not required to complete an additional CT/MRI scan for study Screening. CT/MRI scans completed during Screening prior to signing the main ICF must have been performed and available for submission per the image acquisition guidelines.

[y] After the 30-day (±7 days) safety follow-up visit, post-treatment follow-up assessments should be done every 90 days (following the last dose of investigational product and/or other study treatments and where allowable can be completed by telephone), as referenced in the table. GSK may request that updated survival data be collected on randomized participants outside the protocol window noted in the schedule of events. At the time of the request, the site will determine survival status for each participant by the method agreed with the participant, unless the participant has withdrawn consent for survival FU. Public records may be utilized where allowed, per local regulations.

[z] Applies to those participants who receive IDS only.

[aa] After completing 1 year of maintenance treatment (=17 cycles [±1] of niraparib) and 9 cycles [±1] of dostarlimab/placebo, and if not receiving bevacizumab, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration. If receiving bevacizumab, following completion of bevacizumab treatment, participants may return for clinic visits and assessments every 6 weeks, to coincide with the dostarlimab/placebo IV administration. Participants do not need to return to the clinic Q3W but have the option to return to the clinic every 6 weeks, if preferred. Because both 3- and 6-week options are allowed per protocol, this will not lead to protocol deviations.

[ab] If participant had the required CT/MRI and/or laboratory assessments within the 28-day Screening window before C1D1 but prior to signing the informed consent form (ICF), the participant is not required to complete additional CT/MRI scan and/or laboratory assessments for study.

Table 18: Schedule of Events for Unblinded Participants in Arm 1 who then Receive Niraparib Treatment in Maintenance Treatment Period

Visit[a]	**Maintenance Treatment Period**[c, d, p]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[o]
Procedure[b]	**C1**			**C2**		**C(n)**			
Day	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Physical examination							X	X	
Vital signs and weight[e]	X	X	X	X	X	X	X		
Adverse event monitoring[f]	X			X		X	X	X	X
ECOG performance status	X			X		X	X		
CBC with differential[g]	X	X	X	X	X	X	X	X	
Coagulation	As clinically indicated[h]								
Blood chemistry[i]	X			X		X	X	X	
Serum or urine pregnancy test[j]	X			X		X		X	

Visit[a] **Procedure**[b]	**Maintenance Treatment Period**[c, d, p]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[o]
	C1			**C2**		**C(n)**			
Day	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Serum-based tumor markers (e.g., CA 125)[k]	X			X		X			
CCI [redacted] CCI [redacted] CCI [redacted]	X						X		
HRQoL: EQ-5D-5L EORTC-QLQ-C30, and EORTC-QLQ-OV28[m]	X			X		X	X	X	X[m]
Symptom-directed PE	X			X		X			
Concomitant medications	X	X	X	X		X	X	X	
Oral niraparib dispensed or collected	X			X		X	X		

Visit[a] **Procedure**[b]	**Maintenance Treatment Period**[c, d, p]						**EOT**	**Safety Follow-Up**	**Post-Treatment Assessment**[o]
	C1			**C2**		**C(n)**			
Day	**1**	**8**	**15**	**1**	**8**	**1**	**Within 7 days of last dose**	**30 (±7) days after last dose**	**Every 90 (±14) days**
Anticancer therapies assessment									X
Survival assessment									X
Bone marrow aspirate and biopsy	For any suspected MDS/AML case reported while on study, a bone marrow aspirate/biopsy must be performed by a local hematologist to confirm MDS/AML.								
RECIST v1.1 assessment Chest/Abdomen/Pelvis CT or MRI[n]	X					X	X		

Abbreviations: AE=adverse event; AESI=AE of special interest; AML=acute myeloid leukemia; C=cycle; C1D1=Cycle 1 Day 1; CA 125=cancer antigen 125; CBC=complete blood count; CT=computed tomography; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; EORTC-QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; EORTC-QLQ-OV28=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Ovarian Cancer Module OV28; EOT=end of treatment; EQ-5D-5L=European Quality of Life 5-Dimension 5-Level Scale; CCI HRQoL=health-related quality of life; HRR=homologous recombinant repair; ICF=informed consent form; MDS=myelodysplastic syndrome; MRI=magnetic resonance imaging; n=number of participants; PD=progressive disease; PE=physical examination; PK=pharmacokinetics; RECIST=Response Evaluation Criteria in Solid Tumors; SAE=serious adverse event.

[a] Treatment cycles are 21 days long; visits and all assessments should occur within ±3 days of the scheduled visit.

[b] All tests and procedures are required to be performed, and results evaluated prior to dosing. The Sponsor and CCI will not review these data prospectively. Prior to dosing of study drug, the PI must review a CBC, blood chemistry, TSH, and amylase assessment. Review of CA 125 prior to dosing is not required.

[c] Niraparib will start in the maintenance period upon hematologic recovery. Principal Investigators at C1D1 sites should confirm that laboratory values remain within the protocol-specified criteria.

[d] All labs in the Maintenance Period may be performed up to -3 days from Day 1 dosing.

[e] Weight will be measured at every visit. Blood pressure, temperature, and heart rate (pulse) will be measured at every visit. Additionally, BP and heart rate will be performed weekly for the first 8 weeks from the first dose of niraparib in the Maintenance Treatment Period.

[f] All AEs are required to be captured through 30 days after cessation of study treatment. SAEs are required to be captured through 90 days after the last dose of study treatment (or to a minimum of 30 days post-treatment discontinuation if the participant starts alternate anticancer therapy). Any pregnancies that occur within 180 days post-treatment discontinuation are to be captured. Study drug-related SAEs and AESIs will be collected every 90 (±14) days after the last dose of study drug until study closeout, or as otherwise indicated in AESI Section 8.2.7.

[g] If dose interruption or modification is required at any point on study because of hematologic toxicity, weekly (±3 days) blood draws for CBC will be monitored until the AE resolves, and to ensure safety of the new dose, weekly (±3 days) blood draws for CBC will also be required for an additional 4 weeks after the AE has been resolved to the specified levels, after which monitoring every 4 weeks may resume. For Maintenance C1, weekly (±3 days) CBC is required for 4 weeks after initial dose of niraparib. After 1 year of maintenance (after cycle 17), CBC will be done every other cycle.

[h] Coagulation will be collected if required due to an AE.

[i] The following blood chemistry parameters will be measured Q21D (±3 days): sodium, potassium, chloride, calcium, magnesium, glucose, total bilirubin, AST, ALT, total protein, albumin, creatinine, and urea or blood urea nitrogen. After 1 year of maintenance (after cycle 17), blood chemistry will be done every other cycle starting with Cycle 19.

[j] For participants of childbearing potential only.

[k] After 1 year of maintenance (after cycle 17), CA 125 will be done every other cycle.

[l] Samples will be collected at C1D1 of the Maintenance Treatment Period, and at the EOT visit.

[m] HRQoL assessments will be collected on site on the day of study treatment administration, prior to dosing and clinical procedures, during the Maintenance Treatment Period at Day 1 of every cycle (i.e., Q21D±7 days) for the first 3 cycles, Day 1 of every 3 cycles (i.e., every 9 weeks±7 days) through 15 cycles, Cycle 17 and every 6 cycles thereafter until PD or end of study treatment. For participants who discontinue treatment, HRQoL assessments should be collected at the EOT Visit, 30 days (±7 days) Safety Follow-up Visit, 90-days (±14 days) Long-Term Follow-up Visit, and every 180 days (±14 days) after the 90-day Long-Term Follow-up Visit, which will continue until death or the end of study data collection. HRQoL assessments may occur remotely if the participant is no longer actively returning to the clinic.

[n] If there are lesions noted in the chest and/or other clinically indicated areas at Screening, then repeat scans of these areas at each follow-up; otherwise, only scans of the abdomen and pelvis are required at each follow-up. During the Maintenance Treatment Period, imaging to assess disease status must occur at C1D1 (±14 days) of the Maintenance Treatment Period, and then every 4 months (±7 days) for 24 months, followed by every 6 months (±7 days) during the third year and every year thereafter until PD or the initiation of follow-up anticancer therapy. Additional unscheduled scans (of any anatomical region that may be clinically indicated) must be performed if participant has increasing CA 125 values or other suspicious symptoms. Imaging modality must be consistent with previous assessments whenever feasible. Alternate imaging modalities are allowed for identification of new lesions in anatomical regions that have not been previously scanned. CCI [redacted] CCI [redacted] CCI [redacted] If a participant discontinues treatment within 28 days of the scan that indicates PD, then the EOT scan will not be performed. Following completion of 3 years of maintenance therapy, participants may be evaluated clinically with annual scans and additional unscheduled scans for suspicion of disease progression based on increases in CA 125 or other suspicious symptoms. Alternatively, participants may be considered for treatment beyond 3 years in consultation with the Sponsor.

[o] After the 30-day (±7 days) safety follow-up visit, post-treatment follow-up assessments should be done every 90 days (following the last dose of investigational product and/or other study treatments and where allowable can be completed by telephone), as referenced in the table. GSK may request that updated survival data be collected on randomized participants outside the protocol window noted in the schedule of events. At the time of the request, the site will determine survival status for each participant by the method agreed with the participant, unless the participant has withdrawn consent for survival FU. Public records may be utilized where allowed, per local regulations.

[p] After completing 1 year of maintenance treatment (=17 cycles [±1] of niraparib), participants may return for clinic visits and assessments every 6 weeks.

APPENDIX 2. PK SAMPLING SCHEDULE

Table 19: Dostarlimab PK and Antidrug Antibodies Sparse Sampling Scheme: Chemotherapy and Maintenance Treatment Periods

Chemotherapy Treatment Period (1 Cycle=21 Days)	**Cycle 2**	**Cycle 3**	**Cycle 4**	**Cycle 6**		**EOT Visit[d]**	**Safety follow-up**	**Post-Treatment assessment**
Pre-dostarlimab infusion[a, e]	X	X	X	X				
End of dostarlimab infusion (+30 minutes)[b]	X							
Post-dostarlimab infusion (2 hours [±30 minutes])[c]	X							
Maintenance Treatment Period (1 Cycle=21 Days, Dostarlimab Dosed Every Other Cycle=42 days)	**Cycle 1**	**Cycle 3**	**Cycle 7**	**Cycle 9**	**Cycle 13**	**EOT Visit[d]**	**Safety follow-up**	**Post-Treatment assessment**
Pre-dostarlimab infusion[a, e]	X	X	X	X	X			
End of dostarlimab infusion (+30 minutes)[b]	X							
EOT (Within 7 days of last dose)						X		
Safety follow-up (30±7 days after last dose)							X	
Post-Treatment assessment (First 90±14 days only)								X

Abbreviations: EOT=End of treatment; PK=pharmacokinetics

[a] Sample must be taken within 30 minutes prior to the start of the infusion.

[b] Sample must be taken after the end of infusion (30-minute infusion) within a window of +30 minutes. All the PK sampling time points are based on the start time of the infusion.

[c] Sample must be taken within 2 hours (±30 minutes) after the start of the infusion. All the PK sampling time points are based on the start of the infusion.

[d] PK sample should be collected at EOT if the participant discontinues before completing the final on-treatment PK blood sample collection.

[e] If dostarlimab is held or discontinued at a visit that requires dostarlimab PK collection per the table above, a single dostarlimab PK sample (the equivalent to what would be the "predose" sample if the participant were receiving treatment) should still be collected.

Table 20: Niraparib PK Sparse Sampling Scheme: Maintenance Treatment Period

Maintenance Treatment Period (1 Cycle=21 Days, Niraparib Dosed QD)	**Cycle 2**[a]	**Cycle 3**[b]	**Cycle 7**	**Cycle 9**
Pre-niraparib (within 30 minutes before scheduled dose)[c]	X	X	X	X
Post-niraparib (2 hours [±15 minutes])	X	X		

Abbreviations: C2D1M=Cycle 2 Day 1, Maintenance; C3D1M=Cycle 3 Day 1, Maintenance; PK=pharmacokinetics; QD=once daily

[a] To allow for a **6-week** delay from recovery from hematologic toxicity (niraparib dosing begins at C2D1M), niraparib PK sampling will occur on Day 1 of Cycle 2, Cycle 3, Cycle 7, and Cycle 9.

[b] To allow for a **9-week** delay from recovery from hematologic toxicity (niraparib dosing begins at C3D1M), niraparib PK sampling will occur on Day 1 of Cycle 3, Cycle 7, and Cycle 9.

[c] If niraparib is held or discontinued at a visit that requires niraparib PK collection per the table above, a single niraparib PK sample (the equivalent to what would be the "predose" sample if the participant were receiving treatment) should still be collected.

APPENDIX 3. CONTRACEPTIVE GUIDELINES

Participants of childbearing potential who are sexually active and their partners must agree to the use of 2 highly effective methods of contraception throughout their participation during the study treatment and for 180 days after last dose of study treatment(s). Acceptable birth control methods include:

- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
  - oral route
  - intravaginal route
  - transdermal route
- Progestogen-only hormonal contraception associated with inhibition of ovulation
  - oral
  - injectable
  - implantable
- Intrauterine device
- Intrauterine hormone-releasing system
- Bilateral tubal occlusion
- Vasectomized partner
- Sexual abstinence, if the preferred and usual lifestyle of the participant

APPENDIX 4. RESPONSE EVALUATION CRITERIA IN SOLID TUMORS V1.1

Response Criteria by RECIST v1.1

Evaluation of Target Lesions

Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

Partial Response (PR): At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters.

Progressive Disease (PD): At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progressions.)

Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

Evaluation of Non-Target Lesions

Complete Response (CR): Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (<10 mm short axis).

Note: If tumor markers are initially above the upper normal limit, they must normalize for a participant to be considered in complete clinical response.

Non-CR/Non-PD: Persistence of one or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits.

Progressive Disease (PD): Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase.

Although a clear progression of “non-target” lesions only is exceptional, the opinion of the treating physician should prevail in such circumstances, and the progression status should be confirmed at a later time by the review panel (or Principal Investigator).

Evaluation of Best Overall Response

The best overall response is the best response recorded from the start of the treatment until disease progression/recurrence (taking as reference for PD the smallest measurements recorded since the treatment started). The participant's best response

assignment will depend on the achievement of both measurement and confirmation criteria.

As surgery is considered part of the treatment paradigm for participants who receive neoadjuvant chemotherapy, all scans that follow IDS (pre-, peri-, or post-maintenance scans) are compared to the original baseline (screening) scan [Schwartz, 2016]. If at the baseline screening scan, the participant has target lesions ± non-target lesions, then the combined response to systemic treatment AND surgery should be reported as: CR, PR, SD, PD, or NE. For example, if a participant had a target lesion in the ovary which was entirely removed during IDS, and the imaging pre-maintenance did not show any visible disease, then the response should be marked as CR. RECIST guidelines above should be used to determine PR, SD, or PD.

If at the baseline screening scan, the participant has non-target lesions only, then the combined response to systemic treatment AND surgery should be reported as: CR, non-CR/non-PD, PD, or NE.

For SD to be assigned BOR, assessments must have met the SD criteria for a minimum of 12 consecutive weeks following randomization. If the minimum time for SD is not met, BOR will depend on the subsequent assessments. For example, if an assessment of PD follows the assessment of SD and SD does not meet the minimum time requirement, the best response will be PD. Alternatively, participants lost to follow-up after an SD assessment not meeting the minimum time criterion will be considered NE.

Table 21: For Participants with Measurable Disease (i.e., Target Disease)

Target Lesions	Non-Target Lesions	New Lesions	Overall Response	Best Overall Response when Confirmation is Required*
CR	CR	No	CR	>4 wks. Confirmation**
CR	Non-CR/Non-PD	No	PR	>4 wks. Confirmation**
CR	Not evaluated	No	PR	
PR	Non-CR/Non-PD/not evaluated	No	PR	
SD	Non-CR/Non-PD/not evaluated	No	SD	Documented at least once >12 wks. from baseline
PD	Any	Yes or No	PD	No prior SD, PR or CR
Any	PD***	Yes or No	PD	
Any	Any	Yes	PD	

Abbreviations: CR=complete response; PD=progressive disease; PR=partial response; RECIST=Response; Evaluation Criteria in Solid Tumors; SD=stable disease; wks=weeks.

* See RECIST 1.1 manuscript for further details on what is evidence of a new lesion.

** Only for non-randomized trials with response as primary endpoint.

*** In exceptional circumstances, unequivocal progression in non-target lesions may be accepted as disease progression.

Note: Participants with a global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time should be reported as "symptomatic deterioration." Every effort should be made to document the objective progression even after discontinuation of treatment.

Table 22: For Participants with Non-Measurable Disease (i.e., Non-Target Disease)

Non-Target Lesions	New Lesions	Overall Response
CR	No	CR
Non-CR/non-PD	No	Non-CR/non-PD*
Not all evaluated	No	Not Evaluated
Unequivocal PD	Yes or No	PD
Any	Yes	PD

Abbreviations: CR=complete response; PD=progressive disease; SD=stable disease.

*'Non-CR/non-PD' is preferred over 'SD' for non-target disease since SD is increasingly used as an endpoint for assessment of efficacy in some trials so to assign this category when no lesions can be measured is not advised

Assessment of New Lesions on the basis of FDG-PET

New lesions on the basis of FDG-PET imaging can be identified according to the following algorithm:

1. Negative FDG-PET at baseline, with a positive* FDG-PET at follow-up is a sign of PD based on a new lesion.
2. No FDG-PET at baseline and a positive FDG-PET at follow-up:

   If the positive FDG-PET at follow-up corresponds to a new site of disease confirmed by CT, this is PD.

If the positive FDG-PET at follow-up is not confirmed as a new site of disease on CT, additional follow-up CT scans are needed to determine if there is truly progression occurring at that site (if so, the date of PD will be the date of the initial abnormal FDG-PET scan).

If the positive FDG-PET at follow-up corresponds to a pre-existing site of disease on CT that is not progressing on the basis of the anatomic images, this is not PD.

Imaging modality must be consistent with previous assessments whenever feasible. Alternate imaging modalities are allowed per RECIST v1.1 for identification of new lesions in anatomical regions that have not been previously scanned.

*A 'positive' FDG-PET scan lesion means one which is FDG avid with an uptake greater than twice that of the surrounding tissue on the attenuation corrected image.

APPENDIX 5. REQUIRED IMAGING

Exam	Screening/ Baseline[1]	Chemotherapy Treatment Period[2] (for participants who receive IDS only)	Maintenance Treatment Period[3]	EOT[4]	Follow-Up[5]
CT/MRI Chest	R	R	RIC/RIP	RIC/RIP	RIC/RIP
CT/MRI Abdomen	R	R	R	R	R
CT/MRI Pelvis	R	R	R	R	R
CT/MRI Clinically Indicated Areas[6]	RIC	RIC/RIP	RIC/RIP	RIC/RIP	RIC/RIP
Additional Imaging Studies[7]	A	A	A	A	A

R: Required. Required exams will be queried as "Missing" if not received.
RIC: Required if clinically indicated, as determined by the Investigator.
RIP: Required if positive. Once received at a post-Screening/Baseline time point, exam will be required at all subsequent time points.
A: Acceptable. If clinically indicated, additional exams may be submitted on-study.

1 According to GSK, the Screening/Baseline imaging must be performed after the PDS (if applicable). Images must also be performed within twenty-eight (28) days before Cycle 1/Day 1 and prior to IDS (if applicable) during the Chemotherapy Treatment Period. If a participant had CT/MRI imaging within the twenty-eight (28) day Screening window before Cycle 1/Day 1 but prior to signing the ICF, the participant is not required to complete additional CT/MRI scans for study Screening/Baseline.

2 Participants indicated for IDS will have pre-operative scans performed during the chemotherapy period.

3 Imaging must be performed at Cycle 1/Day 1 (±14 days) of the Maintenance Treatment Period, and then every four (4) months (±7 days) for twenty-four (24) months, followed by every six (6) months (±7 days) during the third year and every year thereafter until PD or the initiation of follow-up anticancer therapy.

4 EOT tumor imaging must be performed within seven (7) days of the participant's last dose of the study drug. If a participant discontinues treatment within twenty-eight (28) days of the scan that indicates PD, then the EOT scan will not be performed.

5 If a participant discontinues treatment for a reason other than progression or death, withdrawal of consent, or loss to follow-up, the participant will continue radiographic imaging at the specified intervals until PD or the initiation of follow-up anticancer therapy.

6 CT/MRI imaging of clinically indicated areas (as determined by the Investigator) should be performed at Screening/Baseline and repeated on-study.

7 Additional Imaging Studies may be performed at the discretion of the Investigator, but are not required.

APPENDIX 6. EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG) PERFORMANCE STATUS

Description	Grade
Fully active, able to carry on all pre-disease performance without restriction.	0
Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, i.e., light housework, office work.	1
Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.	2
Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.	3
Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.	4
Death	5

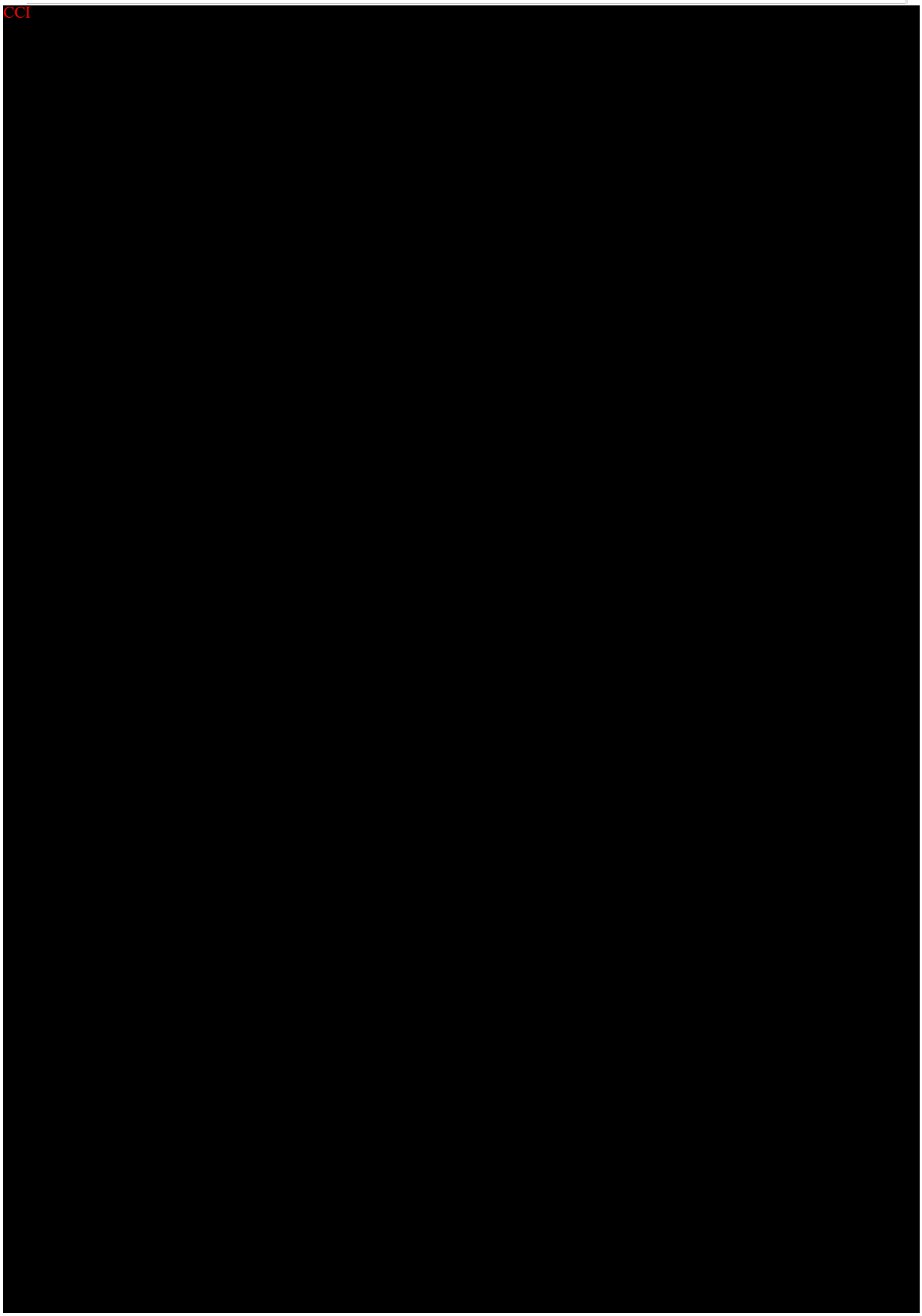
APPENDIX 7. WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

The study will be conducted in line with the most recent version of the Declaration of Helsinki.

CCI

[redacted]

CCI



CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

APPENDIX 11. ADAPTATIONS IN STUDY DESIGN

This study is designed to enable rapid adaptation to evolving treatment paradigms for participants with advanced ovarian cancer. This ensures that study participants will have access to the most current regimen with or without investigational treatment while maintaining the integrity of the study. Full details on adaptations to the study design are located in the protocol.

CCI

[redacted]

CCI

[redacted]

As a result, following Sponsor and Steering Committee discussions, participants were not enrolled into Arm 1 after Amendment 4 was approved at each site. Participants in Arm 1 Chemotherapy Treatment Period who are receiving bevacizumab when Amendment 4 is implemented, may continue the 6 cycles of chemotherapy. Following completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants may start bevacizumab maintenance therapy at the Investigator's discretion. Participants in Arm 1 Maintenance Treatment Period who are receiving bevacizumab when Amendment 4 is implemented may continue bevacizumab maintenance therapy at the Investigator's discretion. Investigators will remain blinded for those participants enrolled in Arm 1 and receiving bevacizumab at the time of implementation of Amendment 4.

Participants in Arm 1 Chemotherapy Treatment Period not receiving bevacizumab when Amendment 4 is implemented, may continue the 6 cycles of chemotherapy. Following completion of the Chemotherapy Treatment Period and confirmation of adequate hematologic parameters, those participants may start niraparib maintenance therapy as "follow-up anticancer treatment" at the Investigator's discretion. Participants in Arm 1, Maintenance Treatment Period not receiving bevacizumab when Amendment 4 is implemented may start niraparib maintenance therapy as "follow-up anticancer treatment" if the time from Cycle 6 Day 1 of the Chemotherapy Treatment Period is ≤12 weeks. Participants will be permitted to remain on study until withdrawal of consent, sponsor decision to terminate study or death. Participants who do not elect to receive niraparib or bevacizumab maintenance will be discontinued from the study treatment and given the option to stay in the study for follow up. In order to facilitate this adaptation, Investigators will be unblinded for those participants enrolled in Arm 1 and not receiving bevacizumab at the time of implementation of Amendment 4. The schedule of events for these participants is shown in Table 18.

CCI

[b] All participants previously randomized to placebo and not receiving bevacizumab will be unblinded and provided the option to receive niraparib maintenance if they have received chemotherapy or discontinued chemotherapy ≤12 weeks.

Prior to implementation of the recommended study adaptation, the Sponsor will amend the study and send to appropriate regulatory authorities for approval. Sites will be notified when there is an adaptation in the randomization schema. There is no plan to hold study enrollment or amend the protocol to accommodate the proposed adaptations unless determined to be necessary by the study Steering Committee and/or regulatory authorities.

Determination of the Final Control Group

The primary efficacy analysis will compare Arm 3 (experimental group) to the appropriate control group that was dynamically determined during the study based on external data. An important goal of this study was to enable rapid adaptation to evolving treatment paradigms in participants with advanced ovarian cancer to ensure that study participants had access to the most current regimen or investigational treatment while still maintaining the integrity of the study. Amendment 4 confirmed that the control arm for the primary efficacy endpoint will be Arm 2.