Statistical Analysis Plan Amendment 2

Study ID: 213353

Official Title of Study: A Phase 2, Open-Label, Single-Arm Study to evaluate the efficacy and safety of the combination of Niraparib and Dostarlimab (TRS-042) in patients with Platinum-Resistant Ovarian Cancer (MOONSTONE)

Other Identifiers: 3000-02-006

Date of Document: 29-OCT-2020

STATISTICAL ANALYSIS PLAN

Protocol Title	A PHASE 2 OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFICACY AND SAFETY OF THE COMBINATION OF NIRAPARIB AND DOSTARLIMAB (TSR-042) IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER (MOONSTONE)
Protocol Number	3000-02-006
Protocol Version	Version 2.0: 22 October 2019 (Amendment 1) Version 1.0: 04 October 2018 (Original)
Study Drug	Niraparib, Dostarlimab (TSR-042)
Study Phase	Phase 2
Methodology	Open-Label, Single-Arm
Sponsor	TESARO, Inc. a GSK Company 1000 Winter Street Waltham MA 02451 Tel: PPD
Analysis Plan Version	Version 2.0
Analysis Plan Date	October 16, 2020

SIGNATURE PAGE

Protocol Title:	A PHASE 2 OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFICACY AND SAFETY OF THE COMBINATION OF NIRAPARIB AND DOSTARLIMAB (TSR-042) IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER (MOONSTONE)
Protocol Number:	3000-02-006
Sponsor:	TESARO, Inc. a GSK Company 1000 Winter Street Waltham MA 02451

Author:
PPD MS
Statistics Leader, Development
Biostatistics, Statistics
Oncology

PPD

16-Oct-2020

Date

By signing this document, I acknowledge that I have read the document and approve of the planned statistical analyses described herein. I agree that the planned statistical analyses are appropriate for this study, are in accordance with the study objectives, and are consistent with the statistical methodology described in the protocol, clinical development plan, and all applicable regulatory guidances and guidelines.

PPD MD
PPD ,
Clinical Development -
Synthetic Lethality -
Medical

PPD

29-Oct-2020

Date

Table of Contents

List of Tables

Table of Figures

Abbreviations and Definitions

Abbreviation	Definition
AE	Adverse event
AESI	Adverse event(s) of special interest
ALP	Alkaline Phosphatase
ALT	Alanine aminotransferase
AML	Acute myeloid leukemia
aPTT	Activated partial thromboplastin time (aPTT)
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body mass index
BOR	Best overall response
BRCA	Breast cancer susceptibility gene
BRCAmut	Breast cancer susceptibility gene mutated
BRCAwt	Breast cancer susceptibility gene wild type
CA-125	Cancer antigen 125
CBC	Complete blood count
CI	Confidence interval
CPS	Combined proportion score
CR	Complete response
CSR	Clinical study report
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DCR	Disease control rate
DNA	Deoxyribonucleic acid
DOR	Duration of response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EE	Efficacy-evaluable
EOT	End of treatment
EU	European Union
FDA	(United States) Food and Drug Administration
FFPE	Formalin fixed paraffin embedded
FIGO	International Federation of Gynecology and Obstetrics
FOSI	Functional Assessment of Cancer Therapy – Ovarian Symptom Index
gBRCA	Germline breast cancer susceptibility gene
gBRCAmut	Germline breast cancer susceptibility gene mutated
gBRCAwt	Germline breast cancer susceptibility gene wild type
GCP	Good Clinical Practice
HRD	Homologous recombination deficiency
HRQoL	Health-related quality of life
IHC	Immunohistochemistry
IND	Investigational New Drug application
INR	International normalized ratio

Abbreviation	Definition
irAE	Immune-related adverse event
ITT	Intent-to-treat
IV	Intravenous
KM	Kaplan-Meier
LLN	Lower limit of normal
MID	Minimally important difference
MDS	Myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MSI H	Microsatellite instability-high
mut	Mutant
NCI	National Cancer Institute
Neg	Negative
NSCLC	non-small cell lung cancer
OC	Ovarian cancer
ORR	Objective response rate
OS	Overall survival
PARP	Poly(ADP-ribose) polymerase
PARPi	PARP inhibitor
PD	Progressive disease (in the context of disease evaluation) or protocol deviation
PD-1	Programmed cell death-1
PD-L1	Programmed cell death-ligand 1
PFI	Platinum-free interval
PFS	Progression-free survival
PO	Orally
PR	Partial response
PROC	Platinum-resistant ovarian cancer
PT	Preferred Term (MedDRA)
Q_1	First quartile
Q_3	Third quartile
Q3W	Every 3 weeks
Q6W	Every 6 weeks
QD	Once daily
RE	Response-evaluable (population)
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious adverse event
SAF	Safety
SAP	Statistical analysis plan
sBRCAmut	Somatic breast cancer susceptibility gene mutation
SD	Stable disease (in the context of disease evaluation) or standard deviation (in the context of statistics)
SDF	Survival distribution function
SMQ	Standard MedDRA Query
SOC	System Organ Class (MedDRA)
tBRCA	Tumor breast cancer susceptibility gene
tBRCAmut	Tumor breast cancer susceptibility gene mutation

Abbreviation	Definition
tBRCAwt	Tumor breast cancer susceptibility gene wild-type
TEAE	Treatment-emergent adverse event
ULN	Upper limit of normal
vCPS	Visually estimated combined positive score
WHO	World Health Organization
WHODD	World Health Organization Drug Dictionary
wt	Wild type

1 Statistical Analysis Plan Scope and Revision History

This statistical analysis plan (SAP) is designed to outline the methods to be used in the analyses of study data in order to answer the study objectives. Patient populations to be used for analyses, data handling rules, statistical methods, and formats for data presentation are identified and provided. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this trial.

This SAP will also outline any differences in the currently planned analyses relative to those described in the study protocol.

The SAP is a living document that will be created during the trial conduct. It will be maintained throughout the lifecycle of the trial. Important changes following approval of SAP v1.0 will be tracked in this section. Table 1 shows the revision history.

Table 1 Revision History

SAP version (date)	Protocol version (date)	eCRF version (date)	Changes from previous version
1.0	2.0 (22 October 2019)	17 March 2020	Original version
2.0	2.0 (22 October 2019)	14 April 2020	• Specified cut-point for PD-L1 assay for determination of subgroups (vCPS<5% and vCPS≥5%). • Added details regarding PFI calculation • Removed lists of preferred terms for analysis of grouped adverse events. The lists be maintained in a separate document. • Clarifications to futility analysis population • Described additional summaries for COVID-19 data.

1.1 Summary of Changes to the Planned Analyses

No changes are noted to the analyses planned in the protocol. The statistical analysis plan provides additional details to the analyses specified in the protocol.

2 Introduction

Niraparib is an orally available, potent, and highly selective poly (adenosine diphosphate-ribose) polymerase (PARP)-1 and PARP-2 inhibitor. Zejula® (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.

Niraparib treatment as monotherapy and in combinations is being studied by TESARO through a global development plan that involves several ongoing company-sponsored clinical studies in ovarian, lung, and breast cancer indications. In addition, TESARO and Janssen have a partnership investigating niraparib for use in prostate cancer.

Dostarlimab (TSR-042) is an anti-programmed death-1 (anti PD-1) humanized monoclonal antibody (mAb) of the immunoglobulin G4 (IgG4)-κ isotype. TESARO submitted the original Investigational New Drug application (IND) for dostarlimab (TSR-042) on 22 December 2015 and obtained the IND approval on 22 January 2016 with Study 4010-01-001 titled "A Phase 1 Dose Escalation and Cohort Expansion Study of TSR-042, an anti-PD-1 Monoclonal Antibody, in Patients with Advanced Solid Tumors." Dostarlimab (TSR-042) is being studied by TESARO in a global development plan as monotherapy in microsatellite instability-high (MSI-H) tumors, including endometrial cancer, and in combination with other approved and investigational drugs under development by TESARO, such as niraparib in other solid tumors, including ovarian cancer and non-small cell lung cancer (NSCLC).

The objective of the proposed study is to evaluate the efficacy and safety of the combination of niraparib and dostarlimab (TSR-042) in patients with advanced, relapsed, high-grade ovarian, fallopian tube, or primary peritoneal cancer without known breast cancer susceptibility gene (BRCA) mutation who have platinum-resistant disease and who have also been previously treated with bevacizumab.

3 Study Objectives and Endpoints

3.1 Study Objectives

3.2 Primary Objective

The primary objective and corresponding endpoint is listed in Table 2.

Table 2 Primary Objective and Endpoint

Primary Objective	Primary Outcome Variable
To evaluate the efficacy, as measured by confirmed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 (Eisenhauer, et al., 2009) based on Investigator assessment, of the combination of niraparib and dostarlimab (TSR-042) in: • patients with platinum-resistant ovarian cancer (PROC) without a known BRCA mutation who have been previously treated with bevacizumab • subset of patients with PROC who have PD-L1 positive tumors (vCPS≥5%) without a known BRCA mutation who have been previously treated with bevacizumab.	Confirmed ORR, which is defined as the proportion of patients achieving confirmed CR or PR as assessed by the Investigator per RECIST v1.1.

3.3 Secondary Objectives

The secondary objectives and corresponding endpoints are listed in Table 3.

Table 3 Secondary Objectives and Endpoints

Secondary Objectives	Secondary Outcome Variables
To evaluate the clinical benefit of the niraparib and dostarlimab combination in the overall population and in the subset of patients with PD-L1 positive tumors as measured by:	
• Duration of response (DOR) per RECIST v1.1 based on Investigator assessment	DOR, defined as the time from first documentation of CR or PR until the time of first documentation of disease progression by RECIST v1.1 based on Investigator assessment or death by any cause in the absence of progression by RECIST v1.1.
• Progression-free survival (PFS) per RECIST v1.1 based on Investigator assessment	PFS, defined as the time from the date of the first dose of study treatment to the earlier date of assessment of progression by RECIST v.1.1 based on Investigator assessment or death by any cause in the absence of progression by RECIST v.1.1.
• Overall survival (OS)	OS, defined as the time from the date of the first dose of study treatment to the date of death by any cause.
• Disease control rate (DCR)	DCR, defined as the percentage of patients who have achieved best overall response (BOR) of CR, PR, or SD per RECIST v.1.1 based on the Investigator's assessment.
To evaluate the ORR, DOR, PFS, and DCR per RECIST v1.1 based on independent review committee assessment	ORR based on independent review committee assessment, defined as the percentage of patients who have achieved confirmed CR or PR per RECIST v1.1 based on the independent review committee assessment.
To evaluate the safety and tolerability of the niraparib and dostarlimab combination in patients with PROC as measured by standard safety assessments	Assessment of AEs, vital signs, symptom-directed physical examination findings and clinical laboratory values (including hematology, serum chemistry, coagulation, and thyroid function).

3.4 Exploratory Objectives

The exploratory objectives and corresponding endpoints are listed in Table 4.

Table 4 Exploratory Objectives and Endpoints

Exploratory Objectives	Exploratory Outcome Variables
Exploratory objectives of this study are as follows and will be evaluated in the overall population and the subset of patients with PD-L1 positive tumors:	
To evaluate efficacy of the niraparib and dostarlimab (TSR-042) combination among patients with BRCAwt tumors as measured by confirmed ORR, DOR, PFS, OS, and DCR based on Investigator assessment using RECIST v1.1	Efficacy endpoints (confirmed ORR, DOR, PFS, OS and DCR based on Investigator assessment using RECIST v1.1) in the BRCAwt population
To evaluate the duration of disease control among patients with BOR of CR, PR, or SD based on Investigator assessment and independent review committee assessment	Duration of disease control, defined as the time from the date of the first dose of study treatment to the earlier date of assessment of progression by RECIST v.1.1 or death by any cause in the absence of progression by RECIST v1.1 among patients whose BOR is CR, PR or SD.
To evaluate health-related quality of life (HRQoL) in patients with PROC treated with the combination of niraparib and dostarlimab (TSR-042), as measured by the Functional Assessment of Cancer Therapy – Ovarian Symptom Index (FOSI)	The observed change from baseline and time to symptom worsening in the FOSI questionnaire.
To identify additional potential disease-related or treatment-related biomarkers that correlate with responses to the niraparib and dostarlimab (TSR-042) combination, including, but not limited to, the measures of homologous recombination repair pathway defects and the optimal PD-L1 level for efficacy to be used in other dostarlimab ovarian cancer trials.	Disease related or treatment-related biomarkers (eg, DNA repair deficiency, PD L1 expression) to explore the correlations with responses to the combination of niraparib and dostarlimab.

4 Study Methods

4.1 General Study Design and Plan

This is an open-label, single-arm Phase 2 study to evaluate the efficacy and safety of the niraparib and dostarlimab (TSR-042) combination in patients with advanced, relapsed, high-grade ovarian, fallopian tube, or primary peritoneal cancer without known BRCA mutation who have platinum resistant disease and who have also been previously treated with bevacizumab.

This study will consist of a screening period (Day -28 to Day -1), a treatment period, an end of treatment period when study treatment is discontinued for any reason, a Safety Follow-up Visit occurring 30 ± 7 days after the last dose of study treatment, and a survival assessment occurring every 90 ± 14 days after the last dose of study treatment. All patients will undergo an End of Treatment Visit within 7 days of the decision to discontinue treatment for any reason.

Patients must provide sufficient tumor tissue for BRCA testing and PD-L1 testing, minimally. Per amendment 1, slides cut from formalin fixed paraffin embedded (FFPE) tissue blocks are not acceptable. Blood samples will be collected at screening for central gBRCA testing. Blood samples will also be collected for exploratory biomarker analysis at screening, at Cycle 3 Day 1, at the time of Investigator-assessed PR (+ 21 days), at the time of Investigator-assessed CR (+ 21 days), and at the End of Treatment Visit.

All patients will receive treatment with niraparib and dostarlimab (TSR-042) (collectively referred to as "study treatment") beginning on Cycle 1 Day 1 using the regimen detailed in Table 5, depending on body weight and platelet count at screening. Treatment Cycles 1 to 4 are 3 weeks long and Cycles 5 and later are 6 weeks long. A window of ± 3 days is allowed to start the following cycle to accommodate holidays, clinic closing due to inclement weather, or other administrative reasons.

Table 5 Treatment Regimen

Niraparib	**Dostarlimab**
Starting doses are as follows: • 300 mg PO QD continuously in patients with screening actual body weight ≥ 77 kg AND screening platelet count ≥ 150,000/µL until PD or toxicity • 200 mg PO QD continuously in patients with screening actual body weight < 77 kg OR screening platelet count < 150,000/µL until PD or toxicity	• 500 mg IV on Day 1 of each 3-week cycle (Q3W Cycles 1 to 4), followed by 1,000 mg IV on Day 1 of each 6-week cycle (Q6W Cycle 5 and later) until PD or toxicity

Abbreviations: IV = intravenous; PD = progressive disease; PO = orally; Q3W = every 3 weeks; Q6W = every 6 weeks; QD = once daily

Safety assessments performed will include collection of adverse events (AEs), vital sign measurements, symptom directed physical examinations, and clinical laboratory assessments.

Radiographic evaluations (i.e., computed tomography/magnetic resonance imaging of chest, abdomen, and pelvis) to assess the extent of disease will be conducted every 9 weeks (63 ± 7 days) for the first year of study treatment, independent of cycle delays or dose interruptions, or at any time when progression of disease is suspected. After 1 year of radiographic assessments, imaging will be performed every 12 weeks (84 ± 14 days). Per RECIST v.1.1, CR or PR should be confirmed; tumor imaging for confirmation of response must be performed at the earliest 28 days after the first indication of PR or CR but no later than 35 days after the response. The subsequent tumor imaging after the confirmatory scan should be obtained per the original scheduled interval (e.g., 9 weeks [63 ± 7 days] from a confirmatory scan during the first year of study treatment and every 12 weeks thereafter). Radiographic evaluations will continue until progressive disease (PD), start of alternate anticancer therapy, withdrawal of consent to study participation, becoming lost to follow-up, death, or end of the study. If a patient discontinues treatment for a reason other than radiographic progression or death, withdrawal of consent, loss to follow-up, or the end of the study, radiographic evaluation and cancer antigen 125 (CA-125) testing should continue at the specified intervals (i.e., every 9 weeks for the first year of study treatment and every 12 weeks thereafter until PD). Also, clinically stable patients should not be discontinued until progression is confirmed. If a patient discontinues treatment for clinical progression and does not meet RECIST criteria for progression, scans and CA-125 testing

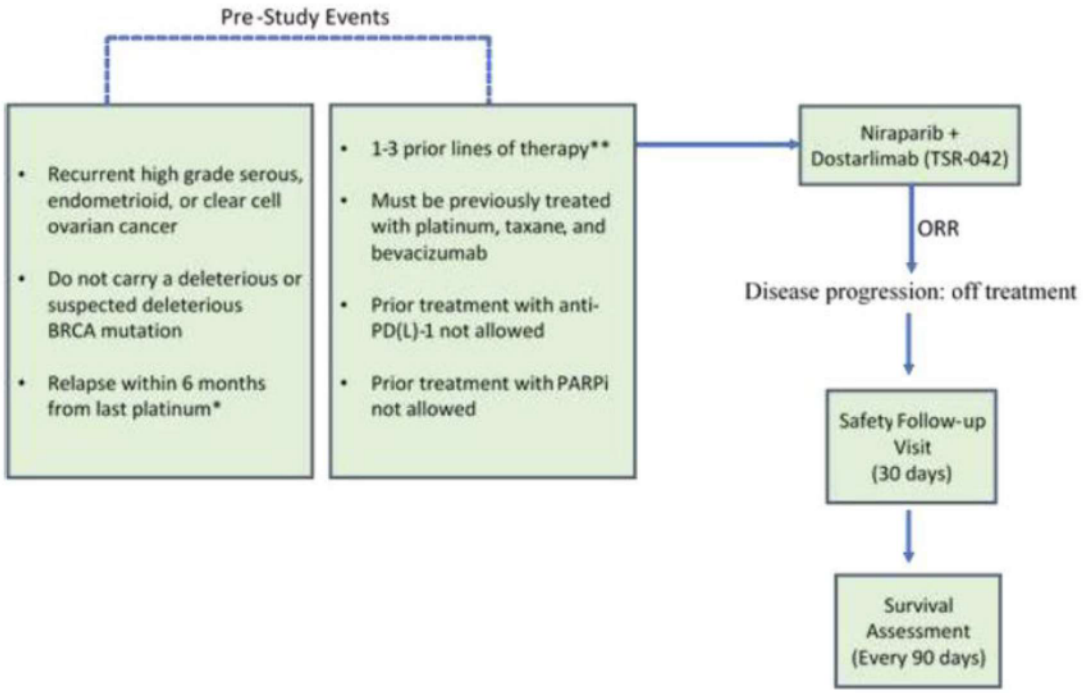
should continue at the specified intervals until progression is confirmed or until the start of subsequent anticancer treatment.

All AEs and serious adverse events (SAEs) will be collected and recorded for each patient from the day of signing the informed consent form until 90 days after last study drug administration or until alternate anticancer treatment has been initiated, whichever occurs earlier; any pregnancies that occur within 180 days post-treatment are to be reported.

Study drug-related SAEs and adverse events of special interest (AESIs) will be collected every 90 ± 14 days after the last dose of study drug until study closeout, or as otherwise indicated in the protocol. AESIs must be reported as soon as the Investigator becomes aware of them. All AEs and SAEs experienced by a patient, 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 patient is lost to follow-up or withdraws consent, or until the patient has died.

A study schema is shown in Figure 1.

Figure 1: Overall Study Schema



Abbreviations: CA-125 = cancer antigen 125; BRCA = breast cancer susceptibility gene; ORR = objective response rate; PARPi = poly(adenosine diphosphate-ribose) polymerase inhibitor; PD = progression of disease; PD(L)-1 = programmed cell death-1 or programmed cell death-ligand 1. RECIST = Response Evaluation Criteria in Solid Tumors.

*Excludes patients who experienced disease progression within 3 months of first-line platinum therapy.

**Neoadjuvant, adjuvant, and the combination of both will be considered as one line of therapy. Treatment with single-agent bevacizumab given as maintenance is not counted as a separate line of therapy. If a therapeutic regimen is modified or changed for a reason other than lack of response or PD (such as allergic reaction, toxicity, or drug availability), this will not be counted as a separate line of therapy. The use of single agent hormonal therapy given for reasons other than progressive disease per RECIST v1.1 (i.e. hormonal therapy given for increasing CA-125 levels) is not counted as a separate line of therapy.

It is anticipated that approximately 150 patients will be enrolled and dosed. The study will be conducted in conformance with Good Clinical Practice (GCP).

4.2 Randomization and Blinding

Not applicable as this is a single-arm study.

4.3 Study Procedures

The schedule of assessments can be found in Section 7.6.1 of the study protocol.

5 Sample Size

A sample size of approximately 150 patients overall will provide sufficient precision for assessment of the primary endpoint of ORR in the overall and PD-L1 positive populations. No inferential testing will be performed, and no adjustments will be made for multiplicity. Primary analysis will be based

on the ORR point estimate and the corresponding 95% exact CI. The PD-L1 positive population is defined in Section 6.1.3.

Standard of care treatment options in BRCAwt population include single chemotherapy, such as paclitaxel, doxorubicin, topotecan, and gemcitabine. The described ORR with these agents is 10% to 20% in first or second relapse (Pignata, et al., 2015; Gynecologic Oncology Group, et al., 2006; Gordon, et al., 2001; Mutch, et al., 2007; DOXIL®, 1995). Therefore, a target ORR of 25% (with sufficient precision such that the lower 95% confidence bound exceeds 15% in the described study population (patients with BRCAwt PROC previously treated with bevacizumab with 1 to 3 prior lines of therapy) with durable response would be considered clinically meaningful.

Table 6 shows 95% CIs at different observed ORR rates (ranging from 20% to 50%) with 150 patients. If the true ORR is 25%, there is 87% chance that the lower bound of the 95% CI will exceed 15%.

Assuming the prevalence of PD-L1 positive disease is 50% in this study population, it is expected that approximately 75 patients with PD-L1 positive tumors will be evaluable. Table 7 shows 95% CIs at different observed ORR rates (ranging from 20% to 50%) for 75 patients with PD-L1 positive tumors. If the true ORR is 30%, there is 84% chance that the lower bound of the 95% CI will exceed 15%.

Table 6: Estimates and 95% CIs with 150 Patients

Sample Size	Number of Responders	ORR (%)	Lower 95% Confidence Limit	Upper 95% Confidence Limit
150	30	20.0	13.9	27.3
	37	24.7	18.0	32.4
	45	30.0	22.8	38.0
	52	34.7	27.1	42.9
	60	40.0	32.1	48.3
	67	44.7	36.6	53.0
	75	50.0	41.7	58.3

Abbreviations: CI = confidence interval; ORR = objective response rate.

Table 7: Estimates and 95% CIs with 75 Evaluable PD-L1 Patients

Sample Size	Number of Responders	ORR (%)	Lower 95% Confidence Limit	Upper 95% Confidence Limit
75	15	20.0	11.7	30.8
	19	25.3	16.0	36.7
	23	30.7	20.5	42.4
	26	34.7	24.0	46.5
	30	40.0	28.9	52.0
	34	45.3	33.8	57.3
	37	49.3	37.6	61.1

Abbreviations: CI = confidence interval; ORR = objective response rate; PD-L1 = programmed cell death ligand 1.

6 General Considerations

6.1 Definitions

6.1.1 Baseline Definitions

For all analyses, baseline is defined as the most recent measurement prior to the first administration of study treatment (considering earlier of niraparib or dostarlimab). If no times are recorded and the assessment is performed on the date of the first administration of study treatment, the assessment will be considered as the baseline.

6.1.2 Study Time Periods

The following study time periods will be defined for analysis:

Treatment Period: the period of time between the date of first dose of any study medication up to and including 90 days after the last dose of study medication or the date of subsequent anticancer drug therapy, whichever occurs first. Safety will generally be reported through the treatment period, unless otherwise specified. The treatment period can be broken down further into the active treatment period and the safety follow-up period as defined below.

- Active treatment: the period of time between the date of first dose and maximum of the following dates:
  - date of last dose of dostarlimab + last interval cycle duration (21 days for cycle 1-4 and 42 days for cycles 5 and beyond),
  - date of last dose of niraparib.

- Safety follow-up: the period of time following active treatment up to and including 90 days after the last dose of study medication or the date of subsequent anticancer drug therapy, whichever occurs first.

Long term follow-up: the period of time following the treatment period, (after the earlier of 90 days post last dose of study medication or date of subsequent anticancer drug therapy).

6.1.3 Biomarker Definitions

Local germline BRCA results are collected during enrollment when available and will be defined as follows:

- Local gBRCA wild type (gBRCAwt): No deleterious or suspected deleterious mutation found in BRCA1 or BRCA2 based on local germline BRCA test result.

- Local unknown gBRCA status (gBRCA-unk): No local gBRCA results available.

Local tumor BRCA results are collected from sites when available and will be defined as follows:

- Local tBRCA wild type (tBRCAwt): Based on local tumor BRCA test result, no deleterious or suspicious deleterious mutation in BRCA1/2 gene
- Local unknown tBRCA status (tBRCA-unk): no local tBRCA results available

Central germline BRCA status is determined using Myriad BRACAnalysis test on blood samples collected at screening and will be defined as follows.

- gBRCA wild type (gBRCAwt): No deleterious or suspected deleterious inherited mutation found in BRCA1 or BRCA2 in the blood

- gBRCA mutant (gBRCAmut): Deleterious or suspected deleterious inherited mutation found in BRCA1 or BRCA2 in the blood
- Unknown gBRCA status: No gBRCA results available (e.g. test canceled, incomplete/ inconclusive, or data missing for a patient).

Central tumor BRCA (tBRCA) status is determined using the Myriad HRD test on tumor samples and is defined as follows.

- tBRCA mutant (tBRCAmut): At least one deleterious or suspected deleterious mutation found in BRCA1 or BRCA2 in the tumor.
- tBRCA wild type (tBRCAwt): No deleterious or suspected deleterious mutation found in BRCA1 or BRCA2 in the tumor.
- Unknown tBRCA status: tBRCA result not available (e.g., test canceled, incomplete/inconclusive, or data missing for a patient)

BRCA status will be determined considering both the central germline BRCA results and central tumor BRCA results as shown in Table 8.

Table 8 Determination of BRCA Status Considering Central gBRCA and tBRCA Results

Central gBRCA	**Central tBRCA**	**BRCA status taking account both central gBRCA and tBRCA**
gBRCAwt	tBRCAwt	BRCAwt
	tBRCAmut	BRCAmut
	tBRCA unknown	BRCA unknown
gBRCAmut	tBRCAwt	BRCAmut
	tBRCAmut	BRCAmut
	tBRCA unknown	BRCAmut
gBRCA unknown	tBRCAwt	BRCA unknown
	tBRCAmut	BRCAmut
	tBRCA unknown	BRCA unknown
Note: local gBRCA status will not be used to determine BRCA status		

Homologous recombination deficiency (HRD) is dysregulation in the homologous recombination pathway (due to genetic mutations or alterations) leading to cellular genomic instability and an inability to efficiently repair damaged DNA. In this study, HRD score is determined using the Myriad HRD test on tumor sample collected prior to enrollment. HRD status will be determined considering HRD score and BRCA status, which considers both central gBRCA and tBRCA results as follows and per Table 9:

- HRD positive: Any tumor with an HRD score ≥42, OR BRCA mutant, is considered HRD positive. The following sub-categories of HRD positive will be determined.
    - BRCAmut
    - (BRCAwt or BRCA unknown) and HRD test score ≥42
- HRD negative: Any tumor with an HRD score <42, AND not BRCAmut (i.e. BRCAwt or BRCA unknown), is considered HRD negative.
- HRD unknown: No sample tested or failed sample AND not BRCA mutant.

Table 9 Determination of HRD Status Considering HRD Score, Central gBRCA and tBRCA Results

HRD Score	**BRCA status taking account both central gBRCA and tBRCA**	**HRD Status**
HRD score ≥42	BRCAwt	HRD positive
	BRCAmut	HRD positive
	BRCA unknown	HRD positive
HRD score <42	BRCAwt	HRD negative
	BRCAmut	HRD positive
	BRCA unknown	HRD negative
HRD score unknown	BRCAwt	HRD unknown
	BRCAmut	HRD positive
	BRCA unknown	HRD unknown

PD-L1 is one of the ligands that bind to PD-1 on tumor infiltrating T cells and renders the T cells inactive. PD-L1 expression has been used as a biomarker for identifying patients who may benefit from anti-PD1/L1 therapies.

In this document, PD-L1 status is determined using the Ventana SP263 immunohistochemistry (IHC) clinical trial assay (CTA) on tumor tissue sample collected prior to enrollment.

- PD-L1 positive (PD-L1 vCPS ≥5%): Any tumor tissue sample with a visually estimated combined positive score (vCPS) ≥5%. vCPS is defined as the percentage of tumor cells and immune cells staining positive within the total tumor area
- PD-L1 vCPS <5%: Any tumor tissue sample with a vCPS score <5%.
- PD-L1 unknown: No sample tested or failed sample.

6.2 Analysis Populations

The following patient populations will be evaluated and used for presentation and analysis of the data:

- Safety (SAF) population is defined as all patients who have received any amount of study treatment.
- Intent-to-Treat (ITT) population is defined as all patients who have received at least 1 complete dose of either study drug and who have measurable disease (which is defined separately under Investigator assessment and Independent Review Committee assessment) at baseline. Measurable disease at baseline is defined by the existence of at least 1 target lesion at baseline tumor assessment by RECIST v1.1 criteria.
- Efficacy-Evaluable (EE) population is defined as all patients who have received at least 1 complete dose of either study drug and who have measurable disease (which is defined separately under Investigator assessment and Independent Review Committee assessment) at baseline and who do not have protocol deviations significantly impacting the interpretation of efficacy results. Patients who are enrolled and dosed who are retrospectively determined to have deviations with respect to the following inclusion/exclusion criteria will be excluded from the EE population:

  Inclusion Criteria
  - Patients must have recurrent high-grade serous, endometrioid, or clear cell ovarian, fallopian tube, or primary peritoneal cancer (Inclusion 2).
  - Patients must be considered resistant to the last administered platinum therapy (Inclusion 3).
  - Patients must have completed at least 1 but no more than 3 prior lines of therapy for advanced or metastatic ovarian cancer (Inclusion 4).
  - Patients must have been previously treated with platinum-based regimen, taxane agent(s), and bevacizumab (Inclusion 5)

  Exclusion Criteria
  - Patients who experienced disease progression within 3 months (as evidenced by radiographic progression per RECIST v1.1) of first-line platinum therapy (Exclusion 1).
  - Patients with known deleterious or suspicious deleterious mutation in breast cancer susceptibility gene (BRCA) 1 or BRCA2 genes (Exclusion 2)
  - Patient has received prior therapy with an anti-PD-1, anti-programmed-death-ligand-1 (anti-PD-L1), or anti-programmed death-ligand-2 (anti-PD-L2) agent (Exclusion 3).
  - Patient has received prior therapy with a poly (adenosine diphosphate-ribose) polymerase (PARP)-1/PARP-2 inhibitor (Exclusion 4).

  Patients who withdraw without a post-baseline tumor assessment due to withdrawal of consent, loss to follow-up or non-compliance with no evidence of early death or clinical progression will also be excluded from the EE population.

The SAF population is the primary population for the analysis of safety endpoints.

The ITT population is the primary population for the analysis of efficacy endpoints. The EE population will be used in supportive efficacy analyses when applicable.

6.3 Withdrawals, Dropouts, Loss to Follow-up

Patients who are withdrawn or discontinue from the study will not be replaced.

6.4 Covariates and Subgroups

ORR, as assessed by the Investigator, will be descriptively summarized by subgroup using the ITT population. Subgroups are defined as follows:

- BRCA status (BRCAwt, BRCAmut, BRCA unknown)
- HRD status
  - HRD negative,
  - HRD positive
    - BRCAmut
    - BRCAwt/BRCA unknown
  - HRD unknown
- PD-L1 status (PD-L1 positive (vCPS≥5%), PD-L1 vCPS<5%, PD-L1 unknown)
- Age (<65, ≥65, <70 and ≥70 years,)
- Race (White, non-White)
- Ethnicity (Hispanic/Latino, Not Hispanic/Latino)
- Baseline ECOG (0, 1)
- Previous lines of therapy (1, 2, 3)
- Response to last platinum therapy (refractory, resistant).

Additional efficacy endpoints (DOR, PFS, DCR and OS), as assessed by the Investigator, will be descriptively summarized by biomarker status (BRCA status, HRD status and PD-L1 status) and response to last platinum therapy.

For ORR and DCR, the rate and corresponding 95% CI will be calculated in accordance with the methodology described in Section 7.1 for binomial endpoints for each subgroup.

For DOR, PFS and OS, descriptive analyses will be performed using KM in accordance with the methodology described in Section 7.1 for time to event endpoints for each subgroup.

If applicable, other exploratory subpopulations may be further defined and analyzed.

6.5 Missing Data

In general, there will be no substitutions made to accommodate missing data points. Methods for handling incomplete FOSI questionnaires will be performed according to the FOSI scoring manual. All data recorded on the eCRF will be included in data listings that will accompany the CSR.

Incomplete dates for disease history and prior anti-cancer therapy (e.g. initial diagnosis date, chemotherapy start/end dates) will be imputed as follows:

- If the day is missing, it will be imputed to the 1st day of the month.
- If both day and month are missing, the month and day will be imputed as January 1st.
- If the date is completely missing, no imputation will be performed.

Per inclusion criteria, patients must be considered resistant to the last administered platinum therapy, ie, the time from last administered platinum dose until the initial documented progression (as evidenced by radiographic progression per RECIST v.1.1) must be less than 6 months. As platinum-free interval (PFI) is a critical inclusion criterion, missing dates associated with the last platinum therapy should be minimized. In the case of incomplete dates, the following imputation rules will be used for the calculation of PFI:

- Platinum start/end dates will be imputed as above for chemotherapy start/stop dates.

- Date of progression for last-administered platinum therapy:
    - If the day is missing, it will be imputed to the 1st day of the month.
    - If day and month are missing, the start of the next anti-cancer regimen will be used.
    - If the date is completely missing and reason for discontinuation is progressive disease by RECIST or clinical criteria, the start of the next anti-cancer regimen will be used.
    - If the date is completely missing and the reason for discontinuation is not progressive disease, the PFI will be considered unknown.

  For patients whose last therapy was platinum-based, the start date of the next anti-cancer regimen would be the first dose of study treatment received on the MOONSTONE study. If the imputed date of the disease progression following the last platinum-based therapy is earlier than the end date of the last platinum-based therapy, the imputed date of the disease progression will be set equal to the end date of the last platinum-based therapy.

Imputation of partial dates is used only to estimate PFI; data listings will present the partial date as recorded in the eCRF.

Incomplete dates for adverse event and concomitant medication dates will be imputed as follows:

Start Date:

- If only 'day' is missing, and the month and year are not the same as the month and year of first dose, then impute day with '01'. Otherwise, if the month and year are the same as first dose date, use first dose date.
- If 'day' and 'month' are missing, and 'year' is not missing, then impute month and day with month and day of first dose date (assuming same 'year').
- If the year is not the same as the year of first dose, impute 01 for day and 01 for month.
- If the start date is completely missing, it will be set to the first dose date.

Stop Date:

- If only 'day' is missing, impute day with last day of the month.
- If 'day' and 'month' are missing, and 'year' is not missing, then impute month with '12' and day with '31' (or date of study discontinuation/completion if earlier than 12-31).
- If the stop date is completely missing, it will be set to the date of study discontinuation/completion. A stop date will not be applied to ongoing AEs.
- If the imputed stop date is greater than last contact date, then set to last contact date.

Imputation of partial dates is used to determine whether an event is treatment-emergent; or classification of medications as prior/concomitant. In addition, imputed partial dates will be used to determine the appropriate cycle for analyses by cycle. Data listings will present the partial date as recorded in the eCRF.

6.6 Visit Windows

It is expected that all visits should occur according to the protocol schedule. By-visit summaries and analyses will be by nominal visit (all data will be tabulated per the evaluation visit as recorded on the eCRF even if the assessment is outside of the visit window for analysis).

In data listings, the relative day of all assessment dates will be presented.

6.7 Interim Analyses and Data Monitoring

An interim futility analysis will be performed after the first 40 patients (regardless of PD-L1 status) have had the opportunity for at least 1 scan (approximately 9 weeks after initial dose). Eligible patients with a non-evaluable scan will not be included. In addition, patients who withdraw without a post-baseline tumor assessment due to withdrawal of consent, loss to follow-up or non-compliance with no evidence of early death or clinical progression will also be excluded from the interim analysis population. Patients who withdraw due to AE will be included in the interim analysis population .

Interim futility analysis will be performed considering confirmed and unconfirmed responses that have the potential to be confirmed with additional follow-up. Enrollment will continue at the discretion of the sponsor while obtaining response data on the first 40 patients.

The nonbinding rule for futility criteria is ≤ 5 responses (complete or partial responses, considering both confirmed and unconfirmed) in 40 patients. The probability of early termination is 79% and 43% when the true ORR is 10% and 15%, respectively.

In addition to objective response rate, demographics, baseline characteristics, primary cancer history, prior anticancer treatment, baseline biomarker status (as data is available), will be summarized. ORR by subgroups may also be explored.

If the interim analysis demonstrates futility, the protocol may be amended as a result to enroll patients with PD-L1 positive tumors only.

6.8 Multi-Center Studies

Data will be pooled across study sites.

6.9 Multiple Testing

There will be no adjustment for multiplicity as there is no formal hypothesis testing planned and the efficacy objectives are related only to estimation.

7 Summary of Study Data

7.1 General Considerations

In general, all presentations, unless otherwise noted, will be performed for the overall patient population as well as the subset of patients with PD-L1 positive tumors.

All data listings that contain an assessment date will also contain a relative study day. Pre-treatment and on-treatment study days are numbered relative to the day of the first dose of study treatment which is designated as Day 1. The preceding day is Day -1, the day before that is Day -2, etc.

In general, categorical data will be summarized using number of patients (n), frequency and percentages, with the denominator for percentages being the number of patients in the analysis set for each cohort. Percentages will be rounded to 1 decimal place except for 100%, which will have no decimal place. Counts of zero in any category will be presented without percentage.

Continuous data will be summarized using the number of patients, mean, standard deviation, median, first quartile (Q1), third quartile (Q3), minimum, and maximum. In general, the mean, median and quartiles (Q1, Q3) will be presented to 1 decimal place greater than the original data; the standard

deviation will be presented to 2 decimal places greater than the original data; and the minimum and maximum will have the same number of decimal places as the original data.

Two-sided exact 95% confidence intervals (CIs) based on the Clopper-Pearson method (Clopper & Pearson, 1934) will be provided to summarize the binomial proportion where applicable. The Clopper-Pearson CI can be carried out using the FREQ procedure in SAS v9.4 or higher by appending the "/ BINOMIAL(EXACT)" option to the end of the appropriate "TABLE" statement.

Time-to-event analyses will be performed using Kaplan-Meier (KM) methods. Quartile estimates and associated 2-sided 95% CIs (Brookmeyer & Crowley, 1982) will be provided. Survival distribution function (SDF) estimates from product-limit method along with the corresponding 95% confidence using the log-log transformation will be provided at 3-month intervals as data allows. Kaplan-Meier plots of the SDF will be presented and will include the number of patients at risk over time.

Subgroup analyses will be performed using descriptive statistics and are considered exploratory.

In addition:

- P-values greater than or equal to 0.0001, in general, will be presented to 4 decimal places; p-values less than 0.0001 will be presented as "<0.0001"
- CIs will be presented to 1 decimal place
- Study Day 1 will be considered the first day of study treatment, as the minimum of (first dose of niraparib, first dose of dostarlimab)
- Study day will be calculated as follows:
    - Days prior to first dose: study day=date – first dose date
    - Days on or after first dose: study day = date – first dose date + 1
- Weeks will be calculated as number of days divided by 7
- Months will be calculated as number of days divided by 30.4375
- Years will be calculated as number of days divided by 365.25
- All tables, figures, and listings will include footers at the bottom of the page reflecting the path of the program used to generate the tables, figures, and listings, and date and time of the generation of the output.

Some minor modifications may be necessary to the planned design of tables, figures, and listings to accommodate data collected during the actual study conduct.

7.2 Patient Enrollment

The number of patients screened (who have signed informed consent) and the number of patients in each analysis population will be summarized.

The number of patients screened and who received at least one dose of study medication by center will be provided.

7.3 Patient Disposition

Patient disposition will be tabulated and include the following:

- number of patients ongoing study treatment at the time of the data cut
- number who discontinued each treatment and primary reason for withdrawal of each treatment
- number of patients on-study at the time of the data cut

- number who discontinued study and the primary reason for withdrawal from study

In addition, the number of deaths on active treatment, during safety follow-up and during long term follow-up, as defined in Section 6.1.2, will be tabulated along with the primary reason for death.

A by-patient data listing of study completion information including the reasons for treatment discontinuation and/or study discontinuation will be presented.

7.4 Protocol Deviations

Protocol deviations will be assessed as important or significant per Sponsor's SOP.

A protocol deviation is classified as important if there is the potential to impact the completeness, accuracy, and/or reliability of the study data, or affect a patient's rights, safety, or well-being.

An important protocol deviation is classified as significant if it is confirmed to adversely impact the completeness, accuracy, and/or reliability of the study data, or affect a patient's rights, safety, or well-being.

All protocol deviations will be identified and finalized prior to database lock.

The following protocol deviation summaries will be provided:

- Number and percentage of patients with a significant protocol deviation by type of deviation.
- Number and percentage of patients with an important protocol deviation by type of deviation.
- A listing of all protocol deviations.

7.5 Demographic and Baseline Variables

Demographics, baseline and disease characteristics will be summarized using descriptive statistics using the safety population. If there is a large difference between the analysis populations, tables may also be generated to reflect other analysis populations.

Demographic, baseline and disease characteristic data for each patient will be provided in data listings.

The demographic and baseline characteristics tables will include the following variables:

- Sex
- Reproductive status (childbearing/non-childbearing potential)
- Race (White, Black, Asian, American Indian/Alaska native, native Hawaiian or other Pacific Islander, other, unknown, and not reported). If more than one race is selected, the patient will be counted in the 'Multiple Race' category.
- Ethnicity (Hispanic, non-Hispanic, unknown, and not reported)
- Age at time of screening (years), age as reported on the eCRF, will be used
- Age categories (<65, ≥65 which will be further sub-categorized as 65 to <70, 70 to < 75 and ≥75)
- Baseline weight (in kilograms, last value prior to first dose; if weight is reported in pounds, convert to kilograms by dividing by 2.2)
- Baseline height (in centimeters, last value prior to first dose; if height is reported in inches, convert to centimeters by multiplying by 2.54)

- Baseline body mass index (BMI) (kg/m^2), calculated using the patient's height and weight at baseline [BMI (kg/m^2) = weight (kg) / height (m)^2]
- ECOG performance status at baseline

Primary cancer history will be summarized, including the following variables

- Primary tumor site (ovarian, primary peritoneal, or fallopian tube)
- Time from first diagnosis to first dose (years), defined as:
  - (date of first dose of study treatment – date of diagnosis + 1)/365.25, where missing data is handled per Section 6.5.
- International Federation of Gynecology and Obstetrics (FIGO) stage at time of initial diagnosis
- Metastatic Disease (yes/no)
- Histology and grade of disease at diagnosis and most recent biopsy, if additional biopsy performed

Prior ovarian cancer treatment will be summarized by Type, Sub-type as applicable and Preferred Term as classified in Table 10 by setting (any setting, neo-adjuvant/adjuvant, maintenance, recurrence, other). Additional treatments may be added as required to accommodate other prior cancer treatments that are used in this study.

Table 10 Classification of Prior Ovarian Cancer Treatment

Type	Sub-type	Preferred Term (PT) /CRF Term
Chemotherapy	Anthracycline	Doxorubicin, Pegylated liposomal doxorubicin hydrochloride
	Platinum	Cisplatin, Carboplatin
	Taxane	Docetaxel, Paclitaxel
	Other	Cyclophosphamide Etoposide Gemcitabine Pemetrexed Topotecan Trabectedin
Hormonal Therapy		Tamoxifen Anastrozole Letrozole Emexestane Fulvestrant
Monoclonal Antibody		Bevacizumab
Investigational Drug		Investigational Drug Investigational Antineoplastic Drugs

In addition, the following prior ovarian cancer treatment variables will be summarized:

- Any radiotherapy prior to enrollment
- Any surgeries/procedures related to the study indication
- Number of prior lines of therapy, where the following rules will be applied:

  - Neoadjuvant, adjuvant, and the combination of both will be considered as one line of therapy.
  - Treatment with single-agent bevacizumab given as maintenance is not counted as a separate line of therapy.
  - If a therapeutic regimen is modified or changed for a reason other than lack of response or PD (such as allergic reaction, toxicity, or drug availability), this is not counted as a separate line of therapy.
  - The use of single agent hormonal therapy given for reasons other than progressive disease per RECIST v1.1 (i.e. hormonal therapy given for increasing CA-125 levels) is not counted as a separate line of therapy.
- Months between last treatment regimen and first dose of study treatment, defined as:
  - (date of last treatment regimen (end date) – first dose of study treatment + 1)/30.4375, where missing data is handled per Section 6.5.
- Number of prior platinum-containing lines of therapy
- Months between last platinum dose and first dose of study treatment, defined as:
  - (date of last platinum regimen (end date) – first dose of study treatment + 1)/30.4375, where missing data is handled per Section 6.5.
- PFI (days) after the last platinum-based therapy (summarized as a continuous variable and a categorical variable – refractory (PFI ≤ 28 days), resistant (PFI >28 days to <190 days, unknown)). PFI is defined as:
  - date of progression on last platinum regimen – date of last platinum regimen (end date) + 1, where missing data is handled per Section 6.5.

  For patients who continue on treatment despite progression (i.e. date of last platinum regimen is after date of progression), PFI will be set as 0.

Biomarker status will be summarized, including:

- Local gBRCA status [gBRCAwt, gBRCA unknown]
- Local tBRCA status [tBRCAwt, tBRCA unknown]
- Centralized gBRCA status [gBRCAwt, gBRCAmut, gBRCA unknown]
- Centralized tBRCA status [tBRCAwt, tBRCAmut and tBRCA unknown]
- BRCA status, considering both gBRCA and tBRCA results [BRCAwt, BRCAmut, BRCA unknown]
- HRD status [HRD positive, HRD negative, and HRD unknown; HRD positive will be further classified as BRCAmut, BRCAwt, BRCA unknown]
- PD-L1 status [PD-L1 positive (vCPS≥5%), PD-L1 vCPS<5%, PD-L1 unknown]

7.6 Concurrent Illnesses and Medical Conditions

General medical history will be coded using MedDRA v22.0 or later, and the number and percentage of patients experiencing at least 1 such diagnosis by MedDRA System Organ Class (SOC) and preferred term (PT) will be reported.

Prior Grade 3 or Grade 4 blood disorders (thrombocytopenia, leukopenia, anemia, or neutropenia) will be summarized separately.

7.7 Prior and Concurrent Medications

All medications (other than per-protocol study treatments) will be coded using the September 2018 or later version of the WHO Drug Dictionary (WHODD). Medication start and stop dates will be compared to the date of first dose of study drug to allow medications to be classified as prior or concomitant using the following definitions.

- Prior medications: any medications, which started prior to the first dose date of study treatment.
- Concomitant medications: any medications, being taken on or after the initial study treatment dosing date through 90 days after the last dose of study medication or the date of subsequent anticancer drug therapy, whichever occurs first.

Using the definition above, medications can be classified as both prior and concomitant. For example, a patient who starts a medication before first dose and continues during study treatment will be considered as having both prior and concomitant medications. Medications starting after the safety follow-up period will be listed but will not be classified or summarized.

Both prior medications and concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) classification drug class level 3 and WHO preferred name using the number and percentage of patients. A patient reporting the same medication more than once will be counted only once when calculating the number and percentage of patients who received that medication in a given time category (prior or concomitant). The summary of concomitant medications will be ordered by descending frequency with respect to drug class and by descending frequency of preferred name in total within the drug class. For drugs with the same frequency, sorting will be done alphabetically. Summaries will be based on the safety population.

Prior and concomitant medications will be provided in a by-patient listing sorted by patient ID number and administration date in chronological order.

Anti-cancer systemic therapy, radiotherapy and surgery that occurs post discontinuation of study treatment is captured separately from concomitant medication as the existence of such therapies can lead to censoring of time to event endpoints. These data will be listed.

8 Efficacy Analyses

Table 11 provides a summary of the efficacy endpoints and the respective analysis populations and subgroups that will be evaluated. Further details for each endpoint are provided in the subsequent sections.

Table 11 Overview of Analyses for Efficacy Endpoints Performed in Overall Population and Subset of Patients with PD-L1 Positive Tumors

Assessor	Endpoint	Analysis Method	Analysis Populations	Descriptive Subgroup Analysis in ITT Population
Investigator-Assessment	ORR	Rate and 95% CI;	-ITT -EE	All subgroups defined in Section 6.4
	DCR	Rate and 95% CI	-ITT -EE	Biomarker status, Response to last platinum therapy
	DOR	Kaplan-Meier analysis	Patients with BOR of confirmed CR or PR in: -ITT -EE	Biomarker status, Response to last platinum therapy
	PFS	Kaplan-Meier analysis	-ITT -EE	Biomarker status, Response to last platinum therapy
	Duration of Disease Control	Kaplan-Meier analysis	Patients with BOR of confirmed CR, PR or SD in: -ITT -EE	None
Independent-Review Committee (IRC) Assessment	ORR	Rate and 95% CI;	-IRC ITT -IRC EE	None
	DCR	Rate and 95% CI	-IRC ITT -IRC EE	None
	DOR	Kaplan-Meier analysis	Patients with BOR of confirmed CR or PR in: -IRC ITT -IRC EE	None
	PFS	Kaplan-Meier analysis	-IRC ITT -IRC EE	None
	Duration of Disease Control	Kaplan-Meier analysis	Patients with BOR of confirmed CR, PR or SD in: -IRC ITT -IRC EE	None
Not Applicable	OS	Kaplan-Meier analysis	-ITT -EE	Biomarker status, Response to last platinum therapy
	FOSI overall score and change from baseline	Descriptive summary statistics,	-ITT	None
	FOSI time to symptom worsening	Kaplan-Meier analysis	-ITT	None

Abbreviations: BOR=best overall response; CI=confidence interval; CR=complete response; DCR=disease control rate; DOR=duration of response; EE=efficacy-evaluable; FOSI= Functional Assessment of Cancer Therapy – Ovarian Symptom Index (FOSI); IRC=independent review committee; ITT=intent-to-treat. ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PR=partial response; SD=stable disease; wt=wild-type.

8.1 Primary Efficacy Analysis

The primary efficacy parameter will be based on the Investigator-assessed confirmed ORR per RECIST v1.1. Analyses will be performed in the overall population and in the subset of patients with PD-L1 positive tumors.

At each evaluation, the RECIST v1.1 (Eisenhauer, et al., 2009) criteria in Table 12 will be used to define each patient's overall response at that evaluation. These responses will be entered into the eCRF.

Table 12 Time Point Response for Patients with Measurable Disease at Study Entry

Target Lesions	Non-Target Lesions	New Lesions	Overall Response
CR	CR	No	CR
CR	Non-CR/Non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-CR/Non-PD/Not evaluated	No	PR
SD	Non-CR/Non-PD/Not evaluated	No	SD
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD
Abbreviations: CR = complete response; PD = progressive disease; PR = partial response; SD = stable disease.			

As confirmed CR/PR is required, the best overall response (BOR) will be determined as shown in Table 13 per RECIST v1.1 (Eisenhauer, et al., 2009).

The protocol scheduled tumor assessment interval is every 9 weeks (63 ± 7 days) for the first year of study treatment, and then every 12 weeks (84 ± 7 days) until progression. The minimum criteria for SD duration are at least 8 weeks from the date of first dose of study treatment.

Table 13 Best Overall Response when Confirmation of CR and PR Required

Overall Response First Time Point	Overall Response Subsequent Time Point (at least 4 weeks)	Best Overall Response (BOR)
CR	CR	CR
CR	PR	SD, PD or PR [a]
CR	SD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
PR	CR	PR
PR	PR	PR
PR	SD	SD provided minimum criteria for SD duration met, otherwise, NE
PR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
SD	SD	SD provided minimum criteria for SD duration met, otherwise, NE
SD	PD	SD provided minimum criteria for SD duration met, otherwise, PD
SD	NE	SD provided minimum criteria for SD duration met, otherwise, NE
NE	NE	NE

Abbreviations: CR = complete response; NE = not evaluable; PD = progressive disease; PR = partial response; SD = stable disease.

[a] If a CR is truly met at first time point, then any disease seen at a subsequent time point, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However, sometimes 'CR' may be claimed when subsequent scans suggest small lesions were likely still present and in fact the patient had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

Note: The minimum criteria for SD duration are at least 8 weeks from the date of first dose of study treatment.

For each patient, BOR will be determined based on the overall responses at all time points between the date of first dose and the date of first documented radiological disease progression, or the date of subsequent anti-cancer therapy, whichever occurs first. Radiotherapy to lesions other than target or non-target lesions will not be considered subsequent anti-cancer therapy.

Patients with a BOR of either confirmed CR or PR are considered to have responded to treatment ("responders") for the primary efficacy variable (ORR). All other patients are considered to have not responded to treatment ("non-responders") for the primary efficacy variable.

The ORR and 2-sided 95% confidence interval will be provided, in accordance with the methodology described in Section 7.1.

The primary analysis population will be the ITT population. Supportive analyses will also be performed using the EE population. Exploratory subgroup analyses will be performed using the ITT population as described in Section 6.4.

Tumor size (sum of longest (non-nodal) dimension and shortest (nodal) axes of all target lesions identified at baseline) will be presented graphically using waterfall plots, to present each subject's best percentage change in tumor size as a separate bar, with the bars ordered from the largest increase

to the largest decrease. Best percentage change is defined as the largest decrease in sum of diameters for patients who experience a decrease; if there is no decrease, it is considered the smallest increase in the sum of diameters. Bars will be color coded and annotated to display biomarker status. A reference line at the –30% change in tumor size levels will be added to the plots, which corresponds with the definition of 'partial' response. Note: new lesions will not be included in the total tumor size. Patients must have a baseline and post-baseline tumor assessment to be included in the waterfall plot.

Swimmer plots will also be produced. This depicts each patient's nature and duration of response as a separate bar (horizontally) over time. Bars will be color coded and annotated to display biomarker status.

8.2 Secondary Efficacy Analyses

Analyses of secondary efficacy endpoints will be performed in the overall population and in the subset of patients with PD-L1 positive tumors. Censoring rules for the analysis of DOR, PFS and the exploratory endpoint of duration of disease control are provided in Table 14.

Table 14 Censoring Rules used in the DOR, PFS Analysis and Duration of Disease Control

Situation	Date of Event or Censoring	Outcome
No baseline tumor assessments [a]	First dose date	Censored
No post-baseline tumor assessments and no death ≤ 18 weeks after first dose [a]	First dose date	Censored
Start of subsequent anti-cancer therapy prior to a documented radiological progression or death [b]	Date of last post-baseline radiological tumor assessment prior to or on the date of initiation of the subsequent anti-cancer therapy	Censored
Free of radiological progression and no subsequent anti-cancer therapy started and no death [b]	Date of last post-baseline radiological tumor assessment	Censored
Documented radiological progression or death after 2 or more consecutive missing radiologic assessments (i.e. > 18 weeks).	Date of last post-baseline radiological tumor assessment prior to the missed radiological assessment	Censored
Documented radiological progression or death	Earliest date of radiological progression or death	Event

Abbreviations: DOR=duration of response; PFS=progression-free survival.
Note: When considering censoring on last post-baseline assessment, the assessment must not be non-evaluable.
[a] Applied to PFS analysis only.
[b] Radiotherapy to lesions other than target/non-target lesions will not be considered as subsequent anti-cancer therapy.

8.2.1 Investigator Assessed Duration of Response

For patients with confirmed response (CR or PR), DOR (in months) is defined as the time from first documentation of response (CR or PR) until the time of first documentation of disease progression by RECIST v1.1 based on Investigator assessment or death by any cause in the absence of progression by RECIST v1.1, calculated as:

[Earlier of (date of radiological PD or death) – First documentation of response + 1] / 30.4375

Censoring rules for the analysis of DOR are provided in Table 14.

A time-to-event analysis of DOR will be performed in accordance with the methodology described in Section 7.1 for time to event endpoints.

The analysis population will be patients in the ITT analysis set with a confirmed CR or PR. Supportive analyses will be performed using patients with a confirmed CR or PR in the EE analysis population. Exploratory subgroup analyses will be performed using the ITT population as described in Section 6.4.

8.2.2 Investigator Assessed Progression-Free Survival

PFS (in months) is defined as the time from the date of first dose to the earlier date of radiological PD as assessed by the Investigator or death from any cause, calculated as:

[Earlier of (date of radiological PD or death) – First dose date + 1] / 30.4375

Censoring rules used in PFS analysis are the same as those used for DOR and are provided in Table 14.

A time-to-event analysis of PFS will be performed in accordance with the methodology described in Section 7.1 for time to event endpoints.

The analysis population will be the ITT population. Supportive analysis will be performed in the EE population. Exploratory subgroup analyses will be performed using the ITT population as described in Section 6.4.

8.2.3 Overall Survival

Overall survival (in months) is defined as the time from the date of the first dose to the date of death for any cause, calculated as:

[Date of death – First dose date + 1] / 30.4375

Patients who are known to be alive will be censored at the last contact date.

The date of last contact date will be derived using the last complete date among the following data sources:

- Patient assessment dates (laboratory blood draws, vital signs, performance status, ECG, tumor assessments, ECOG, pregnancy test, physical exams, tumor measurement, or tumor biopsy dates)
- Start and end dates of anti-cancer therapies, including anticancer therapy, surgeries or radiotherapy, administered after study treatment discontinuation.
- AE start and end dates (non-imputed dates only)
- Concomitant medications, growth factors, transfusions start and end dates (non-imputed dates only)
- Last date of contact collected on the 'Survival information' eCRF where patient status is alive
- Date of death, collected on the Study Discontinuation CRF form
- Study treatment (niraparib and dostarlimab) start and end dates

- Date of discontinuation on disposition eCRF pages (do not use if reason for discontinuation is lost to follow-up).

Only dates associated with actual examinations of the patient will be used in the derivation. Dates associated with a technical operation unrelated to patient status such as the date a blood sample was processed will not be used in the derivation.

A time-to-event analysis of OS will be performed in accordance with the methodology described in Section 7.1 for time to event endpoints.

The analysis population will be the ITT population. Supportive analysis will be performed in the EE population. Exploratory subgroup analyses will be performed using the ITT population as described in Section 6.4.

8.2.4 Investigator Assessed Disease Control Rate

Patients who achieved a best overall response rate of confirmed CR, PR, or SD (SD must have met the 8-week duration criteria) will be considered "responders" for this endpoint. All other patients will be considered "non-responders" for this endpoint.

The DCR and 2-sided 95% CI will be provided in accordance with the methodology described in Section 7.1 for binomial endpoints.

The analysis population will be the ITT population. Supportive analyses will also be performed using the EE population. Exploratory subgroup analyses will be performed using the ITT population as described in Section 6.4.

8.2.5 Efficacy Endpoints Based on Independent Review Committee Assessment

ORR, DOR, PFS, and DCR will be also evaluated using Independent Review Committee assessment. The analysis methods will be the same as those described for efficacy parameters as assessed by the Investigator in Section 8.1, 8.2.1, 8.2.2 and 8.2.4. Waterfall plots and swimmer plots as described in Section 8.1 will be produced as derived by the Independent Review Committee assessments.

8.3 Exploratory Efficacy Analyses

Analyses of secondary efficacy endpoints will be performed in the overall population and in the subset of patients with PD-L1 positive tumors.

8.3.1 Efficacy in Patients with Documented BRCAwt Tumors

Efficacy endpoints (ORR, DOR, PFS, DCR and OS) as assessed by the Investigator will be assessed in patients with documented BRCAwt tumors. This assessment will be performed as part of the subgroup analyses by BRCA status where patients with BRCAwt, BRCAmut and BRCA unknown tumors are evaluated, considering both central gBRCA and tBRCA results as described in Table 8. The ITT population will be used for analysis.

8.3.2 Duration of Disease Control

Duration of disease control is defined as the time from the date of the first dose of study treatment to the earlier date of assessment of progression by RECIST v.1.1 or death by any cause in the absence of progression by RECIST v1.1 among patients whose BOR is confirmed CR, PR or SD. It is calculated as:

[Earlier date of radiological PD or death – First dose date) + 1] / 30.4375

Table 14 provides a summary of the censoring rules used in calculating duration of disease control.

A time-to-event analysis of duration of disease control will be performed in accordance with the methodology described in Section 7.1 for time to event endpoints.

The analysis population will be ITT patients with SD or confirmed CR or PR. Supportive analyses will be performed using the EE population.

Duration of disease control will be analyzed using the Investigator assessment of response as well as the Independent Review Committee assessment.

8.3.3 Functional Assessment of Cancer Therapy – Ovarian Symptom Index (FOSI)

The FOSI is a validated 8 item measure of symptom response to treatment for ovarian cancer based on a subset of questions from the Functional Assessment of Cancer Therapy – Ovarian Cancer questionnaire (see Protocol Appendix 5). Patients respond to their symptom experience over the past 7 days using a 5-point Likert scale ranging from CCI to CCI.

For items 1 through 6 and item 8, the score used for calculating the total score is the difference between the patient's response and 4. For item 7, the score used for calculating the total score is the patient's response. The total score is calculated by multiplying the sum of all items scored by 8 and dividing the result by the number of responses. If 5 or more responses are recorded, the FOSI can be scored; otherwise, the FOSI score is recorded as missing. The FOSI score range is PPD to PPD; a higher score indicates a better Quality of Life (QOL).

At each time point, the number and percentage of patients who completed the questionnaires will summarized in a table, as well as the reasons for non-completion of these measures. The denominator will be based on the number of patients expected to complete the form at the visit. Expected forms will be derived as those who are still on at least one of the components of study treatment at the visit where FOSI was to be collected.

Descriptive summary statistics will be provided for the overall total score and the change from baseline by time point using the ITT population with valid FOSI data at each timepoint. No imputation will be performed for missing data.

Time to symptom worsening will be defined as the time from randomization to the first FOSI assessment with a worsening score compared to its baseline score using minimally important difference (MID) thresholds (defined as 2-point change) (Beaumont, et al., 2007), which will be categorized at each visit as follows:

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Any patient with only improved or stable FOSI scores will be censored at the date of the last evaluable FOSI assessment, i.e. FOSI score is not missing. Patients who have no valid baseline FOSI assessment or any post-baseline FOSI assessment will be censored at the date of first dose of study medication. Kaplan-Meier methodology, in accordance with the methodology described in Section 7.1

for time to event endpoints, will be used to summarize time to symptom worsening on the overall FOSI score.

8.3.4 Duration of Survival and PFS Follow-Up

Duration of survival follow-up, defined as the time from first dose until date of death or date of last contact (i.e., date patients were censored for overall survival Section 8.2.3), will be summarized. The KM estimate of the median potential survival follow-up, using reverse censoring of survival data (i.e., treating death as censored observations, and censored survival observations as events), will also be presented (Schemper & Smith, 1996). Duration of PFS follow-up will be analyzed in a similar fashion, defined as the time from first dose until date of progression or death or date of censoring (Section 8.2.2).

8.3.5 Estimation of Optimal Threshold for PDL-1 and Derivation of Combinatorial Biomarker Signatures for Identifying Responders and non-Responders

An ensemble statistical algorithm, called BATTing (Bootstrapping and Aggregating Thresholds from Trees), as proposed in (Huang, et al., 2017) and illustrated in (McKeegan, et al., 2015), will be used to estimate the optimal threshold (cut-point) value of PDL-1 that would help identify patients that are likely to have a tumor response with the combination treatment of Niraparib and Dostarlimab. In general, this algorithm selects the optimal cut-point that yields the best differentiation of patient subgroups with respect to the clinical endpoints of interest. First a large number (B) of datasets are randomly drawn with replacement (bootstrapped) from the original dataset. Then a Tree model with a single split on the PDL-1 values is built for each of these B datasets, such that the two terminal nodes of the tree will yield the best possible separation of the groups with respect ORR for the patients receiving Niraparib-Dostarlimab combination treatment. The threshold value from the split formed by each of these B trees is obtained. The median of the B threshold values is the BATTing threshold estimate. B=100 will be used in this dataset, per the recommendation in (Huang, et al., 2017) for B to be set at 50 or higher for ensuring a stable estimate of the threshold. This procedure is expected to yield a more reliable estimate of the PDL-1 threshold because a threshold from just a single Tree built on the original dataset or a single Receiver Operating Characteristic (ROC) curve or a single Precision Recall Curve tends to be highly unstable and not robust enough to small perturbations in the data and outliers, as illustrated clearly in (Huang, et al., 2017).

9 Safety Analyses

9.1 Extent of Exposure

The dosing schedule for niraparib and dostarlimab is provided in Table 5.

The number and percentage of patients at the starting prescribed dose by cycle will be summarized.

Exposure parameters as defined in Table 15 will be summarized. In addition, the number and percentage of patients who have a niraparib dose reduction, dose interruption, missed dose, or dose escalation beyond the starting dose will be summarized. Dostarlimab infusion interruption or infusion delay will also be summarized.

For patients treated beyond Investigator-assessed progression (those dispensed with niraparib post-progression and/or receiving dostarlimab infusion post-progression), the duration of treatment beyond progression will be summarized, along with the best overall response observed post-progression as

recorded by the Investigator (relative to the baseline scan). Duration of post-progression treatment is defined as:

max(date of last niraparib dose + 1, dostarlimab infusion + x) - date of Investigator assessed radiologic progression via RECIST v1.1;

where:

x=21 for last cycle=1-4;

x=42 for last cycle ≥5.

Dosing information as well as derived exposure parameters will be presented for each patient in data listings.

Table 15 Exposure Parameters for Niraparib, Dostarlimab and Overall Study Treatment

Parameter	Niraparib	Dostarlimab	Overall Study Treatment
Number of treatment cycles initiated	# of niraparib cycles initiated (dose given)	# of dostarlimab cycles initiated (infusion started)	# of cycles where either dostarlimab or niraparib initiated.
Duration of treatment (Unit: months)	(date of last niraparib treatment-first niraparib dose +1)/30.4375 NOTE: date of last niraparib treatment will consider the maximum date recorded on the niraparib discontinuation eCRF and the dates recorded on the niraparib study treatment eCRF.	(date of last dostarlimab infusion+x - first dostarlimab infusion)/30.4375, where: x=21 for last cycle=1-4; x=42 for last cycle ≥5 (not to be extended beyond date of death, if applicable)	max(date of last niraparib dose+1, dostarlimab infusion+x)-min(date of first niraparib dose, first dostarlimab infusion); where: x=21 for last cycle=1-4; x=42 for last cycle ≥5 (not to be extended beyond date of death, if applicable)
Cumulative dose (Unit: mg)	Sum of all niraparib doses consumed. This will be derived using pill count data (dispensed - returned). If the number of returned capsules is missing in a cycle, the number of capsules consumed will be assumed to be the prescribed number of capsules/day (eg, 3/2/1 capsules per day) multiplied by the treatment duration in that cycle.	Sum of all dostarlimab doses infused.	NA
Actual dose intensity (Unit: mg/day)	Cumulative dose/niraparib treatment duration (days)	Cumulative dose/dostarlimab treatment duration (days)	NA
Intended daily dose (Unit: mg/day)	200 mg/day or 300 mg/day	23.81 mg/day	NA
Relative dose intensity* (Unit: %)	100*(Actual dose intensity/intended daily dose)	100* (Actual dose intensity/intended daily dose)	NA
Abbreviations: NA=not applicable.			

9.2 Adverse Events

9.2.1 Overview

All AEs and serious adverse events (SAEs) will be collected and recorded for each patient from the day of signing the informed consent form until 90 days after last study drug administration or until alternate anticancer treatment has been initiated, whichever occurs earlier; any pregnancies that occur within 180 days post-treatment are to be reported. Study drug-related SAEs and adverse events of special interest (AESIs) will be collected every 90 ± 14 days after the last dose of study drug until study closeout, or as otherwise indicated in the protocol. 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.

Per protocol, treatment-Emergent Adverse Events (TEAEs) are events that were not present prior to the initiation of study treatment or events already present that worsen in either intensity or frequency following exposure to study treatment.

For analysis, the following will be considered treatment emergent:

- all AEs and SAEs with an onset on or after the first dose of study treatment throughout 90 days after the last dose of study treatment (or until the start of alternate anticancer therapy, whichever occurs earlier).
- all study drug-related SAEs and AESIs with an onset on or after the first dose of study treatment, including new malignancies reported on the survival follow-up form.
- all pregnancies with an onset on or after the first dose of study treatment until 180 days after the last dose of study treatment.
- all AEs with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dose date of either study treatment

Adverse events not considered treatment emergent will be included in the listings, but will not be included in the summaries, unless otherwise specified. All analyses of adverse events will be performed using the Safety Population.

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 subject's disease, these AEs/SAEs must be reported per AE/SAE reporting requirements.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) v22.0 or later. All AEs will be assessed by the Investigator for severity according to CTCAE v4.03. Relationship to each study drug, niraparib and dostarlimab, will be assessed by the Investigator as either related or not-related. Any TEAE for which the relationship to study drug is missing will be considered as related. Within the same MedDRA PT, the AE with the highest ranked relationship to treatment for each patient will be counted in tabulations by relationship to treatment. Within a MedDRA SOC, patients with more than 1 MedDRA PT will be counted only once for the AE that is most related to treatment. The imputation for a missing relationship will take place prior to determining the most related AE within a SOC or PT for a given patient.

Overall, patients with the same AE more than once will have that event counted only once within each SOC, and once within each PT. When summarized by severity, patients with the same AE more than

once will have the maximum severity of that event counted within each SOC, and once within each PT. When summarized by relationship, the AE will be counted towards each study drug to which a related-attribution is given. For example, if an AE is attributed to both study drugs, it will be counted as being related to study treatment, related to niraparib, and related to dostarlimab.

A high-level overview of AEs will be presented in a summary table. This table will include the numbers and percentages of patients who had:

- Any TEAE
- Any treatment-related TEAE
  - Related to niraparib
  - Related to dostarlimab
- Any TEAE with CTCAE Toxicity Grade >=3
- Any treatment-related TEAE with CTCAE Toxicity Grade >=3
  - Related to niraparib
  - Related to dostarlimab
- Any serious TEAE
- Any treatment-related serious TEAE
  - Related to niraparib
  - Related to dostarlimab
- Any TEAE leading to study drug interruption/reduction/delay
  - TEAE leading to niraparib interruption
  - TEAE leading to niraparib dose reduction
  - TEAE leading to dostarlimab infusion interrupted
  - TEAE leading to dostarlimab infusion delay
- Any TEAE leading to study drug withdrawal
  - TEAE leading to niraparib withdrawal
  - TEAE leading to dostarlimab withdrawal
- Any TEAE with outcome of death
- Any treatment-related TEAE leading to death
  - Related to niraparib
  - Related to dostarlimab

Subgroup analyses of TEAEs will be conducted in the following subgroups:

- Age (<65 vs ≥65 years)
- Race (white, non-white)

The following lists the AE tables to be displayed; those designated with an '*' will be produced for the subgroups described above. Tables summarizing treatment-related adverse events will summarize adverse events related to study treatment (either niraparib or dostarlimab), related to niraparib and related to dostarlimab.

- Overview of AEs*
- TEAE by SOC and PT*
- TEAE by PT (sorted by frequency)
- Treatment-related TEAE by SOC and PT*

- Treatment-related TEAE by PT (sorted by frequency)
- TEAE by SOC, PT, and maximum grade
- Grade ≥3 TEAEs by SOC and PT*
- Grade ≥3 TEAEs by PT (sorted by frequency)
- Treatment-related Grade ≥3 TEAEs by SOC and PT*
- Treatment-related Grade ≥3 TEAEs by PT (sorted by frequency)
- Treatment-emergent SAEs by SOC and PT*
- Treatment-related treatment-emergent SAEs by SOC and PT
- TEAEs with outcome of death by SOC and PT
- Treatment-related TEAEs with outcome of death by SOC and PT
- Non-serious TEAEs by SOC and PT (required by ClinicalTrials.gov)
- TEAEs resulting in study treatment modification by SOC and PT (niraparib dose reduction; niraparib dose interruption; dostarlimab infusion interruption; dostarlimab infusion delay)
- TEAEs resulting in study treatment withdrawal by SOC and PT (withdrawal of either study treatment; niraparib; dostarlimab)*

Tables structured as listings will be provided for the following:

- Patients with treatment emergent AEs with Outcome of Death
- Patients with treatment emergent SAEs
- Patients with TEAEs leading to study treatment modification (niraparib dose reduction/interruption or dostarlimab infusion interruption or delay)
- Patients with TEAEs leading to study treatment withdrawal (niraparib and/or dostarlimab)
- Patients with treatment emergent immune-related adverse events as described in Section 9.2.2
- Patients with adverse events of Special Interest as described in Section 9.2.4

Adverse event summaries will be ordered in terms of decreasing frequency for SOC (alphabetically for SOCs with the same number of AEs reported), and decreasing frequency for PT within SOC (alphabetically for PTs with the same number of AEs reported within a SOC).

9.2.2 Immune-Related Adverse Events (irAEs)

irAEs are identified according to a pre-specified search list (Section 12.2, Appendix 3). The incidence of treatment-emergent immune related events will be summarized by Preferred Term overall and by maximum CTCAE grade. Similar summaries will be produced for irAEs related to niraparib and dostarlimab.

9.2.3 Myelosuppression Events

Myelosuppression events will be grouped for analysis. **Table 16** outlines all the grouped events with the criteria of mapping MedDRA PTs for each group using Standardized MedDRA Queries (SMQs) and/or select PTs. The list of terms corresponding to each grouped term is provided in Section 12.2, Appendix 2.

The incidence of myelosuppression events will be summarized by grouped term and Preferred Term overall and by maximum CTCAE grade. Similar summaries will be produced for myelosuppression events related to niraparib and dostarlimab.

Table 16 Myelosuppression Events

Group Term	MedDRA Criteria for Selection of Preferred Terms
Thrombocytopenia events	Haematopoietic thrombocytopenia SMQ (Broad)
Anemia events	Haematopoietic erythropenia SMQ (Broad)
Leukopenia events	Haematopoietic leukopenia SMQ (Broad)
Neutropenia events	Selected PTs related to neutropenia in the Haematopoietic leukopenia SMQ (Broad)
Pancytopenia events	Haematopoietic cytopenias SMQ (Broad)

Abbreviations: MedDRA = medical dictionary for regulatory activities; PT = preferred term; SMQ = Standardized MedDRA Query.

9.2.4 Adverse Events of Special Interest (AESI)

AESIs for this study are the following:

- MDS and AML
- Secondary cancers (new malignancies other than MDS or AML)
- Pneumonitis
- Embryo-fetal toxicity

AESIs will be identified using the AESI field on the AE eCRF. The incidence of AESIs will be summarized by Preferred Term overall and by maximum CTCAE grade. Similar summaries will be produced for AESIs related to niraparib and dostarlimab.

9.2.5 Adverse Events By Treatment Cycle

Incidence and prevalence of adverse events will be summarized by cycles of therapy for all TEAEs and TEAEs with CTCAE Toxicity Grade ≥3. The number of patients initiating study treatment (i.e., dispensed niraparib or started dostarlimab infusion) at the start of the reporting interval will be used as the denominator for incidence and prevalence calculations.

Given the planned cycle duration for Cycles 1-4 is 21 days and Cycle 5 and beyond is 42 days, Cycles 1-2 and 3-4 will be summarized together to ensure a similar duration. In addition, adverse events occurring in Cycle 10 and beyond will be grouped together as Cycle ≥10. Cycles will be defined by the earlier date that niraparib was dispensed or dostarlimab was infused.

For incidence rates by cycle, the specific AE will be assigned to the relevant time period if the start date of the AE occurs within the period. For recurrent events during a reporting interval, the first event occurrence is reported. For events that recur in more than 1 reporting interval (event start date is in different reporting intervals), the event will be reported in the first applicable reporting interval.

For prevalence rates by cycle, the specific AE will be assigned to the relevant time period if the AE occurs within the period, regardless of the interval in which the event started. Events that are present in more than 1 reporting interval will be reported in each applicable reporting interval. Events occurring multiple times within the same interval will be counted only once. Patients with ongoing AEs will be assumed to have the AE until the corresponding last known dosing interval.

9.3 Clinical Laboratory Evaluations

Laboratory assessments will be performed locally at each center's laboratory by means of their established methods.

For the purposes of summarization in both the tables and listings, all laboratory values will be converted to standardized units. If collected as a percent, differentials of white blood cell (WBC) count will be converted to absolute counts, in SI units, for summarization. Only the numeric part in laboratory values that contain non-numeric qualifiers, such as less than (<) a certain value, or greater than (>) a certain value, will be considered for analysis.

Corrected calcium is derived with the following formula:

Corrected calcium (mmol/L) = (0.02 * (40 (g/L) – albumin (g/L))) + calcium (mmol/L).

Laboratory data will be summarized both as continuous data and categorically as classified by severity grades using CTCAE v.4.03.

Continuous Summaries

Absolute values and change from baseline will be summarized by scheduled visit. In addition, the largest post-baseline increase and largest post-baseline decrease relative to baseline will be summarized (including all post-baseline scheduled and unscheduled visits through the treatment period).

The following tests will be summarized:

- Hematology: Hemoglobin, WBC count, absolute neutrophil count, eosinophils, basophils, lymphocytes, monocytes, platelets
- Chemistry: Albumin, alanine aminotransferase (ALT), amylase, aspartate aminotransferase (AST), alkaline phosphatase (ALP), sodium, urea, blood urea nitrogen, total bilirubin, corrected calcium, chloride, creatinine, glucose, magnesium, potassium, total protein
- Coagulation Factors: International normalized ratio (INR) and activated partial thromboplastin time (aPTT)
- Tumor Markers: CA-125

Analysis by CTCAE Severity Grades

NCI CTCAE v 4.03 grades will be determined for the following lab parameters:

- Hematology: hemoglobin (anemia), WBC (white blood cell decreased), lymphocytes (lymphocytes decreased), neutrophils (neutrophil count decreased), and platelets (platelet count decreased)
- Chemistry: albumin (hypoalbuminemia), ALT (alanine aminotransferase increased), AST (aspartate aminotransferase increased), ALP (alkaline phosphatase increased), amylase, total bilirubin (blood bilirubin increased), corrected calcium (hypocalcemia, hypercalcemia), creatinine (creatinine increased), glucose (hyperglycemia, hypoglycemia), magnesium (hypermagnesemia, hypomagnesemia), potassium (hyperkalemia, hypokalemia), and sodium (hyponatremia, hypernatremia)

  As fasting glucose is not a requirement of the study protocol, hyperglycemia will only be coded to grades ≥ 3

The derivation of CTCAE grades will consider only numeric results; clinical assessments will not be considered (Section 12.2, Appendix 1). Laboratory measurements that are within their institutional limits of normal and are not graded as 1-4, per the CTCAE, will be summarized as "Grade 0," which is defined as normal. Additionally, if a lab parameter is graded in both directions (e.g. glucose: hyperglycemia and hypoglycemia), then low direction toxicity grades at baseline and post baseline will be set to 0 when the variables are derived for summarizing high direction toxicity, and vice versa.

A shift summary of baseline to maximum severity on-study treatment (including all post-baseline scheduled and unscheduled visits through the treatment period) will be produced for the coded hematology and chemistry laboratory parameters above. Missing values for baseline and on-study treatment will be displayed; percentages for each parameter will be based on the total number of patients in the safety population.

Liver function tests

Summary of liver function tests will include the following categories to assess possible drug induced liver toxicity. The number and percentage of patients with each of the following (including all post-baseline scheduled and unscheduled visits through the treatment period) will be summarized:

- ALT ≥ 3×ULN, ALT ≥ 5×ULN, ALT ≥ 10×ULN, ALT ≥ 20×ULN
- AST ≥ 3×ULN, AST ≥ 5xULN, AST ≥ 10×ULN, AST ≥ 20×ULN
- (ALT or AST) ≥ 3×ULN, (ALT or AST) ≥ 5×ULN, (ALT or AST) ≥ 10×ULN, (ALT or AST) ≥ 20×ULN
- Total bilirubin ≥ 2×ULN
- Concurrent ALT ≥ 3×ULN and total bilirubin ≥ 2×ULN
- Concurrent AST ≥ 3×ULN and total bilirubin ≥ 2×ULN
- Concurrent (ALT or AST) ≥ 3×ULN and total bilirubin ≥ 2×ULN
- Concurrent (ALT or AST) ≥ 3×ULN and total bilirubin ≥ 2×ULN and ALP ≥ 2×ULN
- Potential Hy's law: Concurrent (ALT or AST) ≥ 3×ULN and total bilirubin ≥ 2×ULN and ALP < 2×ULN or missing

Concurrent measurements are those occurring on the same date.

Categories will be cumulative, i.e., a patient with an elevation of AST ≥ 10×ULN will also appear in the categories ≥ 5×ULN and ≥ 3×ULN. Liver function elevation and possible Hy's Law cases will be summarized using frequency and percentage.

Listings

A by-patient listing of all laboratory data with laboratory reference ranges, abnormal values highlighted, and CTCAE toxicity grading, when available, will be provided for each panel of laboratory data (hematology, serum chemistry, urinalysis, coagulation factors, thyroid panel, CA-125). Screening serology and virology results and urine/serum pregnancy tests will also be listed.

Separate listings will be created for abnormal laboratory values and laboratory values with CTCAE grade ≥3.

9.4 Vital Signs

Summaries of vital signs parameters (systolic and diastolic blood pressures, heart rate, and temperature) and weight will be presented. Observed and change from baseline will also be summarized and analyzed by scheduled visit. In addition, the largest post-baseline increase and largest post-baseline decrease relative to baseline will be summarized during the on-study treatment period (including all post-baseline scheduled and unscheduled visits through the treatment period).

Vital sign measurements will be presented for each patient in a data listing.

9.5 Electrocardiogram

All patients will undergo a single ECG assessment at the screening visit to verify eligibility into the study. Clinically significant findings will be reported on the Medical History eCRF and presented per Section 7.6.

9.6 Physical Examinations and Other Safety Parameters

All new clinically significant abnormal findings or clinically significant worsening of the existing conditions in physical examinations will be reported on the AE eCRF and presented per Section 9.2.

The ECOG shift from baseline to highest score during the on-study treatment period (including all post-baseline scheduled and unscheduled visits through the treatment period) will be summarized.

All ECOG assessments will be presented for each patient in a data listing.

9.7 COVID-19

A summary of the number and percentage of participants for the following assessments will be produced: Case Diagnosis, COVID-19 Test performed, and Results of the COVID-19 test. Additional summaries may be produced, as appropriate.

10 Computing Environment

All statistical analyses will be performed using SAS statistical software v9.4 or later, unless otherwise noted. Programming will be performed by PRA Health Sciences. Quality control procedures will be documented separately in the study-specific quality control plan.

11 References

Beaumont, J., Yount, S., Lalla, D., Lubeck, D., Derynck, M., & al., e. (2007). Validation of the Functional Assessment of Cancer Therapy - Ovarian (FACT-O) Symptom Index (FOSI) in a Phase II Clinical Trial of Pertuzumab in Patients with Advanced Ovarian Cancer. *Journal of Clinical Oncology, 25*, 16021-16021.

Brookmeyer, R., & Crowley, J. (1982). A confidence interval for the median survival time. *Biometrics, 38*, 29-41.

Clopper, C., & Pearson, E. (1934). The use of confidence or fiducial limits illustrated in the case of the binomial. *Biometricka, 26*, 404-413.

DOXIL®. (1995). *doxorubicin hydrochloride liposome injection) for intravenous use [prescribing information]*. Bedford, OH: ALZA Corporation.

Eisenhauer, E., Therasse, P., Bogaerts, J., Schwartz, D., Sargent, D., & Ford, R. (2009). New response evaluation criteria in solid tumours; revised RECIST guidline (version 1.1). *European Journal of Cancer, 45*(2), 228-247.

Gordon, A., JT, F., Guthrie, D., Parkin, D., Gore, M., & Lacave, A. (2001). Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. *Journal of Clinical Oncology, 14*, 3312-3322.

Gynecologic Oncology Group, Markman, M., Blessing, J., Rubin, S., Connor, J. H., & Waggoner, S. (2006). Phase II trial of weekly paclitaxel (80 mg/m2) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers; a Gynecologic Oncology Group study. *Gynecol Oncol, 101*(3), 436-440.

Huang, X., Sun, Y., Trow, P., Chatterjee, S., Chakravartty, A., Tian, L., & Devanarayan, V. (2017). Patient subgroup identification for clinical drug development. *Statistics in Medicine*, 1414-28.

Kalbfleisch, J., & Prentice, R. (1980). *The Statistical Analysis of Failure Time Data.* New York: John Wiley & Sons.

McKeegan, E., Ansell, P., Davis, G., Chan, S., Chandran, R., Gawel, S., . . . Devanarayan, V. (2015). Plasma biomarker signature associated with improved survival in advanced non-small cell lung cancer patients on linifanib. *Lung Cancer, 90(2)*, 296-301.

Mutch, D., Orlando, M., Goss, T., Teneriello, M., Gordon, A., & McMeekan, S. (2007). Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. *Journal of Clinical Oncology, 25*(19), 2811-2818.

Pignata, S., Lorusso, D., Scambia, G., Sambataro, D., Tamberi, S., & Cinieri, S. (2015). Pazopanib plus weekly paclitaxel versus weekly paclitaxel alone for platinum-resistant or platinum-refractory advanced ovarian cancer (MITO 11): a randomized open-label, phase 2 trial. *Lancet Oncology, 16*(5), 561-568.

Schemper, M., & Smith, T. (1996). A Note on Quantifying Follow-up in Studies of Failure Time. *Controlled Clinical Trials, 17*, 343-346.

12 APPENDIX

12.1 APPENDIX 1: Common Terminology Criteria for Adverse Events (CTCAE) v4.03

Lab Test Name	Lab Test Code	Standard Unit	CTCAE v4.03 SOC	CTCAE v4.03 Term	Grade 1	Grade 2	Grade 3	Grade 4
HEMATOLOGY								
Hemoglobin	HGB	g/L	Blood and lymphatic system disorders	Anemia	<LLN - 100 g/L	<100 - 80g/L	<80 g/L	
Leukocytes	WBC	10^9/L	Investigations	White blood cell decreased	<LLN - 3.0 × 10^9/L	<3.0 - 2.0 × 10^9/L	<2.0 - 1.0 × 10^9 /L	<1.0 × 10^9/L
Lymphocytes	LYM	10^9/L	Investigations	Lymphocyte count decreased	<LLN - 0.8 x10^9 /L	<0.8 - 0.5 × 10^9 /L	<0.5 - 0.2 × 10^9 /L	<0.2 × 10^9 /L
Neutrophils	NEUT	10^9/L	Investigations	Neutrophil count decreased	<LLN - 1.5 × 10^9/L	<1.5 - 1.0 × 10^9/L	<1.0 - 0.5 × 10^9/L	<0.5 × 10^9/L
Platelets	PLAT	10^9/L	Investigations	Platelet count decreased	<LLN - 75.0 × 10^9/L	<75.0 - 50.0 × 10^9/L	<50.0 - 25.0 × 10^9/L	<25.0 × 10^9/L
CHEMISTRY								
Albumin	ALB	g/L	Metabolism and nutrition disorders	Hypoalbuminemia	<LLN - 30 g/L	<30 - 20 g/L	<20 g/L	
Alanine Aminotransferase	ALT	U/L	Investigations	Alanine aminotransferase increased	>ULN - 3.0 × ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 × ULN
Amylase	AMYLASE	U/L	Investigations	Serum amylase increased	>ULN- 1.5 x ULN	>1.5-2.0 x ULN	>2.0 – 5.0 x ULN	>5.0 x ULN
Aspartate Aminotransferase	AST	U/L	Investigations	Aspartate aminotransferase increased	>ULN - 3.0 × ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 × ULN
Alkaline phosphatase	ALP	U/L	Investigations	Alkaline phosphatase increased	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Bilirubin	BILI	umol/L	Investigations	Blood bilirubin increased	>ULN - 1.5 × ULN	>1.5 - 3.0 × ULN	>3.0 - 10.0 × ULN	>10.0 × ULN
Calcium (corrected)	CA	mmol/L	Metabolism and nutrition disorders	Hypocalcemia	<LLN - 2.0 mmol/L	<2.0 - 1.75 mmol/L	<1.75 - 1.5 mmol/L	<1.5 mmol/L

Calcium (corrected)	CA	mmol/L	Metabolism and nutrition disorders	Hypercalcemia	>ULN - 2.9 mmol/L	>2.9 - 3.1 mmol/L	>3.1 - 3.4 mmol/L	>3.4 mmol/L
Creatinine	CREAT	umol/L	Investigations	Creatinine increased	>ULN - 1.5 × ULN	>1.5 - 3.0 × ULN	>3.0 - 6.0 × ULN	>6.0 × ULN
Glucose	GLUC	mmol/L	Metabolism and nutrition disorders	Hypoglycemia	<LLN - 3.0 mmol/L	<3.0 - 2.2 mmol/L	<2.2 - 1.7 mmol/L	<1.7 mmol/L
Glucose	GLUC	mmol/L	Metabolism and nutrition disorders	Hyperglycemia	NA	NA	>13.9 - 27.8 mmol/L	>27.8 mmol/L
Magnesium	MG	mmol/L	Metabolism and nutrition disorders	Hypomagnesemia	<LLN - 0.5 mmol/	<0.5 - 0.4 mmol/L	<0.4 - 0.3 mmol/L	<0.3 mmol/L
Magnesium	MG	mmol/L	Metabolism and nutrition disorders	Hypermagnesemia	>ULN - 1.23 mmol/L		>1.23 - 3.30 mmol/L	>3.30 mmol/L
Potassium	K	mmol/L	Metabolism and nutrition disorders	Hypokalemia	<LLN - 3.0 mmol/L		<3.0 - 2.5 mmol/L	<2.5 mmol/L
Potassium	K	mmol/L	Metabolism and nutrition disorders	Hyperkalemia	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L
Sodium	SODIUM	mmol/L	Metabolism and nutrition disorders	Hyponatremia	<LLN - 130 mmol/L		<130 - 120 mmol/L	<120 mmol/L
Sodium	SODIUM	mmol/L	Metabolism and nutrition disorders	Hypernatremia	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L	>160 mmol/L

12.2 APPENDIX 2: Myelosuppression Events

The list of MedDRA PTs is provided in a separate document.

12.3 APPENDIX 3: Immune-Related Adverse Events (irAEs)

The list of MedDRA PTs is provided in a separate document.

12.4 **APPENDIX 4: Statistical Output Shells**

The list of statistical output and corresponding table/figure/listing shells are provided in a separate document.