



STATISTICAL ANALYSIS PLAN (SAP)
STUDY CORT125134-556

Title	A Phase 3 Study of Relacorilant in Combination with Nab-Paclitaxel versus Nab-Paclitaxel Monotherapy in Advanced, Platinum-Resistant, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian-Tube Cancer (ROSELLA)
Study Protocol	CORT125134-556
Phase	3
Investigational Product	Relacorilant (CORT125134)
Indication	Ovarian Cancer
Protocol Version	Amendment 4
Protocol Version (date)	15 February 2025
Sponsor	Corcept Therapeutics Incorporated
IND Number	[128631]
EudraCT Number	[2022-000662-18]
EU CT Number	[2024-514080-25-00]
Document Author	████████████████████ ██████████████████ ████████████████████████ ██████████████████████████
SAP Version / Date	V1.0 / 18 February 2025

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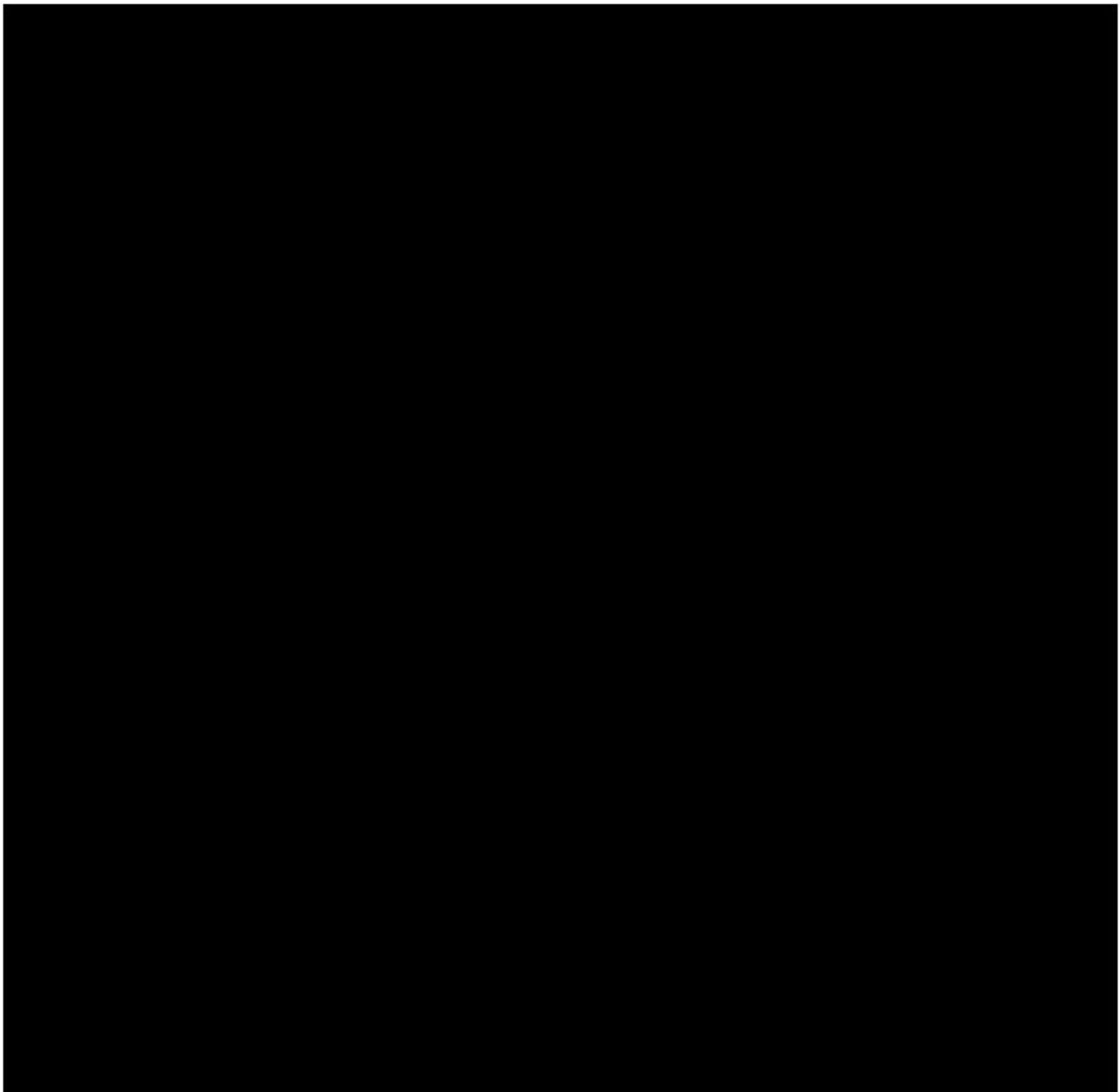


APPROVAL SHEET

STATISTICAL ANALYSIS PLAN

CORT125134-556: A Phase 3 Study of Relacorilant in Combination with Nab-Paclitaxel versus Nab-Paclitaxel Monotherapy in Advanced, Platinum-Resistant, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian-Tube Cancer (ROSELLA)

Reviewed and Accepted at Corcept Therapeutics by



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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
ATC	Anatomical therapeutic chemical
BICR	Blinded Independent Central Review
BoR	Best overall response
CA-125	Cancer antigen 125
CBR	Clinical-Benefit Rate
CEA	Carcinoembryonic antigen
CI	Confidence interval
CR	Complete response
CT	Computed tomography
DoR	Duration of response
EAIR	Exposure adjusted incidence rate
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EDC	Electronic data capture
EORTC	European Organization for Research and Treatment of Cancer
EOT	End of Treatment
EQ-5D-5L/VASc	EuroQoL 5 Dimensions, 5 Levels
GCIG	Gynecologic Cancer Intergroup
G-CSF	Granulocyte colony-stimulating factor
GI	Gastrointestinal
GR	Glucocorticoid receptor
HR	hazard ratio
ICF	informed-consent form
ICH	International Council for Harmonisation
IDMC	Independent Data Monitoring Committee
ITT	Intent-to-treat
IXRS	Interactive voice and web-response system
LLOQ	Lower limit of quantification
LS	Least squares



MedDRA	Medical dictionary for regulatory affairs
MRI	Magnetic resonance imaging
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
ORR	Objective response rate
OS	Overall survival
PD	Pharmacodynamic(s)
PD	Disease progression (progressive disease per RECIST v1.1)
PFS	Progression-free survival
PK	Pharmacokinetic(s)
PKA	Pharmacokinetics analysis population
PRO	Patient-reported outcomes
PR	Partial response
PT	Preferred term
QoL	Quality of life
RECIST	Response evaluation criteria in solid tumors
SAE	Serious adverse event
SAF	Safety analysis population
SAP	Statistical analysis plan
SD	Stable disease (clinical)
SD	Standard Deviation (statistical)
SI	Standard international
SOC	System organ class
TEAE	Treatment-emergent adverse event
ULOQ	Upper limit of qualification
WHODD	World health organization drug dictionary

1 INTRODUCTION

This statistical analysis plan (SAP) contains definitions of analysis populations and endpoints, outlines the timing of statistical analyses, and provides a comprehensive description of statistical analyses to be implemented to assess the clinical efficacy and safety of protocol CORT125134-556, Amendment 4, dated 15 February 2025. A Phase 3 Study of Relacorilant in Combination with Nab-Paclitaxel versus Nab-Paclitaxel Monotherapy in Advanced, Platinum-Resistant, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian-Tube Cancer (ROSELLA).

2 STUDY OVERVIEW

This is a Phase 3, randomized, two-arm, open-label study to evaluate efficacy, safety, pharmacokinetics (PK), pharmacodynamics (PD), patient-reported outcomes (PRO) and quality of life (QoL) of intermittent dosing of relacorilant in combination with nab-paclitaxel (Arm A) versus nab-paclitaxel monotherapy (Arm B).

The study population is women with recurrent platinum-resistant high-grade epithelial, non-mucinous and non-clear cell ovarian, primary peritoneal, or fallopian-tube cancer following at least one treatment, but less than 4 lines of therapy with the following specific histological subtypes:

- High-grade (Grade 3) serous epithelial ovarian, primary peritoneal, or fallopian-tube carcinoma.
 - High-grade (Grade 3) endometrioid epithelial carcinoma.
 - Carcinosarcoma with a $\geq 30\%$ endometrioid epithelial tumor component.

Screening procedures will be performed within the 28 days prior to the first dose of study treatment.

The eligible patients will be randomized in a 1:1 ratio to one of the 2 treatment arms described below. Randomization will be stratified by the following stratification factors: region (North America versus Europe versus the rest of the world) and line of therapy (1 versus more than 1).

- Arm A (experimental arm): Patients will receive relacorilant 150 mg, administered orally, once daily for three consecutive days on the day before (excluding Cycle 1 Day -1), the day of, and the day after nab-paclitaxel infusion, in combination with nab-paclitaxel (80 mg/m² IV) administered on Day 1, 8, and 15 of each 28-day cycle. Relacorilant will not be administered on Cycle 1 Day -1.
- Arm B (comparator; nab-paclitaxel arm): Patients will receive nab-paclitaxel (100 mg/m² IV) administered on Day 1, 8, and 15 of each 28-day cycle.

Study treatment will start on Cycle 1, Day 1 in both treatment arms.

Tumor assessments will be conducted using computerized tomography (CT) with contrast or magnetic resonance imaging (MRI) scans of the chest, abdomen, and pelvis. A baseline tumor scan (prior to initiating therapy) is required within 45 days prior to the first dose of study

treatment and then every 8 weeks (± 7 days) from Cycle 1, Day 1 for the first 40 weeks of the study followed by every 12 weeks (± 7 days) for all patients in Arms A and B until unequivocal progressive disease (PD) by RECIST v1.1 is documented, including in patients who prematurely discontinue therapy. Tumor response will be assessed by Blinded Independent Central Review (BICR) and the investigator (or local radiologist) using RECIST v1.1.

CA-125 will be assessed within 14 days prior to the first dose of study treatment and then every 8 weeks from Cycle 1 Day 1 until progression. Once the best CA-125 response is determined, after 28 days a confirmatory CA-125 is required of the best CA-125 response.

A combined response endpoint based on both RECIST v1.1 and GCIG criteria will also be reported. Tumor response will be assessed by the Investigator or local radiologist using RECIST v1.1. CA-125 response and the combined response will be derived based on CA-125 results.

At the End-of-Treatment Visit, a final radiographic tumor assessment will be done if ≥ 4 weeks have elapsed since the last radiographic tumor assessment, unless there is documented PD. The same method of assessment and the same technique should be used at Baseline and throughout the study. Radiographic scans will be quality checked, anonymized, submitted, read, and stored centrally.

For patients with PD, or for patients who decline further radiographic tumor assessments, survival and subsequent treatment information will be collected every 3 months (± 7 days) after the last dose of study treatment (long-term follow up). Long-term follow-up (survival assessments) will continue until the end point of death, the patient is lost to follow-up, or other study exit criteria are met (see Protocol Section 4.5.2).

To ensure comparability, the Baseline radiographs/scan, and subsequent radiographs/scans to assess response, should be performed using consistent methods and identical techniques, and assessed by the same individual on each occasion when possible.

Safety, PK (only Arm A), PRO, QoL and pharmacodynamic/biomarker profiles will also be assessed in the two dosing regimen arms.

Patients who discontinue treatment at any time (See Protocol Section 4.5.1) will continue to be followed for study endpoints (see Protocol Section 7.12) after the last dose of study treatment until the endpoint of death, the patient is lost to follow-up, or until other study exit criteria are met (see Protocol Section 4.5.2).

This SAP will be developed and approved prior to database lock and data analysis. Any deviations from the SAP will be documented as such in the clinical study report.

The analysis of PFS, one of the two dual primary endpoints, will be conducted when at least 230 PFS events by BICR have been observed. An interim analysis of the dual primary endpoint of overall survival (OS) will be performed at the time of primary analysis of PFS. The formal analysis of OS will be conducted when approximately 292 deaths have been observed and will be performed using the ITT population.

An Independent Data Monitoring Committee (IDMC) will be established to conduct periodic reviews of data to ensure the safety of patients. The committee will operate independently from the Sponsor and the Investigators as described in the IDMC charter.

3 STUDY OBJECTIVES

For all efficacy objectives and corresponding endpoints listed below, assessment for response and disease progression are according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by BICR, unless otherwise noted.

3.1 Primary Objective

To evaluate PFS by BICR and OS in patients treated with an intermittent regimen of relacorilant in combination with nab-paclitaxel compared with patients treated with nab-paclitaxel monotherapy.

3.2 Secondary Objectives

3.2.1 Secondary Efficacy Objectives

The secondary efficacy objectives are to evaluate patients treated with the intermittent regimen of relacorilant in combination with nab-paclitaxel compared with nab-paclitaxel monotherapy:

- To evaluate PFS as assessed by the Investigator (or local radiologist)
- To evaluate objective response rate (ORR)
- To evaluate best overall response (BoR)
- To evaluate duration of response (DoR)
- To evaluate clinical benefit rate (CBR) at 24 weeks
- To evaluate response according to cancer antigen 125 (CA-125) using Gynecologic Cancer Intergroup (GCIG) criteria. A combined-response endpoint based on RECIST v1.1 and GCIG criteria will also be reported.

3.2.2 Safety Objective

- To assess the safety of relacorilant treatment in combination with nab-paclitaxel compared with nab-paclitaxel monotherapy.

3.3 Exploratory

3.3.1 Pharmacodynamics / Biomarkers

- To assess the relationship between baseline and pharmacodynamic markers (e.g., glucocorticoid receptor [GR] and expression of other genes) and the patient's response to relacorilant in combination with nab-paclitaxel.
- To assess pharmacodynamic effects of the intermittent regimen of relacorilant in combination with nab-paclitaxel.
- To explore mechanisms of resistance to relacorilant in combination with nab-paclitaxel.

3.3.2 Patient-Reported Outcomes and Quality of Life

- To describe changes from baseline of Patient-Reported Outcomes (PRO) and Quality of Life (QoL) scores in the study population and to describe differences between treatment arms.

3.3.3 Pharmacokinetic Objective

- To assess the PK of relacorilant and estimate its plasma exposures using population PK models.

4 STUDY ENDPOINTS

4.1 Primary Endpoints

The dual primary efficacy study endpoints include the following:

- PFS: Time from randomization until first documented progressive disease (PD) by RECIST v1.1 per BICR, or death due to any cause, whichever occurs first.
- OS: Time from randomization to death by any cause.

4.2 Secondary Endpoints

4.2.1 Efficacy

- PFS (Investigators): Time from randomization until PD or death whichever occurred first as assessed by Investigator using RECIST v1.1.
- ORR: Proportion of patients with measurable disease at Baseline who attain complete response (CR) or partial response (PR) by RECIST v1.1 as assessed by BICR and as assessed by Investigator.
- BoR: The best response recorded from the date of randomization until PD/recurrence (or death) as assessed by BICR and as assessed by Investigator.
- DoR: Time from the first objective response (CR or PR) to first objectively documented PD or death (whichever occurs first) as assessed by BICR and as assessed by Investigator.
- CBR at 24 weeks: proportion of patients who attain CR, PR, or stable disease (SD) for 24 weeks as per RECIST v1.1 as assessed by BICR and as assessed by Investigator.
- CA-125 response will be assessed per GCIG criteria (Rustin et al. 2011) defined as $\geq 50\%$ reduction in CA-125 from a pre-treatment sample and maintained for ≥ 28 days in patients with a pretreatment sample that is at least twice the upper limit of the reference range (within 2 weeks before starting the treatment). In addition, patients who have a CA-125 response and whose CA-125 level falls to within the reference range will be classified as CA-125 complete responders.
- Combined response according to RECIST v1.1 + GCIG criteria. Responses will be reported separately and combined for RECIST v1.1 by Investigator and CA-125/GCIG

criteria.

4.2.2 Safety

The safety of each treatment group will be assessed by evaluating:

- Incidence of adverse events (AEs), serious AEs (SAEs), treatment-related AEs, AEs by severity, and deaths due to AEs, all deaths, and changes in laboratory determinations, and vital sign parameters
- Discontinuations of treatment and study withdrawal due to AEs

4.3 Exploratory Endpoints

4.3.1 Pharmacokinetic Endpoint

- Sparse PK sampling for relacorilant population PK.

4.3.2 Pharmacodynamics

Baseline assessment of:

- Tumor GR expression.
- Expression of GR-regulated genes in whole blood.
- Salivary cortisol.

Change from Baseline of:

- Expression of GR-regulated genes in whole blood

4.3.3 Exploratory Pharmacodynamics/Biomarker Assessments

Descriptive statistics will be presented for all the biomarker endpoints. Additional exploratory biomarker analyses of these and other assessments may be conducted and described in a separate Biomarker SAP.

4.3.4 Patient-Reported Outcomes

Changes from baseline of PRO and QoL assessments scores using European Organization for Research and Treatment of Cancer (EORTC) ovarian cancer specific quality of life questionnaire (QLQ-OV28), European Organization for Research and Treatment of Cancer (EORTC QLQC30) questionnaires, and the EuroQol-5 Dimension 5-level (EQ-5D-5L) questionnaires. A higher score represents a better quality of life.

The primary patient-reported outcome will be the number of patients achieving at least 15-point absolute improvement at Week 8 or Week 9 in the abdominal/gastrointestinal (GI) scale of the QLQ-OV28 questionnaire. A higher score represents a better quality of life.

5 SAMPLE-SIZE CONSIDERATIONS

To estimate the total sample size and the number of events needed in this study, estimates of median PFS were considered from previous studies for the treatment of recurrent or persistent platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer.

In the Phase 2 study CORT125134-552, the observed median PFS was 3.8 months with nab-paclitaxel alone (95% CI: 3.5–5.4) versus 5.6 months with relacorilant plus nab-paclitaxel (95% CI: 3.7–7.2). The observed results are the basis for the assumptions for study CORT125134-556.

For PFS, based on 1:1 randomization allocation ratio, a total of 230 events ensures the study has 86.4% power for a 2-sided log-rank test with a $\alpha=0.04$ level of significance, to detect a 50% increase in PFS (hazard ratio [HR]=0.66). Assuming an exponential distribution of PFS, this corresponds to an increase in median PFS from 3.8 months to 5.8 months, which is greater than the scheduled RECIST scan interval of 8 weeks.

Up to 360 patients will be randomized (1:1) and followed until the required number of events are observed. This sample size allows for a 10% dropout rate in the first 12 months of follow-up.

For OS, approximately 292 events will provide the study with 80% power for a 2-sided log-rank test with an overall 0.01 level of significance to detect a 50% increase in OS (HR=0.67).

Assuming an exponential distribution of OS, this corresponds to an increase in median OS from 13 months to 19.4 months.

6 ANALYSIS POPULATIONS

6.1 Screened population

All patients who signed the informed consent form (ICF).

6.2 Intent-To-Treat Population

Intent-to-Treat Population (ITT) will include all randomized patients, analyzed according to the randomized treatment arm. This population will be used for analysis of the primary endpoints of PFS and OS as well as all secondary efficacy endpoints.

6.3 Safety Analysis Population

Safety Analysis Population (SAF) will include all randomized patients who receive at least one dose of study treatment, analyzed according to the treatment actually received. This population will be used for all safety endpoints.

6.4 Pharmacokinetic Analysis Population

Pharmacokinetics Analysis Population (PKA) will be all patients in the SAF who have PK data collected and available for analysis. Summary tables for PK parameters will be based on this set of patients.

7 DEFINITIONS, COMPUTATIONS AND CONVENTIONS

The statistical principles applied in the design and planned analyses of this study are consistent with International Council for Harmonisation (ICH) E9 guidelines (ICH 1998) and Guidance for Industry Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (2007). All statistical analyses detailed in this SAP will be conducted using SAS version 9.4 or higher.

7.1 Definitions

Study day for efficacy: Study day for efficacy will be calculated in reference to the date of randomization (study day 1). For assessments conducted on or after the randomization date, study day is calculated as (assessment date – randomization date + 1). For assessments conducted before the randomization date, study day is calculated as (assessment date – randomization date). There is no study day 0.

Study day for safety: Study day for safety will be calculated in reference to the date of the first dose of study drug. For assessments conducted on or after the date of the first dose of study drug, study day will be calculated as (assessment date – date of first dose of study drug + 1). For assessments conducted before the date of the first dose of study drug, study day is calculated as (assessment date – date of first dose of study drug). There is no study day 0.

Treatment-emergent period: The treatment-emergent period is defined as the period of time from the date and time of the first dose of either study treatment through 30 days after the last dose of either study treatment or the initiation of a new anticancer therapy (whichever occurs first). The treatment-emergent period will be used in the summaries of treatment-emergent adverse events (TEAEs).

Baseline and postbaseline value: Unless otherwise specified, a baseline value will be defined as the most recent value prior to the first dose of study treatment (relacorilant or nab-paclitaxel, whichever occurs first) including PRO, QoL and baseline characteristics. In addition, pre-treatment C1D1 values could serve as baseline. A postbaseline value is defined as an assessment obtained after the first dose of study drug.

Baseline values for tumor assessment and CA-125 marker will be collected within 14 days of start of study treatment.

Baseline and postbaseline value for safety analyses: Unless otherwise specified, a baseline value for safety analyses is defined as the last value before the date/time of first dose of study drug for laboratory tests, vital sign assessments, and electrocardiogram (ECG) data. A postbaseline value for safety analyses is defined as a measurement taken after the date/time of the first dose of study drug. If multiple values are present for the same visit and collected on different dates, the first value will be used in the summaries by visit. If multiple values are present for the same date, the average of these values will be used in the summaries by visit, and the worst toxicity grade will be used in the summaries of toxicity grade by laboratory tests.

Last dose date: Date of the last nonzero dose from the drug administration electronic case report

form (eCRF).

7.2 Reporting Conventions

Unless otherwise specified, the following conventions will be applied to all analyses:

- Mean and median values will be formatted to 1 more decimal place than the measured value. Standard deviation values will be formatted to 2 more decimal places than the measured value; minimum and maximum values will be presented to the same number of decimal places as the measured value.
- Percentages will be rounded to 1 decimal place. Number and percentage values will be presented as xx (xx.x%).
- Listings will be sorted for presentation in order of treatment group, patient identifier (ID), and date of procedure or event.
- Analysis and summary tables will have the analysis population sample size (i.e., number of patients).
- Laboratory data will be reported using standard international (SI) units; as local laboratories are used for this study, conversion factors from conventional units will be listed in the clinical study report.
- 1 inch = 2.54 cm.
- Time-to-event or duration of event endpoints will be based on the actual date the radiograph was obtained rather than the associated visit date.
- Hazard ratios and odds ratios will be rounded to 2 decimal places.
- For by-visit observed data analyses, percentages will be calculated based on the number of patients with nonmissing data as the denominator unless otherwise specified.
- For time-to-event right-censored data, the summary statistics and descriptions will include Kaplan-Meier plots and/or life tables.
- For other continuous endpoints, the summary statistics will include mean, standard deviation, median, and range (minimum and maximum).
- For categorical endpoints, the summary statistics will include frequency counts and percentages.
- Confidence intervals (CIs), when presented, will generally be constructed at the 95% level. For binomial variables, exact methods will be employed unless otherwise specified.
- P-values will be rounded to 4 decimal places. P-values that round to 0.0000 will be presented as '<0.0001' and p-values that round to 1.000 will be presented as '>0.9999'.
- Medical history and adverse events will be coded using the Medical Dictionary for

Regulatory Activities (MedDRA version 27.0 or higher)

- Adverse event severity will be evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE v.5.0).
- Prior therapies and concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Global B3 March 2024 coding dictionary and summarized by Anatomical Therapeutic Chemical (ATC) therapeutic subgroup and preferred drug names.

7.3 Conventions for Dates

Conventions for calculations with dates are as follows:

- Dates will be stored as numeric variables in the SAS analysis files and reported in DDMMYY format (i.e., the Date9. datetime format in SAS).
- Dates recorded in comment fields will not be imputed or reported in any specific format.
- Intervals that are presented in weeks will be transformed from days to weeks by using the following conversion formula, and rounding to 1 decimal place:
 - $\text{WEEKS} = \text{DAYS} / 7$
- Intervals that are presented in months will be transformed from days to months by using the following conversion formula, and rounding to 1 decimal place:
 - $\text{MONTHS} = \text{DAYS} / 30.4375$

Detailed rules for imputation of missing/partially missing dates for adverse events, prior/concomitant medications/procedures, and primary cancer diagnosis are provided in [Section 12.1](#).

7.4 Treatment Group Presentation

Patient disposition, protocol deviations, demographics and baseline characteristics, medical history, prior medications and procedures, and efficacy data summaries will be presented by randomized treatment group. Unless otherwise specified, safety data summaries will be presented by the actual treatment received.

7.5 Handling of Missing Data

Unless stated otherwise in sections below, missing data will not be replaced with imputed values.

Missing dates or partially missing dates will be imputed conservatively for adverse events and prior/concomitant medications/procedures. Specific rules for handling of missing or partially missing dates for date of birth, adverse events, prior/concomitant medications/procedures, and diagnosis of ovarian cancer are provided in [Appendix 12.1](#).

7.6 Visit Windows

Visit windows are defined in Appendix [12.2](#).

8 TIMING OF ANALYSES

8.1 Primary Analyses

The analysis of PFS, will be conducted when at least 230 PFS events by BICR have been observed. An interim analysis of OS will be conducted at the time of the primary analysis of PFS. The formal analysis of OS will be conducted when approximately 292 deaths have been observed and will be performed using the ITT population.

9 STATISTICAL METHODS

9.1 Patient Disposition

Patient populations will be summarized by treatment group and overall, for all patients randomized and will include the number and percentage of patients in the ITT, safety, and PKA populations.

The number of patients screened will be provided based on the IRT data source, as well as the number and percentage of screened patients who were subsequently randomized.

Disposition summaries will present the number of patients who discontinued treatment based on the End of Treatment CRF. Primary reason for discontinuation of relacorilant and nab-paclitaxel, including any of the following, will be summarized:

- Adverse Event
- Clinical Progression
- Death
- Investigator Decision
- Lost to Follow-up
- Patient Decision
- Progressive Disease
- Protocol Deviation
- Site Terminated by Sponsor
- Study Terminated by Sponsor
- Withdrawal of Consent
- Other

Counts and percentages of patients who discontinue the study based on the End of Study CRF will be summarized:

- Adverse events
- Clinical Progression
- Death
- Lost to Follow-up
- Progressive Disease
- Protocol Deviation

- Site Terminated by Sponsor
- Study Terminated by Sponsor
- Withdrawal of consent
- Other

Counts and percentages of patients who discontinued treatment completed 30 days and long-term follow-up will also be summarized.

9.2 Protocol Deviations

Protocol deviations will be categorized as important or other according to the protocol deviation specification document. Important protocol deviations that occur during the study will be summarized by deviation category for all patients in the ITT population by treatment group as randomized. A by-patient listing of all deviations will be provided.

Patient eligibility (all inclusion and exclusion criteria met) at randomization will be listed for all patients in the ITT population.

9.3 Demographic Characteristics

The following patient characteristics collected for the ITT Population will be presented in data listings and summarized by treatment regimen and overall:

- Age at informed consent (continuous and categorical variable: <50, ≥50 to <65, ≥65) will be summarized.
- Sex
- Of childbearing potential (Yes/No)
- Ethnicity
- Race
- Height
- Baseline Weight
- Geographic region: North America (United States and Canada), Europe, rest of the world (South Korea, Brazil, Argentina, Australia)
- Lines of therapy: 1 line of therapy vs more than 1 line of therapy as reported in IRT and in EDC

9.4 Disease Characteristics and Previous Therapies

All medical history verbatim terms will be coded using the MedDRA version 27.0 or higher and ordered by system organ class (SOC) and preferred term (PT). At each level of summation (SOC, PT), patients reporting more than one medical condition will be counted only once.

Study-Specific Disease History: For each patient, date and stage of initial diagnosis, primary site of disease (ovarian, fallopian tube, or primary peritoneal), histologic features, and current extent and location of disease will be listed. A summary table will summarize these disease history characteristics by treatment arm and overall.

Prior Procedures/Surgeries for Disease Under Study: All previous procedures or surgeries will be

listed by date of procedure. By treatment arm and overall, number of patients reporting at least one prior procedure/surgery will be summarized. Additional characteristics summarized will include whether primary debulking, or interval debulking surgery with neoadjuvant therapy were performed, outcomes, as well as any debulking surgeries performed for recurrent disease.

Prior Anticancer Therapy for Disease Under Study: All prior anticancer therapies received, and whether ongoing, will be listed by date of first dose. A summary table will be provided by treatment arm and overall for the number of lines of prior anticancer therapy, number of patients reporting at least one prior anticancer therapy, number of patients with platinum resistant disease, previous treatment-free, platinum-free, and taxane-free intervals, received a taxane therapy as the last line before study entry, number of lines in platinum resistant setting, prior exposure at any time to common approved treatments, and for the last therapy: the therapy type, best response achieved, and reason for discontinuation of therapy (toxicity, disease progression, or other) and related information.

Prior Radiotherapy for Disease Under Study: A listing will display all entries for prior radiotherapies received by date of first dose. Patients who received at least one prior radiotherapy for disease under study, its site, administrative setting, and months from first dose of radiotherapy until randomization will be summarized by treatment arm and overall.

9.5 Medical History

Medical History: As noted on the eCRF, a complete medical history, including any clinically significant medical conditions, will be collected during Screening, and presented in a listing and summary table. Verbatim terms will be coded using the MedDRA version 27.0 or higher and ordered by SOC and PT. At each level of summation (SOC, PT), patients reporting more than one medical condition will be counted only once.

Prior Cancer Panel/Molecular Profiling Results: Analysis will be described in the Biomarker SAP. For each patient, the BRCA mutation (mutant, wildtype, unknown) and HRD status (HRD+, HRD-, unknown) will be listed. A summary table will summarize BRCA and HRD status by treatment arm and overall.

9.6 Concomitant Medications and Subsequent Therapies

Any concomitant and prior medication used by patients will be recorded on eCRF. Indication for use, whether taken for medical history or AE, start and end date, ongoing, dose, dose formulation, frequency, and route of administration will be noted. Medications are considered concomitant if exposure occurs during the treatment-emergent period and can start either prior to or after the first dose of study treatment. A prior medication is defined as any medication administered that ended prior to the date of the first dose of study treatment. A patient reporting use of the same medication more than once will be counted once in the calculation of the number and percentage of patients who received that medication. Exposure to medications up to and including 30 days after administration of the last dose of either study treatment or up to the initiation of a new anticancer therapy (whichever occurs first) will be reported as concomitant.

The imputation rules for missing start and end date of a concomitant medication are described in Appendix 12.1.

Verbatim terms from the eCRF will be mapped to Anatomical/Therapeutic Chemical (ATC) drug class (level 4) and generic drug names using the WHODD Global B3 March 2024 coding dictionary.

For each treatment arm, a listing will display all entries for medications received by a patient, ordered by “Start date”. The listing will display the recorded term from the eCRF and, the ATC level 2 class (therapeutic subgroup) and the preferred/generic drug name.

Summary table will be organized to display the therapeutic subgroup (level 2) and preferred/generic drug name separately for Prior Medications, Concomitant Medications, and Prior/Concomitant Medications. It will include counts and percentages of patients who reported using at least one medication in each therapeutic subgroup by treatment arm and overall.

A data listing will be provided for all prior and concomitant procedures and/or surgeries.

Concomitant radiotherapy, blood transfusions, and subsequent anticancer therapies received will be listed and summarized by treatment arm and overall.

9.7 Extent of Exposure and Study Drug Compliance

All recorded information on oral dosing of relacorilant, including whether taken during fasting, any dose reductions and related reason, actual dose, any dose interruption and discontinuation during the cycle and end date, as well as drug accountability will be presented in a data listing by patient and by date of administration. A table of the number of patients with a dose adjustment (i.e., dose interruption, dose reduction) and number of dose adjustments will be presented.

A separate data listing and summary table will present data collected on nab-paclitaxel administered via an IV infusion. Body surface area, whether dose reduced prior to infusion and reason, volume of prepared and administered dose, actual dose administered, whether infusion was interrupted and reason, and discontinuation will be included. A table of the number of patients with a dose reduction, a dose adjustment (e.g., dose interruption) and number of dose adjustments will be presented.

A table by treatment arm and all patients will provide summary statistics on the following:

- Number of Cycles of Treatment: The number of cycles for each study drug will be presented based on the last visit when the patient received treatment.
- Duration of Exposure: The duration of exposure for each study drug will be presented in days and calculated as the date of last dose of study drug minus the date of the first dose of study drug, plus one.
- Total Dose Received: The total dose received for each study drug will be the sum of the actual dose administered for the duration of exposure. For subjects where their dose received is either zero or missing, a received dose of zero is included in the total dose

received derivation.

- Total Dose Expected: The total dose expected is calculated for each study drug. The expected study drug dosing schedule is as follows:

For Arm A patients relacorilant is expected to be taken once daily on the day before (excluding Cycle 1 Day -1), the day of, and the day after nab-paclitaxel. Nab-paclitaxel is expected to be taken on Day 1, 8, and 15 of each 28-day cycle.

For Arm B nab-paclitaxel is expected to be taken on Day 1, 8, and 15 of each 28-day cycle.

The expected dosing schedule is used in combination with the actual date and dose of study drug administration to calculate the total dose expected. A subject will have expected dose calculations based on all days within a cycle as determined by the earliest start date and the latest end date within a given cycle. For subjects where their dose received is either zero or missing, an associated expected dose is included in the total dose expected derivation.

The planned dose for relacorilant will be 150 mg and the planned dose for nab-paclitaxel will be 80 mg/m² for Arm A and 100 mg/m² for Arm B. A maximum of two reductions of relacorilant is allowed in the study. The reduction of relacorilant dose cannot be below 100 mg.

- Relative Dose Intensity: Relative dose intensity is calculated for each study drug as the total dose received divided by the total dose expected, multiplied by 100.

Patient use of G-CSF factors, start and end date and reason for taking will be presented in a listing. A summary table will tabulate the G-CSF and reason for taking by treatment arm and overall.

9.8 Efficacy Analyses

The ITT analysis population will be used to address the primary as well as secondary efficacy objectives of the study. Disease response and progression assessed according to RECIST v1.1 by the BICR will provide the basis for efficacy endpoints.

Per the BICR Imaging Review Charter v1.0 dated 10 February 2023, two Readers (Reader 1 and Reader 2) will assess all scans. Adjudication is performed at the time point level when one of the triggers is met (i.e., discordance between the two BICR Readers in their assessment of PD vs Non-PD, or Response vs Non-Response). For all analyses in this SAP, when an adjudication is available at one or more time points for a patient, the Reader with whom the Adjudicator agrees with at the last adjudicated time point will be used. All time points for the patient will use that Reader's assessments. When adjudication is not available at any time points, the assessments of Reader 1 will be used for each time point for the patient.

Additionally, the GCIG criteria for definitions of response and progression in ovarian cancer

clinical trials (Rustin 2011) will be employed for select outcomes, as calculated using CA-125 local laboratory results.

At all scheduled visits, data recorded for target, non-target, and new lesions, and BICR response assessment will be presented in by-patient listings. Summary tables and figures will be provided for endpoints as described in the following sections.

Stratified analyses will use the same stratification factors that were used to stratify the randomization schedule as documented in the interactive voice and web-response system (IXRS). The stratification factors include the following:

- Region (North America versus Europe versus the rest of the world)
- Line of therapy (1 versus more than 1)

9.8.1 Multiplicity Adjustment for Efficacy Analyses

To maintain experiment-wise 2-sided type I error at 0.05, a group sequential weighted Holm procedure will be used for the dual primary endpoints PFS and OS. The study will be considered to have a positive outcome if either of the 2 primary endpoints reaches statistical significance.

For the primary efficacy endpoint of PFS by BICR, the null hypothesis of no difference in PFS among the 2 study groups will be tested at a 2-sided $\alpha = 0.04$ level of significance using a stratified log-rank test. The alternative hypothesis is that there is a difference between groups.

The primary endpoint of OS will be allocated a 2-sided $\alpha = 0.01$ level of significance for the stratified log-rank test. If PFS by BICR is rejected, then per the Holm procedure OS will be tested at $\alpha = 0.05$, using a stratified log-rank test.

The OS data is not expected to be mature at the time of interim analysis (at the time of primary PFS analysis). Therefore, the OS data is only summarized with the intent to detect a trend. The study will not be stopped or adjusted based on the interim OS look. At the time of the interim OS analysis a 2-sided stratified log-rank test will be conducted at $\alpha = 0.0001$ as significance level (this constitutes the alpha spending function). The formal final analysis of OS will be conducted when approximately 292 deaths have been observed and will be performed at $\alpha = 0.0499$ significance level if PFS by BICR is significant or $\alpha = 0.0099$ if PFS by BICR is not significant.

The group sequential testing for OS will use a Haybittle-Peto boundary as a spending function. The target number of OS events when the final analysis is conducted is the same in the context of this group sequential design.

All other secondary endpoints will be tested at a nominal 2-sided 0.05 level of significance, with no additional adjustment for multiplicity. P-values from secondary tests and exploratory tests will be considered descriptive.

9.9 Dual Primary Efficacy Endpoints

The dual primary endpoints PFS and OS are defined in Section 4.1.

9.9.1 Primary Analysis of PFS

The first primary efficacy endpoint of PFS is defined as time from date of randomization to the date of first documented progressive disease per RECIST v1.1 (as determined by BICR) or death from any cause, whichever comes first.

PFS (months) = (earliest date of progression, death, or censoring – date of randomization + 1)/30.4375

All events of disease progression or death will be counted regardless of whether the event occurred while the patient was on study drug or had previously discontinued treatment. Patients who do not experience disease progression or death before the analysis cutoff date will be censored at the date of last adequate tumor assessment. Censoring will also be applied to patients with a disease progression event or death that occurs after two or more consecutively missed tumor assessments. Date of censoring for these patients will be based on the last tumor assessment prior to missing the assessments. Censoring rules are summarized in [Table 1](#).

Table 1: Censoring Rules for the Primary Analysis of PFS

Censoring Categories	Date of Censoring
Patients who did not have baseline or postbaseline tumor assessments and did not die on or before the data cutoff date	Randomization date
Patients who did not have documented progression as determined by BICR and did not die on or before the data cutoff date	Date of the last adequate tumor assessment on or before the data cutoff date
Patients who did not have documented progression as determined by BICR on or before initiation of a new anticancer therapy and did not die on or before the data cutoff date	Date of the last adequate tumor assessment on or before initiation of a new anticancer therapy and on or before the data cutoff date
Patients who had 2 or more consecutive missed scheduled tumor assessments (no scans within 119 days of event if last available assessment is on or before week 24, 147 days if last assessment is at week 32 and 175 days if last assessment is at week 40 or later) immediately prior to disease progression or death	Date of the last adequate tumor assessment without evidence of disease progression before the 2 missed tumor assessments and on or before the data cutoff date.

If a patient meets the criteria for more than 1 censoring rule, PFS will be censored at the earliest censoring date.

A stratified log-rank 2-sided test with a 0.04 level of significance will be used to compare treatment groups. The stratification factors will be the same used to stratify the randomization schedule as documented in the interactive voice and web-response system (IXRS): region (North America versus Europe versus the rest of the world) and line of therapy (1 versus more than 1).

Median PFS will be estimated for each treatment group using the Kaplan-Meier method and 95%

CIIs will be calculated using the Brookmeyer-Crowley method. Survival across treatment arms will also be graphically displayed in Kaplan-Meier plots.

The hazard ratio (HR; $\lambda_{\text{active}}/\lambda_{\text{control}}$) and the associated 95% CI will be estimated using a stratified Cox regression model with treatment group as the only main effect in the presence of stratification factors at randomization. An unstratified HR and the associated 95% CI will also be presented. If the p-value for the stratified log-rank test is statistically significant (<0.04 , two-sided) and the observed HR ($\lambda_{\text{active}}/\lambda_{\text{control}}$) is <1 , the null hypothesis of no difference in PFS will be rejected and it will be inferred that PFS is statistically prolonged in the group receiving relacorilant + nab-paclitaxel compared with the group receiving nab-paclitaxel monotherapy. The median follow-up time for PFS in months will be summarized by treatment and overall, along with 95% confidence interval.

The event-free rate with a two-sided 95% CI using Greenwood's formula will be presented for the selected time points (i.e., 6, 12 months). The censoring reasons will be summarized categorically with the number and percentage of patients tabulated.

9.9.2 Primary Analysis of OS

The second primary efficacy endpoint OS is defined as the time from the date of randomization to the date of death due to any cause. If a patient has not died before the analysis cutoff date, OS will be censored at the date of last contact on or before the data cutoff date. The date a patient was last known to be alive before the data cutoff date is described in Section 12.3.

$$\text{OS (months)} = (\text{earliest date of death or censoring} - \text{date of randomization} + 1)/30.4375$$

Date and cause of death, along with any post-therapy information, will be collected for all patients, including those who discontinue treatment, at 3-month intervals starting from the date of progression to death, loss to follow-up, or study termination by Sponsor. For patients who withdraw consent, public records will be searched for survival status as allowed per local laws.

There will be an interim and final analysis for OS. The interim analysis of OS will be conducted at the time of the primary analysis of PFS. At the interim analysis, OS data will be summarized to detect a trend in OS. The formal analysis of OS will be conducted when approximately 292 deaths have been observed and will be performed using the ITT population.

The testing of OS will be conducted using a stratified log-rank 2-sided test. The stratification factors will be the same used to stratify the randomization schedule as documented in the IXRS. The median of OS and the associated 95% CI for each treatment arm and overall will be estimated using the Kaplan-Meier method. Kaplan-Meier estimates with two-sided 95% CI calculated using the Brookmeyer-Crowley method will be provided for OS time quartiles.

The HR and the associated 95% CI will be estimated using a Cox regression model with treatment group as the main effect and the same stratification factors as the stratified log-rank test. An unstratified HR and the associated 95% CI will also be presented. The survival rate at 6 and 12 months with two-sided 95% CI using Greenwood's formula will be presented. The

censoring reasons will be summarized categorically with the number and percentage of patients tabulated.

9.9.3 Sensitivity Analyses

A sensitivity analysis of PFS to assess the impact of postbaseline anticancer therapies will be performed. For this analysis, PFS is defined as the time from randomization until the date of progression as determined by the BICR, initiation of a new anticancer therapy, or death due to any cause, whichever occurs first.

Additionally, a sensitivity analysis of PFS to assess the impact of treatment discontinuation for any reason will be performed. For this analysis, patients who discontinue treatment before radiographic progression as determined by BICR or death will be considered to have a PFS event at the time of the study treatment discontinuation. PFS is defined as the time from randomization until the date of progression as determined by the BICR, study treatment discontinuation for any reason, or death due to any cause, whichever occurs first.

A third sensitivity analysis will look at clinical progression in addition to radiographic progression. In this analysis, patients who progress clinically as determined by the Investigator will be considered to have a PFS event. In this analysis, PFS is defined as the time from randomization until the date of clinical progression as determined by the Investigator or radiographic progression as determined by BICR, or death due to any cause, whichever occurs first. Censoring rules described in Table 1 will apply.

A fourth sensitivity analysis will count all death events as PFS events even if they occur after 119 days from most recent evaluable scan if they are due to disease under study. In this analysis, PFS is defined as the time from randomization until the date of progression as determined by the BICR, or death due to any cause, including deaths due to disease progression occurring after 2 or more consecutively missed tumor assessments. The remainder of the censoring rules described in Table 1 will apply.

A fifth sensitivity analysis will censor patients with a disease progression event or death that occurs after two or more consecutively missed tumor assessments, defined as no scans within 119 days of progression or death. The remainder of the censoring rules described in Table 1 will apply.

A sixth sensitivity analysis will look at the evaluation of the discordance rate between Investigator and BICR on assessing the PFS data.

Potential evaluation bias between the Investigator and BICR assessments will be assessed with respect to either disease progression status or the timing at which progression occurs using 2 measures, the early discrepancy rate and late discrepancy rate (Amit et al, 2011). The agreement between the investigator and BICR within a treatment arm is described as follows:

Investigator	BICR	
	PD	No PD
PD	$a=a1+a2+a3$	b
No PD	c	d

Note: In practice, an investigator PD occurring later than an BICR assessed PD (a2) would rarely be observed.

a1 = number of agreements on timing and occurrence of PD where the difference between the two PD dates is less than or equal to 14 days.

a2 = number of times investigator declares PD more than 14 days later than BICR.

a3 = number of times investigator declares PD more than 14 days earlier than BICR.

b = number of subjects whose investigator declared PD, but BICR did not.

c = number of subjects whose BICR declared PD, but investigator assessment did not.

d = number of subjects neither investigator nor BICR assessments declared PD.

The early discrepancy rate (EDR) is defined as:

$$EDR = (b + a3) / (a + b)$$

The EDR represents the positive predictive value of investigator assessment and quantifies the frequency with which the investigator declares progression early relative to BICR within each arm as a proportion of the total number of investigator assessed PD's.

The late discrepancy rate (LDR) is defined as:

$$LDR = (c + a2) / (b + c + a2 + a3)$$

The LDR quantifies the frequency that investigator declares progression later than BICR as a proportion of the total number of discrepancies within the arm. If the distribution of discrepancies is similar between the arms, then this suggests the absence of evaluation bias favoring a particular arm.

The EDR and LDR can be calculated for each treatment arm and the differential discordance around each measure can be defined as the rate on the experimental arm minus the rate on the control arm. A negative differential discordance for the EDR and/or positive differential discordance for the LDR are suggestive of a bias in the investigator favoring the experimental arm. The LDR and EDR will be summarized for each treatment arm.

In addition, the time to first, second, third, fourth, etc., tumor assessment visits will be summarized by treatment group using the median and the 95% CI. The number of missing tumor assessments will be summarized based on investigator and BICR assessment.

9.10 Secondary Efficacy Endpoints

Each secondary efficacy endpoint will be evaluated at the 2-sided 0.05 level of significance without adjustment for multiplicity of testing. P-values from secondary tests (other than OS) and exploratory tests will be considered descriptive.

9.10.1 Progression Free Survival by Investigator

The PFS by Investigator is defined as the time from randomization until the date of radiologic progressive disease per RECIST v1.1 or death from any cause, whichever comes first, as determined by Investigator (or local radiologist). The censoring rule for this endpoint will be same as the rules defined in Table 1 for the primary endpoint except for assessment done by BICR will be replaced with investigator (or local radiologist) based assessment. The analysis of this endpoint will follow the same approach as elaborated for primary endpoint.

9.10.2 Best Overall Response

For each patient, BoR as determined by BICR is defined as the best response by RECIST v1.1 will be derived from the date of randomization to PD or death, or the start of new anticancer therapy, whichever occurs first. BoR rates will be summarized by the number and percentage of patients within each response category (CR, PR, stable disease, PD, or not evaluable) for the ITT population.

Waterfall plots will visually illustrate the maximum percent change in the target lesions' sum of longest diameters measured on the response axis, with vertical bars representing the BoR of CR, PR, SD, or PD.

The same analysis will be repeated for BoR as determined by the Investigator.

9.10.3 Objective Response Rate

ORR will be determined by BICR and is defined as the proportion of patients who achieve a complete response (CR) or partial response (PR) by RECIST v1.1. Confirmed and unconfirmed ORR will be reported. The primary analysis of ORR will be performed among the patients with baseline measurable disease in the ITT population. In the analysis of ORR, patients who do not have any post-baseline adequate tumor assessments will be counted as non-responders.

Confirmed objective response will consider as responders the patients with BOR of PR or CR by BICR, confirmed by the subsequent tumor assessment (at least 4 weeks later) at the data cutoff date.

A stratified Cochran-Mantel-Haenszel test at a two-sided 0.05 significance level will be used to test differences in ORR between treatment arms. The stratification factors will be the same used to stratify the randomization schedule as documented in the IXRS. The CR responders will be

reported separately for the patients with non-measurable disease at Baseline.

An unstratified p-value will also be provided as a sensitivity analysis. Point estimates of ORR, the difference in response rates between treatment groups and the two-sided 95% CIs for the point estimates and the differences will be provided using exact Pearson Clopper confidence interval method.

The same analysis will be repeated for ORR as determined by the Investigator.

9.10.4 Clinical Benefit Response Rate

CBR by RECIST v1.1 as assessed by BICR is defined as the proportion of patients who achieve a complete response (CR), partial response (PR) or stable disease (SD) at 24 weeks. In the analysis of CBR, patients who do not have any post-baseline adequate tumor assessments will be counted as non-responders.

A stratified Cochran-Mantel-Haenszel test at a two-sided 0.05 significance level will be used to test differences in CBR between treatment arms. The stratification factors will be the same used to stratify the randomization schedule as documented in the IXRS. An unstratified p-value will also be provided as a sensitivity analysis.

Point estimates of CBR, the difference in response rates between treatment groups and the two-sided 95% CIs for the point estimates and the differences will be provided using exact Pearson Clopper confidence interval method.

The same analysis will be repeated for CBR as determined by the Investigator.

9.10.5 Duration of Response

DoR is defined as the time from the date of first documented CR or PR (whichever came first) by BICR until first observation of PD or death due to any cause, whichever is earlier. DoR will be assessed only in patients with baseline measurable disease in the ITT population who have an objective response (CR or PR) at any time on study, prior to the start of a new anticancer therapy. Patients who do not experience PD and are alive as of the analysis cutoff date will be censored at the date of last adequate tumor assessment. Censoring rules in [Table 1](#) will be applied as well.

$\text{DoR (months)} = (\text{earliest date of progression, death, or censoring} - \text{date of first documented objective response} + 1) / 30.4375$

Estimates of median DoR with 95% CIs will be computed for each treatment arm using the Kaplan-Meier method. Kaplan-Meier estimates with two-sided 95% CI calculated using Brookmeyer and Crowley method will be provided for DoR time quartiles. Kaplan-Meier graphs will visually display DoR by treatment arm. The rate with a two-sided 95% CI using Greenwood's formula will be presented for 6 and 12 months. The censoring reasons will be summarized categorically with the number and percentage of patients tabulated.

The hazard ratio (HR; $\lambda_{\text{active}} / \lambda_{\text{control}}$) and the associated 95% CI will be estimated using a

stratified Cox regression model with treatment group as the only main effect in the presence of stratification factors at randomization. An unstratified HR and the associated 95% CI will also be presented. The median follow up time for DoR in months will be summarized by treatment and overall, along with 95% confidence interval.

The same analysis will be repeated for DoR as determined by the Investigator.

9.10.6 Disease Response via RECIST v1.1 and GCIG Criteria

Disease response in this study will primarily be evaluated via RECIST v1.1. The GCIG criteria ([Rustin 2011](#)) for definition of response in ovarian cancer clinical trials will also be utilized for determining efficacy. Patients in the ITT population who have an initial CA-125 level of at least twice the upper limit of the reference range within 2 weeks before starting treatment will be considered eligible and evaluable for the GCIG response criteria. Results will be presented separately and combining both criteria for RECIST v1.1 and CA-125 response.

CA-125 Response: Patients without initial measurable disease either because no measurable disease is evident on radiological imaging or because appropriate imaging was not performed may be evaluated using the GCIG criteria. A 50% or greater reduction in CA-125 from a pre-treatment sample that is confirmed and maintained for at least 28 days will be defined as a CA-125 response. The date when CA-125 level is first reduced by 50% will be the date of CA-125 response. Patients who achieve a CA-125 response and whose CA-125 level falls within the reference range will be classified as CA-125 complete responders.

To calculate response per GCIG criteria, an intent-to-treat analysis will be used that includes all randomized patients with an initial CA-125 level of at least twice the upper limit of the reference range as eligible and evaluable. In addition, as a separate analysis, those patients who have a CA-125 response and whose CA-125 level falls to within the reference range can be classified as CA-125 complete responders. In [Table 2](#) and [Table 3](#), where CA-125 is stated as normalized or normal, means within the reference range.

In addition, a summary table for descriptive statistics for CA-125 by visit for observed values and change from Baseline will be provided by treatment arm and overall. Change from Baseline will be calculated as the post-baseline minus the baseline measurement. If either value is missing, the observation will not be included in the summary statistics.

9.10.6.1 Evaluation of Best Overall Response in Patients without Initial Measurable Disease and Evaluable by CA-125 (GCIG)

CA-125 may be used to evaluate response in patients without initial measurable disease either because no measurable disease is evident on radiological imaging or because appropriate imaging has not been performed as demonstrated in [Table 2](#).

Table 2: Evaluation of Best Overall Response in Patients Without Initial Measurable Disease and Who are Evaluable by CA-125 (GCIG)

CA-125	Nontarget Lesions ^a	New Lesions	Overall Response	Best Response for This Category Also Requires
Response and Normalized	CR	No	CR	Confirmed and maintained for at least 28 days
Response	Non-PD	No	PR	
Normalized but no response	Non-CR/Non-PD	No	SD	
Non-PR/non-PD	Non-PD	No	SD	
PD	Any	Yes or No	PD	
Any	PD ^b	Yes or No	PD	
Any	Any	Yes	PD	

Abbreviations: CR, Complete response; PD, progressive disease; PR, partial response; SD, stable disease.

^a Nontarget lesions include ascites and peritoneal thickening, which are not measurable according to RECIST.

^b Unequivocal progression in nontarget lesions may be accepted as disease progression.

9.10.6.2 Evaluation of Best Overall Response in Patients with Initial Measurable Disease and Who are Also Evaluable by CA-125 (GCIG)

A report that combines both CA-125 and RECIST v1.1 criteria is likely to include patients who are measurable by one or both of the criteria and who may have events at different time points. Best overall response should be determined according to [Table 3](#). In patients who have measurable disease by both criteria, the date of response will be the date of the earlier of the 2 events if this approach to combined response reporting is to be used. In the combined assessment of CA-125 and RECIST v1.1 response, the following algorithm applies when determining the best overall response. If patients have progressive disease (PD) according to RECIST v1.1 within 28 days of CA-125 response, they are classified as having PD. If the PD according to RECIST v1.1 occurs more than 28 days from the CA-125 response, they are classified as having partial response.

Patients whose best response according to RECIST v1.1 is stable disease but who have a CA-125 response are classified as CA-125 responders.

Table 3: Best Overall Response in Patients with Measurable Disease and Who are also Evaluable by CA-125 (GCIG)

Target Legion ^a	Nontarget ^b	New Lesion	CA-125	Best Overall Response
CR	CR	No	Normal	CR
CR	Non-CR Non-PD	No	Not PD	PR
CR	CR	No	PR but not normal	PR
CR	NE	No	PR	PR
PR	Non-PD or NAE	No	Not PD	PR
NAE	Non-PD	No	PR	PR
PD or New >28 days from CA-125 PR ^c			PR	PR
SD	Non-PD	No	PR	PR
SD	Non-PD or NAE	No	Not PR and not PD	SD
PD or New ≤28 days From CA-125 PR ^c			PR	PD
PD	Any	Yes or No	Any	PD
Any	PD	Yes or No	Any	PD
Any	Any	Yes	Any	PD
Any	Any	Yes or No	PD	PD

Abbreviations: CA-125, cell surface antigen 125; CR, Complete response; NE, Not evaluated; NAE, not all evaluated; PD, progressive disease; PR, partial response; SD, stable disease.

^a Target lesions include up to 5 measurable lesions (2 per organ) as defined by RECIST v1.1.

^b Nontarget lesions include ascites and peritoneal thickening which are not measurable according to RECIST v1.1.

^c Patients who have a CA-125 response that occurs more than 28 days from PD according to RECIST v1.1 are considered a PR, according to best response, but PD if the RECIST v1.1 PD is within 28 days of CA-125 response.

9.10.6.3 Reporting of Response According to both RECIST v1.1 and CA-125 (GCIG) Criteria

In this study, responses will be reported separately for both tumor response per RECIST v1.1 and CA-125 response per GCIG. A combined response endpoint based on both RECIST v1.1 and CA-125/GCIG criteria will also be reported. Tumor response will be assessed by the Investigator or local radiologist using RECIST v1.1. CA-125 response and the combined response will be derived based upon local CA-125 results.

9.10.7 Exploratory Efficacy Endpoints

9.10.7.1 Restricted Mean Survival Time (RMST)

As a summary of treatment effect on OS without assuming proportional hazards, an RMST model will be presented. RMST is the expected survival time subject to a specific time horizon, and it is an alternative measure to summarize the survival profile. The RMST will be reported by treatment group along with the difference in RMST and 95% CI at 18 months. The SAS code to estimate RMST is provided in Appendix [12.5](#).

9.10.7.2 Exploratory Pharmacodynamic/Biomarkers Analyses

During this study, with the consent of patients, biological samples (e.g., blood, plasma, serum, or tumor tissue) will be obtained either for analysis during the study or future analysis. These samples will be used to develop a better understanding of the mechanisms of both treatment response (predictive biomarkers) and disease processes (prognostic biomarkers) and ultimately to identify which patients have a high probability to benefit from treatment with relacorilant and those who do not.

Corcept-audited Specialty laboratories will conduct tests using a variety of techniques (e.g. immunohistochemistry and DNA/RNA analysis). Pharmacodynamic assays may be performed to correlate results of biomarker assessments to the physiological effects of relacorilant.

Pharmacodynamic/biomarker endpoints may include, but not limited to, analysis of baseline assessment and change from Baseline of:

- Tumor immunohistochemistry: Glucocorticoid receptor (GR) and immune markers such as PDL1, CD3, CD8, CD4, MPO, CD163, FOXP3, Ki67.
- RNA analyses from circulating cells and tumor, where feasible.
- Cancer antigens such as CA-125, CA15-3, CA19-9 and/or carcinoembryonic antigen (CEA).
- Cytokines

Data listings will be provided for whether archival or recent (pre-treatment) tumor biopsy, optional paired tumor biopsies, and blood samples were obtained, the date of collection, as well as additional information recorded on the eCRFs.

Descriptive statistics will be presented for all the biomarker endpoints. Additional exploratory biomarker analyses of these and other assessments may be conducted and described in a separate Biomarker document.

9.10.7.3 Patient-Reported Outcomes and Quality of Life Assessment.

Health-related PRO and QoL will be assessed in the Safety population using three standard and validated instruments. Baseline measures will be collected prior to the first dose of relacorilant or nab-paclitaxel, whichever is earlier, at the Screening visit. If not performed at Screening, these

assessments can be completed at Cycle 1 Day 1 prior to the administration of study treatment.

Post-baseline assessments will be completed at Cycle 2 Day 1, Cycle 3 Day 1, and Cycle 4 Day 1. After Cycle 4 Day 1, assessments will be performed every other cycle (starting from Cycle 6 Day 1) through the end of treatment Visit. Patients will be asked to complete the European Organization for Research and Treatment of Cancer (EORTC) ovarian cancer specific quality of life questionnaire (EORTC QLQ-OV28) first, followed by EORTC QLQ-C30 and EuroQol-5 Dimension 5-level (EQ-5D-5L). A healthcare resource utilization (HRU) questionnaire will also be administered at these visits.

EORTC QLQ-C30 version 3: this is an extensively validated and widely used measure of HRQOL. Patient responses to the 30 items of the instrument will be scored to obtain an overall and five domains of functioning (physical, role, emotional, social, cognitive) global HRQOL, and 9 symptoms that commonly occur in cancer (pain, fatigue, nausea, vomiting, constipation, diarrhea, dyspnea, problems with sleep, appetite). The scoring of EORTC QLQ-C30 is provided in Appendix 12.7.

A data listing will include patient responses to all items reported at scheduled visits, as well as derived overall and domain scores.

Descriptive statistics (mean, standard deviation, 95% CI, median, range) of the observed scores at Baseline, post-baseline visits, and change from Baseline will be summarized at each time point by treatment arm and overall, for each subscale and overall.

Overall and within each subscale, mean change in linear transformed scores between the groups will be assessed, using a linear mixed model for repeated measures (MMRM) analysis using mixed effects model that considers the scores at each assessment point up to EOT.

When a patient has a missing scheduled assessment, it will be imputed with an unscheduled assessment or EOT assessment which is within one month of the scheduled timepoint, if available. All other unscheduled assessments will not be included. The remainder of the EOT assessments will be summarized in the EOT visit for the summary statistics outputs. To aid in convergence for the MMRM analysis, only those visits up to and including Cycle 6 Day 1 will be used in the model.

The variables in the model will be treatment, visit, treatment-by-visit, with baseline used as a covariate. The MMRM model will include patients within treatment arms as random effects. An unstructured covariance structure will be used to model within-patient error. In case of convergence issues, the following covariance structures will be used until the convergence criteria is met, in this order: unstructured covariance, heterogeneous compound symmetry, compound symmetry. The Kenward and Roger method for calculating the denominator degrees of freedom for tests of fixed effects will be used.

The LS mean scores for each treatment arm, with 95% CIs and P values (considered descriptive) will be reported (See Appendix for SAS code to estimate LS mean).

EORTC QLQ-OV28: this assesses abdominal/gastrointestinal (GI) symptoms, peripheral neuropathy, other chemotherapy side effects, hormonal/menopausal symptoms, body image, attitude to disease/ treatment and sexual functioning. The scoring of EORTC QLQ-OV28 is provided in Appendix 12.8.

A data listing will include patient responses to all items reported at scheduled visits, as well as derived overall and domain scores.

The number of patients achieving at least 15-point absolute improvement at Week 8 or Week 9 in the abdominal/ GI scale of the QLQ-OV28 questionnaire will be summarized by treatment arm along with 95% CI. The CI will be computed using an exact binomial method. Similarly, the number of patients achieving at least 10-point absolute improvement at Week 8 or Week 9 in the abdominal/ GI scale will be summarized as a sensitivity analysis.

Descriptive statistics (mean, standard deviation, 95% CI, median, range) of the observed scores at Baseline, post-baseline visits, and change from Baseline will be summarized at each time point by treatment arm and overall, for each subscale and overall.

Overall and within each subscale, mean change in linear transformed scores between the groups will be assessed, using a linear MMRM analysis using mixed effects model that considers the scores at each assessment point up to EOT.

When a patient has a missing scheduled assessment, it will be imputed with an unscheduled assessment or EOT assessment which is within one month of the scheduled timepoint, if available. All other unscheduled assessments will not be included. The remainder of the EOT assessments will be summarized in the EOT visit for the summary statistics outputs.

The variables in the model will be treatment, visit, treatment-by-visit, with baseline used as a covariate. The MMRM model will include patients within treatment arms as random effects. An unstructured covariance structure will be used to model within-patient error. In case of convergence issues, the following covariance structures will be used until the convergence criteria is met, in this order: unstructured covariance, heterogeneous compound symmetry, compound symmetry. The Kenward and Roger method for calculating the denominator degrees of freedom for tests of fixed effects will be used.

The LS mean scores for each treatment arm, with 95% CIs and p-values will be reported.

EQ-5D-5L: The five dimensions of this instrument, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, along with a visual analog score for overall health will be assessed at designated visits. Patients will respond to each dimension on a 5-level Likert-type scale and also quantitatively rate their overall health from 0 to 100, with 0 indicating the worst health imagined. Based on preferences identified by the US general population, a weighted index value will be calculated from patient responses to the 5 dimensions (van Hout 2012).

Patient responses recorded at each visit as well as the derived index score will be included in a data listing.

By treatment arm, a summary table will present health profile results as the proportion of patients reporting problems at each level for each dimension at baseline and follow-up visits.

A linear MMRM analysis using mixed effects model will be constructed to obtain mean differences in the weighted index value and visual analog score for patients in treatment Arm A versus Arm B. Associated 95% CIs and p-values (considered descriptive) will also be presented. When a patient has a missing scheduled assessment, it will be imputed with an unscheduled assessment or EOT assessment which is within one month of the scheduled timepoint, if available. All other unscheduled assessments will not be included. The remainder of the EOT assessments will be summarized in the EOT visit for the summary statistics outputs. To aid in convergence for the MMRM analysis, only those visits up to and including C6D1 will be used in the model.

The variables in the model will be treatment, visit, treatment-by-visit, with baseline used as a covariate. The MMRM model will include patients within treatment arms as random effects. An unstructured covariance structure will be used to model within-patient error. In case of convergence issues, the following covariance structures will be used until the convergence criteria is met, in this order: unstructured covariance, heterogeneous compound symmetry, compound symmetry. The Kenward and Roger method for calculating the denominator degrees of freedom for tests of fixed effects will be used.

Healthcare utilization: Health care facility use, emergency department visits and inpatient hospital services will be summarized by treatment arm and presented in by- subject listing.

9.10.7.4 Time to second progression:

The time to second progression (PFS2) will be defined as time from randomization to progression on the next regimen of subsequent anticancer therapy or death due to any cause, whichever occurs first. PFS2 analysis will be performed in the ITT population. Patients alive and for whom a second objective disease progression has not been observed should be censored at the last time known to be alive and without second objective disease progression. Censoring rules for PFS2 are described in [Table 4](#).

Table 4: Censoring Rules for PFS2

Censoring Rules	Date of Censoring
Patients with no postbaseline assessments	Date of randomization.
Patients who had no first documented disease progression per RECIST 1.1 or death on study before data cutoff date	Date of the last tumor assessment before data cutoff date
Patients who had a documented first disease progression on study but did not continue with a subsequent anticancer therapy	Date of treatment discontinuation or date of the last tumor assessment before data cutoff date, whichever comes last
Patients who did not have a second documented disease progression on subsequent anticancer therapy before data cutoff	Date of the last available tumor assessment on or before the analysis data cutoff date or date of discontinuation of treatment, whichever comes last
Patients who started subsequent anticancer treatment but had no further tumor assessment information	Date of the start date of subsequent anticancer therapy
Patients who initiate a new anticancer therapy after start of subsequent anticancer therapy without evidence of a second documented disease progression	Date of the discontinuation of subsequent anticancer therapy or the analysis data cutoff date, whichever comes first

Kaplan-Meier methods will be used for calculating the median time to second progression in each treatment arm. A 2-sided 95% CI will be provided for this estimate.

Summary statistics for duration on subsequent therapy will also be reported. Duration on subsequent therapy (months) = (end date – start date + 1)/30.4375

9.10.8 Subgroup Analyses

Additional subgroup analyses will be conducted if there are 10 or more patients in each group:

- Prior lines of therapy: 1 vs 2 vs 3 vs 2-3 per EDC
- Prior lines of therapy per IRT 1 vs 2-3
- Prior PARP inhibitor (olaparib, rucaparib, niraparib) vs no prior PARP inhibitor.
- Region: North America vs Europe vs rest of world (South Korea, Australia, Argentina, Brazil)
- HRD/BRCA: BRCA1/2 mutant vs BRCA1/2 wild-type vs Unknown; HRD vs HRP vs HRD status unknown
- Age: <65 vs ≥65
- ECOG Performance Status: 1 vs 0
- Primary platinum-free interval, defined as the time from the last dose of platinum therapy to the date of disease progression (or the first dose of the next regimen if the date of

disease progression is not documented) for first-line therapy: ≤ 6 months vs >6 months

- Most recent platinum-free interval, defined as last dose of platinum therapy to randomization date ≤ 3 months vs >3 months
- Taxane in last regimen: Yes vs No
- Taxane-free interval, defined as the time from the last dose of last taxane therapy until randomization: ≤ 6 months vs >6 months vs no prior taxane
- Stage at diagnosis: I, II or III vs IV
- Tumor histological subtype: serous vs non-serous
- Weight at baseline: <60 kg vs ≥ 60 kg
- Size of the largest target lesion at baseline: <5 cm vs ≥ 5 cm

The subgroup analyses will use stratified log rank test and median time to PFS will be estimated for each subgroup by treatment using Kaplan-Meier method and the 95% CI will be calculated using the Brookmeyer-Crowley method. The HR and the 95% CI will be estimated using a stratified Cox regression model. An unstratified HR and the associated 95% CI will also be presented.

The primary endpoint of PFS by BICR will be summarized by all subgroups. Additionally, SAEs and Special Safety topics will be summarized by age and racial subgroups. OS will be summarized by age, racial subgroups and region.

Note, this trial enrolled only female patients. Therefore, subgroup by sex coincides with the full population of female patients.

9.11 Pharmacokinetic and Pharmacokinetic/Pharmacodynamic Exposure/Safety Analyses

Relacorilant plasma exposures will be estimated using population PK methods, which will be described in a separate PK analysis plan finalized before database lock.

9.12 Safety Analyses

All safety analyses will be performed on the SAF population. Patients will be analyzed according to the actual treatment received.

All safety data will appear in by-patient data listings.

9.12.1 Adverse Events

Adverse events will be collected immediately following signing of informed consent and will continue until 30 days after the last dose of relacorilant or nab-paclitaxel, whichever is later. Events that occur after the first dose of either study treatment and up to and including 30 days after administration of the last dose of either study treatment or the initiation of a new anticancer therapy (whichever occurs first) or any event present before treatment that worsens after treatment

will be considered TEAEs. Adverse events reported more than 30 days after the last dose of study treatment will be considered post-treatment AEs.

AE severity is graded by the Investigator according to NCI-CTCAE v5.0 using the guidance provided in the protocol. The Investigator will assess causality of AEs and SAEs based on the causal attribution guidance in the study protocol. Related AEs are defined as AEs assessed by the Investigator as “Possibly related to study drug” or “Probably related to study drug.” If the relationship to study drug is missing, the adverse event will be counted as related. Adverse event listings will show missing relationship as “missing.”

Verbatim terms on case report forms will be mapped to PTs and SOC by the primary hierarchy using the MedDRA version 27 or higher.

Summaries that are displayed by SOC and PT will be ordered by descending incidence of SOC and PT within each system organ class in the relacorilant and nab-paclitaxel arm. Summaries displayed by PT will be ordered by descending incidence of PT in the relacorilant and nab-paclitaxel arm.

Both treatment arms and overall frequencies will be included in all summaries of TEAEs with the exceptions noted below. Percentages are based on the number of patients in each treatment arm. For some displays (as noted below), the risk difference and 95% confidence interval will be displayed for each treatment arm.

The following AE summary tables will be produced:

- Overall summary of TEAEs with risk differences and 95% confidence intervals
- Patient incidence of TEAEs:
 - o By SOC and PT with risk differences and 95% confidence intervals
 - o By PT
 - o By SOC, PT, and maximum severity
 - o By exposure-adjusted incidence rate (EAIR) by SOC and PT with risk differences and 95% confidence intervals
- Patient incidence of TEAEs related to relacorilant (for the relacorilant-containing arm only):
 - o By SOC and PT
 - o By PT
 - o By SOC, PT, and maximum severity
- Patient incidence of TEAEs related to both relacorilant and nab-paclitaxel (for the relacorilant-containing arm only):
 - o By SOC and PT
 - o By PT
 - o By SOC, PT, and maximum severity
- Patient incidence of TEAEs related to nab-paclitaxel:
 - o By SOC and PT with risk differences and 95% confidence intervals

- o By PT
 - o By SOC, PT, and maximum severity
 - o Grade 3 or higher by SOC and PT
- Patient incidence of Grade 3 (Severe) or higher TEAEs by SOC and PT
- Patient incidence of TEAEs leading to discontinuation of relacorilant by SOC and PT (for the relacorilant-containing arm only)
- Patient incidence of TEAEs leading to discontinuation of both relacorilant and nab-paclitaxel by SOC and PT (for the relacorilant-containing arm only)
- Patient incidence of TEAEs leading to discontinuation of nab-paclitaxel by SOC and PT
- Patient incidence of TEAEs with fatal outcome by PT
- Patient incidence of treatment-emergent serious adverse events:
 - o By SOC and PT with risk differences and 95% confidence intervals
 - o By decreasing incidence of PT
 - o By SOC, PT, and maximum severity
 - o Related to relacorilant, relacorilant and nab-paclitaxel, and nab-paclitaxel by SOC and PT
 - o EAIR by SOC and PT with risk differences and 95% confidence intervals
- Patient incidence of TEAEs for PTs with $\geq 5\%$ difference between treatment arms
- Patient incidence of TEAEs for Grade 3 (Severe) or higher TEAEs with $\geq 2\%$ difference between treatment arms
- Patient incidence of TEAEs leading to relacorilant interruptions by PT (for the relacorilant-containing arm only)
- Patient incidence of TEAEs leading to nab-paclitaxel interruptions by PT
- Patient incidence of TEAEs leading to relacorilant dose reduction by PT (for the relacorilant-containing arm only)
- Patient incidence of TEAEs leading to nab-paclitaxel dose reduction by PT
- Patient incidence of TEAEs associated with safety topics of interest (as described in 9.12.1.1)

At each level of summation (e.g., any adverse event, SOC, and PT), patients reporting more than one AE will only be counted once. In the summaries of TEAEs by severity grade, patients will be counted only once at the highest severity reported at each level of summarization; in the summaries of TEAEs by relationship to study drug, patients will be counted once at the closest relationship to study drug.

The Exposure Adjusted Incidence Rate (EAIR) for a TEAE is defined as:

$$\text{Event Incidence rate per 100 PYE} = \frac{\text{Total number of subjects with a event}}{\text{Total PYE}} \times 100$$

The total patient-years-exposure (PYE) to a treatment is the sum of individual patient's PYE within the treatment exposure period and is defined as:

- For patients with an event within the exposure period:

$$PYE = (First\ event\ start\ date - first\ dose\ date + 1)/365.25$$
- For patients with no event within the exposure period:

$$PYE = (Last\ dose\ date + 30 - first\ dose\ date + 1)/365.25$$

The last dose date refers to the last date of either study treatment (i.e., relacorilant or nab-paclitaxel), whichever occurs last. If death occurs, patient discontinues study or a new anticancer therapy is initiated in the 30 days after last dose date, the $PYE = (death\ date/end\ of\ study\ date/start\ of\ subsequent\ anticancer\ therapy - first\ dose\ date + 1)/365.25$.

The exact 95% CI based on Poisson distribution (Ulm 1990) for EAIR is defined as:

$$\left(\frac{\chi^2_{2(Total\ number\ of\ subjects\ with\ an\ event), 0.025}}{2 \times Total\ PYE}, \frac{\chi^2_{2(1+Total\ number\ of\ subjects\ with\ an\ event), 0.975}}{2 \times Total\ PYE} \right) \times 100$$

where $\chi^2_{v,a}$ is the chi-square quantile for upper tail probability on v degrees of freedom.

The exact 95% CI for difference of EAIR between two treatment arms will be calculated based on two independent Poisson distributions using below formula with point estimate of EAIR difference (IRD), $\widehat{IRD} = n_1/PYE_1 - n_2/PYE_2$,

$$x^2 = \left(n_1 - \frac{nPYE_1}{PYE} \right)^2 / \left(\frac{nPYE_1PYE_2}{PYE^2} \right)$$

and

$\widehat{IRD\ CI} = \widehat{IRD} \pm Z_{\alpha/2} \sqrt{\widehat{IRD}^2 / x^2}$ where $n = n_1 + n_2$ with n_1 is the number of patients with event in treatment arm 1 and n_2 is number of patients with event in treatment arm 2, $PYE = PYE_1 + PYE_2$ with PYE_1 is patient-years-exposure in treatment arm 1 and PYE_2 is patient-years-exposure in treatment in treatment arm 2 and $Z_{\alpha/2}$ is a quartile of standard norm distribution with $\alpha = 0.05$ (Sahai and Kurshid, 1996).

The following listings will be produced:

- All AEs, whether treatment-emergent or not, will be listed by treatment arm and sorted chronologically for each individual patient, including dates of onset and resolution (calendar date and safety study day), whether ongoing, serious, NCI-CTCAE toxicity grade, action(s) taken, outcome, and relationship to study treatment.

Serious TEAEs and TEAEs that lead to discontinuation of study drug (relacorilant or nab-paclitaxel), study drug interruptions (relacorilant or nab-paclitaxel), study drug dose reductions (relacorilant or nab-paclitaxel), and safety topics of interest will be listed separately. Serious AEs occurring during Screening will be presented in a listing.

9.12.1.1 Identified Risks and General Safety Topics

A set of safety topics were defined to identify and characterize events possibly associated with the use of relacorilant based on the mechanism of action, observed during the relacorilant pre-clinical and clinical development program, or are of clinical importance to the treated population. Summaries of these special safety topics will be produced to enhance the understanding of safety data.

The safety topics of interest comprise:

- Excessive glucocorticoid receptor (GR) antagonism
- Adrenal insufficiency
- Neutropenia
- Thrombocytopenia
- Anemia
- Peripheral neuropathy
- Cutaneous toxicity
- Oedema
- Sepsis

The following summaries of TEAEs associated with safety topics of interest will be produced:

- Patient incidence of TEAEs
 - By PT
 - By PT and severity
- Time to first onset of TEAEs
 - The time to the start of the first occurrence will be calculated by the date of onset of the first event of interest – date of first dose of study drug + 1
 - Patients who never reported a TEAE in the safety topic of interest will be censored at the date of study discontinuation, start of subsequent anticancer therapy or data cut-off date for the analysis, whichever is earlier.

The analysis of time to event will include the number of patients with an event, the number of patients without an event (censored), descriptive statistics of time for those with an event, and range in days for all patients. Kaplan-Meier estimates will be calculated by the treatment group. The quartiles, including the median time-to-event and their respective 2-sided 95% CIs, will be presented. Kaplan-Meier estimates will be plotted as a cumulative probability plot for each treatment group with the number at risk identified.

9.12.2 Deaths

All deaths, date and primary cause, whether they occurred during treatment or after 30-day follow-up, and whether an autopsy report is available will be listed and summarized.

9.12.3 Clinical Laboratory Tests

Screening Hepatitis B and C serologies and HIV, CA-125, and other clinical laboratory tests for

safety (hematology, serum chemistry, coagulation, urinalysis) will be performed according to the study schedule, data processed by local laboratories, and entered directly into the EDC by site users.

Table 5 lists all laboratory variables evaluated during the study. All results and normal ranges will be presented in data listings. Grade 3 or higher lab abnormalities will be presented in a separate by-patient listing.

Table 5: Clinical Laboratory Variables Evaluated During the Study

Hematology Red blood cell count Hemoglobin Hematocrit Platelet count White blood cell count (WBC) WBC with 5-part differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils	Serum Chemistry Aspartate aminotransferase Albumin Alkaline phosphatase Alanine aminotransferase Bicarbonate Bilirubin (total and direct) Blood urea nitrogen Calcium Chloride Creatinine Magnesium Phosphorus Sodium Potassium Total protein Uric acid	Coagulation Activated partial thromboplastin time International normalized ratio Prothrombin time
		Pregnancy Serum/urine pregnancy test ^a
		Tumor Markers Cancer antigen 125
		Pharmacodynamics See Table 14 in the protocol for details.
		Urinalysis
		Serology HIV immunoassay ^b Hepatitis B/C serology ^c

^a For Women of childbearing potential, must be confirmed as negative prior to randomization within 72-hour of first dose of study drug, and prior to Day 1 of subsequent cycles while on treatment.

^b 4th generation immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen.

^c Serologic assays for hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti-HBc), antibody to hepatitis B surface antigen (anti-HBs), and anti-hepatitis C antibodies.

For continuous values (clinical laboratory values) that are not able to be determined due to being less than the lower limit of quantification (LLOQ) (e.g., “<1.0”) or higher than the upper limit of quantification (ULOQ), the value will be assigned to 1 unit lower than the LLOQ or 1 unit higher than the ULOQ for any analyses performed. The original value will be displayed in any listings provided.

For safety lab panels for hematology and chemistry, summaries of actual values and change from Baseline will be presented by treatment arm and overall at each assessment time point. Change from Baseline will be calculated as the post-baseline minus the baseline measurement. If either value is missing, the observation will not be included in the summary statistics.

Summaries of actual values and change from Baseline in absolute neutrophil count will be presented by treatment arm and overall at each assessment time point for patients who received at least 1 dose of G-CSF on study.

Plots of mean values for hemoglobin, platelet count, and neutrophils will be presented by visit and by treatment arm for the first 10 cycles.

For hematology and chemistry parameters that can be graded using NCI-CTCAE v5.0, shift tables that summarize counts and percentages of patients by severity grade at Baseline and worst post-baseline and last post-baseline result will also be constructed.

Results from a serum or urine pregnancy test for patients of childbearing potential, performed prior to start of study treatment and subsequently every cycle, will be listed.

Laboratory liver test abnormalities will be listed and summarized in a table by treatment arm. An evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) graph will be provided for ALT vs TBL and AST vs TBL.

Additionally, a summary of the number of patients with liver test abnormalities will be provided for the worst value after first dose of study drug including ALT ($>3\times\text{ULN}$, $>5\times\text{ULN}$, $>8\times\text{ULN}$, $>10\times\text{ULN}$, and $>20\times\text{ULN}$); AST ($>3\times\text{ULN}$, $>5\times\text{ULN}$, $>8\times\text{ULN}$, $>10\times\text{ULN}$, and $>20\times\text{ULN}$); total bilirubin ($>\text{ULN}$ and $>2\times\text{ULN}$); ALP ($>1.5\times\text{ULN}$); ALT or AST $>3\times\text{ULN}$ and total bilirubin ($>1.5\times\text{ULN}$ and $>2\times\text{ULN}$); ALT or AST $>3\times\text{ULN}$, total bilirubin $>2\times\text{ULN}$, and ALP ($<2\times\text{ULN}$ or $>2\times\text{ULN}$); ALT or AST $>3\times\text{ULN}$ and $\text{INR}>1.5$. A listing of all patients with liver test abnormalities will be provided including all laboratory values and corresponding abnormality.

Only laboratory parameters collected within the treatment emergent period will be displayed. Summary outputs will include measurements collected up to and including 30 days after administration of the last dose of either study treatment or the initiation of a new anticancer therapy (whichever occurs first).

9.12.4 Vital Signs and Weight

At designated visits, vital signs will be recorded and will include weight, systolic and diastolic blood pressure, resting heart rate, body temperature, and respiratory rate. A listing of all vital signs will be provided. Additionally, data will be summarized by treatment arm and overall, using descriptive statistics at Baseline, each study evaluation, and change from Baseline to evaluation. Change from Baseline will be calculated as the post-baseline minus the baseline measurement. If either value is missing, the observation will not be included in the summary statistics.

9.12.5 Electrocardiograms

At Baseline, Cycle 3 Day 1 and EOT visits, 12-lead ECG data, obtained in triplicate, will be classified as normal, abnormal but not clinically significant, or abnormal and clinically significant by the Investigator or qualified designee. All recorded results will be included in a

listing, and results averaging the triplicate reading at screening and end of study will be summarized for each treatment arm as an absolute value and change from Baseline.

9.12.6 ECOG Performance Status

ECOG performance status assessed at Screening and subsequent study visits will be included in a data listing. Patient performance status will also be summarized by treatment arm and overall for each numeric grade at baseline and change from Baseline. Shift tables will summarize the counts and percentages of patients by ECOG status at Baseline and worst post-baseline/last post-baseline result.

9.12.7 Physical Examination

Confirmation of a physical examination, including date of assessment, will be listed for each scheduled time point.



10 CHANGES FROM PROTOCOL IN STUDY CONDUCT OR STATISTICAL ANALYSIS PLAN

Not applicable.

11 REFERENCES

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12 APPENDIX

12.1 Imputation of Missing/Partially Missing Dates

Missing data will not be imputed unless otherwise specified.

For safety analyses, incomplete date of last dose of study drug and incomplete start date of a new antitumor treatment that are missing the day of the month, the 15th of the month will be used to impute the missing data. When imputing partial last dose dates, the last assessment date and death date will be taken into consideration. This imputation rule will be used to determine the treatment-emergent period.

Adverse Events and Concomitant Medications

The imputation rule for the safety analyses will be used to address the issues with partial dates. The imputed dates will be used to determine the treatment-emergent period. For adverse events with a partial date, available date parts (year, month, and day) of the partial date will be compared with the corresponding date components of the start date and end date of the treatment-emergent period to determine if the event is treatment emergent. When in doubt, the adverse event will be considered treatment emergent by default. The following rules will be applied to impute partial dates for adverse events:

If start date of an adverse event is partially missing, impute as follows:

- If both month and day are missing and year = year of treatment start date, then set to treatment start date
- If both month and day are missing and year $\neq$ year of treatment start date, then set to January 01
- If day is missing and month and year = month and year of treatment start date, then set to treatment start date
- If day is missing and month and year $\neq$ month and year of treatment start date, then set to first of the month
- If only year is missing or start date is completely missing, set to treatment start date as long as adverse event end date is not before treatment start date

If end date of an adverse event is partially missing, impute as follows:

- If both month and day are missing, then set to December 31
- If only day is missing, then set to last day of the month
- If only year is missing or end date is completely missing, do not impute

When the start date or end date of a medication is partially missing, the date will be imputed to determine whether the medication is prior or concomitant (or both). The following rules will be

applied to impute partial dates for medications:

If start date of a medication is partially missing, impute as follows:

- If both month and day are missing, then set to January 01
- If only day is missing, then set to the first of the month

If end date of a medication is partially missing, impute as follows:

- If both month and day are missing, then set to December 31
- If only day is missing, then set to last day of the month

If only year is missing or start date or end date of a medication is completely missing, do not impute.

Primary Cancer Diagnosis

If the diagnosis date of primary cancer is partially missing, the following rules will be applied to impute partial dates:

- If both month and day are missing and year = year of treatment start date, then set to treatment start date.
- If both month and day are missing and year $\neq$ year of treatment start date, then set to December 31.
- If day is missing and month and year = month and year of treatment start date, then set to treatment start date.
- If day is missing and month and year $\neq$ month and year of treatment start date, then set to the last day of the month.

Start of subsequent anticancer therapy

For records with partially missing subsequent anticancer therapy start date, the start date of subsequent anti-cancer therapy will be imputed by the earliest possible date that is not contradicting with any other available data in the database.

- If the day is missing then impute to the earliest day in the month which is after last dose of either study treatment, but before end of study and death date.
- If the start day is completely missing or day and month are both missing, do not impute.

The imputed start of subsequent anticancer therapy will be used in deriving efficacy variables and the treatment emergent period.

12.2 Visit Windows

Visit windows will be used to associate assessments with a scheduled visit for summarizing data by visit.

Study visits will align with nab-paclitaxel infusion days during the Treatment Phase. Screening hematology and chemistry laboratory tests can be used for the Cycle 1 Day 1 values if collected within 3 days prior to the first dose of study treatment. For all other visits, hematology and chemistry should be performed within the prior 24 hours (relative to the study visit/nab-paclitaxel infusion).

The Follow-up Visit should be performed 30 days (± 3 days) after the patient receives their final dose of relacorilant or nab-paclitaxel, whichever is latest.

The Long-term follow-up assessments should be done every 3 months (± 7 days) until the endpoint of death, the patient is lost to follow-up, or until 2 years following the final dose of study treatment in the final patient enrolled.

For efficacy assessments and AEs, data from both planned visits and unscheduled visits will be assessed and summarized.

A serum or urine pregnancy test for female patients of childbearing potential will be performed prior to the first dose of study treatment (48-hour window from the first dose of study treatment) and then every 12 weeks ± 7 days.

Tumor assessments will be performed within 28 days prior to the first dose of study treatment and then every 8 weeks (± 7 days) from Cycle 1, Day 1 irrespective of treatment delays until unequivocal disease progression is documented, including in patients who prematurely discontinue therapy. The same method should be used for each assessment for a particular patient.

The analysis visit window for PRO/QoL assessments are as follows:

Study Day 1 will be considered as day prior to the first dose of relacorilant or nab-paclitaxel, whichever is earlier, at the Screening visit. If not performed at Screening, these assessments can be completed at Cycle 1 Day 1 prior to the administration of study treatment. Table 6 outlines the analysis visit windows.

Table 6: Analysis Visit Windows for PRO Assessments

Visit Name	Target Day	Start	End
Baseline/Screening Visit	1	-	15
C2D1	29	16	43
C3D1	57	44	71
C4D1	85	72	113
C6D1	141	114	169
C8D1	197	170	225
C10D1	253	226	281
CXD1	(X-1)*28+1	Target Day - 27	Target Day +28

C: Cycle; D: Day

12.3 Overall Survival

For the overall survival analysis, deaths that occur on or before the data cutoff date will be considered an event. Data from patients who do not die on or before the data cutoff date will be censored at the last contact date. The last contact date will be derived as follows:

Source Data	Conditions
Date of randomization	No condition
Last contact date/last date patient known to be alive from Long-Term Follow-Up eCRF	Use if patient status is reported to be alive Do not use if patient status is reported unknown
End of study	Not lost to follow up
Start/end dates or PD date of postbaseline anticancer therapy	Nonmissing medication/procedure term
Start/end dates from drug administration record	Nonmissing dose. Doses of 0 are allowed.
End of treatment date from the End of Treatment eCRF	No condition
Tumor assessment (RECIST v1.1) date	Evaluation is marked as done.
Laboratory/PK collection dates	Sample collection marked as done.
Vital signs date	At least 1 nonmissing parameter value
ECOG performance status date	Nonmissing ECOG performance status
Start/end dates of adverse events	Nonmissing verbatim term
Physical examination	At least 1 nonmissing parameter value
ECG	At least 1 nonmissing parameter value

12.4 SAS code for estimating median PFS and the associated 95%CI

-Use the following programming statements to obtain the stratified log rank test P-value and associated Kaplan-Meier estimates:

```
ODS OUTPUT survdiff=p_randst Quartiles=Quart outusrv=survest1;
Proc lifetest Data=<DSN> method=KM;
    Time Aval*CNSR (1);
Strata <RAND STRATA>/group=TRT TEST=logrank diff=control ('ARM B');
Run;
```

-Use the following programming statements to obtain the HR and 95CI:

```
ODS OUTPUT parameterestimates=HRCI_RANDST;
Proc PHREG data=<DSN>;
    Class TRT/param=ref=last;
    Model AVAL*CNSR(1)=TRT/risklimits ties=EFRON;
    HAZARDRATIO TRT;
    STRATA <RAND STRATA>;
Run;
```

-Use the following programming statements to obtain rates at 6 & 12 months for the Kaplan-Meier estimates

```
Proc lifetest Data=<DSN> method=KM timelist=6,12 outsurv=survest reduceout;;
    Time Aval*CNSR (1);
Strata TRT;
Run;
```

12.5 SAS code for estimating RMST

The boundary time τ is assumed to be 18 months.

```
proc rmstreg data=adtte2 tau=18;
    class trt01pn RANDSF RANDA;
    model aval*newcnsr(0) = trt01pn RANDSF RANDA / link=linear
method=ipcw(strata=trt01pn);
    lsmeans trt01pn;
run;
```

12.6 SAS code for estimating mean change, 95% CI and P-value from MMRM

The following programming statements to obtain the mean change, 95% CI and P-value:

```
ODS output diff=diffs ;
proc mixed data=ADQS;
    class ACTARMCD AVISIT SUBJID RANDQ1 RANDQ2;
    Model CHG= ACTARMCD AVISIT ACTARMCD*AVISIT BASE RANDQ1 RANDQ2/s
ddfm=kr;
    Repeated AVISIT/type=UN subject=SUBJID(ACTARMCD);
```

```
lsmeans actarmcd/diff cl;
```

```
run;
```

- Use the following programming statements to obtain the Mean Change, 95% CI and P-value

```
ODS output Diffs=diffs(where=(ACTARMCD ne _ACTARMCD));
```

```
PROC MIXED DATA=ADQS;
```

```
class ACTARMCD AVISIT SUBJID RANDQ1 RANDQ2;
```

```
model CHG = ACTARMCD AVISIT ACTARMCD*AVISIT BASE RANDQ1 RANDQ2/s ddfm=kr;
```

```
repeated AVISIT/type=UN subject=SUBJID(ACTARMCD);
```

```
lsmeans actARMCD/diff cl;
```

```
RUN;
```

12.7 Scoring of EORTC QLQ-C30 core questionnaire

The EORTC QLA-C30 version 3.0 questionnaire (1) has been developed to assess the quality of life of cancer patients.

The QLQ-C30 is composed of both multi-item scales and single-item measures. It consists of 30 items assessing five functional scales, three symptom scales, a global health status / QoL scale, and six single items. All the scales and single-item measures range in score from 0 to 100. A higher scale score represents a higher response level.

Table 7: Scoring the QLQ-C30 version 3.0

EORTC QLQ-C30 Scores dimensions	Abbreviation	Number of questions	Question range*	Version 3.0 question number (q)
Global Health status / QoL				
Global health status/QoL (revised) †	QL2	2	6	29,30
Functional scales				
Physical Functioning (revised) †	PF2	5	3	1 to 5
Role Functioning (revised) †	RF2	2	3	6,7
Emotional Functioning	EF	4	3	21 to 24
Cognitive Functioning	CF	2	3	20,25
Social Functioning	SF	2	3	26,27
Symptom scales/items				
Fatigue	FA	3	3	10,12,18
Nausea and Vomiting	NV	2	3	14,15
Pain	PA	2	3	9,19
Dyspnoea	DY	1	3	8
Insomnia	SL	1	3	11
Appetite loss	AP	1	3	13
Constipation	CO	1	3	16
Diarrhoea	DI	1	3	17
Financial difficulties	FI	1	3	28

* Question range is the difference between the possible maximum and the minimum response to individual questions; most questions take values from 1 to 4, giving range = 3.

† (revised) dimensions are those that have been changed since version 1.0, and their short names are indicated in this manual by a suffix “2” – for example, PF2.

12.7.1 Scoring process

Every dimension (column 1) in Table 2 has a specific number of questions assigned that are used to obtain the score.

For instance, for Global health status (QL2) dimension, there are two questions (number 29 and 30) used to obtain the score. The raw score for each dimension is calculated by averaging all the questions assigned to the specific dimension, as illustrated in Table 3.

For example, for QL2 we obtain the raw score by adding q29 and q30 and dividing by two.

Raw score (RS)= (q29+q30)/2

Once the raw score is obtained a linear transformation is applied. In the case of Global Health status (QL2) the transformation (Table 8) is:

$S = \{(RS-1)/range\} \times 100$

The scoring process for the dimensions (Table 7) is the same in all cases. A summary of the process is described in Table 8 below.

Table 8: Technical Summary for Scoring QLQ-C30 Questionnaire

Technical Summary	
In practical terms, if question Items $q_1, q_2, \dots, q_n$ are included in a scale, the procedure is as follows:	
Raw score	
Calculate the raw score	Raw Score (RS) = $(q_1 + q_2 + \dots + q_n) / n$
Linear Transformation	
Apply the linear transformation to 0-100 to obtain the score S,	
Functional scales:	$S = \{1 - (RS - 1) / \text{range}\} \times 100$
Symptom scales/items:	$S = \{(RS - 1) / \text{range}\} \times 100$
Global Health Status/QoL:	$S = \{(RS - 1) / \text{range}\} \times 100$
Range is the difference between the maximum possible value of RS and the minimum possible value	

12.8 EORTC QLQ-OV28 ovarian cancer

The QLQ-OV28 is a supplementary questionnaire (which is usually employed in conjunction with the QLQ-C30). The EORTC QLQ-OV28 assesses the quality of life of women with ovarian cancer in clinical trials. It was designed for patients with local or advanced disease who receive treatment by surgery with or without chemotherapy. It consists of 28 items assessing abdominal/GI symptoms, peripheral neuropathy, other chemotherapy side effects, hormonal symptoms, body image, attitudes to disease/treatment, and sexuality.

12.8.1 Scoring of the ovarian cancer module

The scoring approach for the ovarian cancer module is identical in principle to that used for the scales/items of the EORTC QLQ-C30 (Table 7). For each multi-item scale, calculate the average of the corresponding items. For each single-item measure, the score of the concerning item corresponds to the raw score. Consider that the scoring of questions 55, 56 and 57 must be reversed prior to statistical analysis.

Table 9: Scoring the QLQ-OV28

EORTC QLQ-OV28 Scores dimensions	Number of questions	Item range*	QLQ-OV28 question number (q)	Reverse scoring questions
Symptom scales / items				
Abdominal/gastrointestinal symptoms	7	3	31-37	
Peripheral neuropathy	3	3	41-43	
Other chemotherapy side-effects ^{a, b}	7	3	38-40, 44-47	
Hormonal/menopausal symptoms	2	3	48,49	
Body image	2	3	50,51	
Attitude to disease and treatment	3	3	52-54	
Sexuality ^c	2/4	3	55-58	55, 56, 57

* “Item range” is the difference between the possible maximum and the minimum response to individual items. All items are scored 1 to 4, giving range = 3.

^a The “other chemotherapy side effects” scale is composed of 7 items which may not be highly intercorrelated depending on the administered treatment. In case of doubt, it is advised to investigate these 7 items individually.

^b Item 39 is conditional and must not be scored if the response to question 38: ‘Have you lost any hair?’ is ‘not at all’.

^c Items 57 and 58 are conditional and must not be scored if the response to question 56 (‘To what extent were you sexually active?’) is ‘not at all’. If items 57 and 58 are not applicable, then the sexuality scale is composed only of items 55 and 56.

If there are missing items in a scale, the scale score will be calculated on the completed items if at least 50% of the component items have been completed; otherwise, the scale score is regarded as missing.

12.9 Safety Topics of Interest

Topic	Definition	Search methodology	Search strategy
<u>Excessive GR antagonism</u>	A syndrome with severe (Grade 3 or higher) symptoms which is caused by excessive antagonism of the glucocorticoid receptor after treatment with a competitive antagonist	Algorithm based on the search strategy	Two or more of the following specified AEs with temporal association (event onset +/- 2 days) and at least 1 has CTCAE toxicity grade = Grade 3 or higher: • Fatigue • Decreased appetite • Nausea • Vomiting • Abdominal pain

Topic	Definition	Search methodology	Search strategy
<u>Adrenal insufficiency</u>	Deficiency of cortisol produced by the adrenal cortex that leads to under-stimulation of both the glucocorticoid receptor AND the mineralocorticoid receptor	MedDRA HLT (Predefined Preferred Term list)	Adrenal cortical hypofunctions (HLT)
<u>Neutropenia</u>	An abnormally low count of neutrophils	Sponsor-defined PT list	Neutropenia, Febrile neutropenia, Neutropenic sepsis, Neutrophil count decreased
<u>Thrombocytopenia</u>	A reduction in platelet count	Sponsor-defined PT list	Thrombocytopenia, Platelet count decreased, Thrombocytopenic purpura
<u>Anemia</u>	A reduction in hemoglobin or hematocrit or red blood cell count	Sponsor-defined PT list	Anaemia, Haematocrit decreased, Haemoglobin decreased, Red blood cell count decreased
<u>Peripheral neuropathy</u>	Impairment of the peripheral motor, sensory and autonomic nervous system	MedDRA SMQ	Peripheral neuropathy (SMQ) (broad)
<u>Cutaneous toxicity</u>	Toxicity that affects the skin	MedDRA SOC (Predefined PT list)	Skin and subcutaneous tissue disorders (SOC)
<u>Oedema</u>	Fluid accumulation in the intercellular tissue space	MedDRA SMQ	Haemodynamic oedema, effusions and fluid overload SMQ
<u>Sepsis</u>	Organ dysfunction caused by a dysregulated host response to infection	MedDRA SMQ	Sepsis (SMQ) (narrow)