Protocol MDV3800-14

A Phase 1, Open-Label Study to Assess the Effects of Talazoparib on Cardiac Repolarization in Patients With Advanced Solid Tumors

Statistical Analysis Plan
Shells and Specifications

Version: 1.0

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FINAL STATISTICAL ANALYSIS PLAN APPROVAL

A Phase 1, Open-Label Study to Assess the Effects of Talazoparib on Cardiac Repolarization in Patients With Advanced Solid Tumors

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1. VERSION HISTORY

This Statistical Analysis Plan (SAP) for study MDV3800-14 is based on the protocol amendment 1 dated 19AUG2016.

Table 1 Summary of Major Changes in SAP Amendments

SAP Version	Change	Rationale
1.0		

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in study MDV3800-14.

The data will be analyzed by Medivation (a wholly owned subsidiary of Pfizer Inc.) and ERT Inc. (a designated CRO).

All analyses stated in this Statistical Analysis Plan will be performed using SAS® software version 9.4 or later.

2.1. Study Design

This is a phase 1, open-label safety study of talazoparib (also known as MDV3800, BMN 673), a poly(ADP-ribose) polymerase (PARP) inhibitor in development for treatment of a variety of human cancers. This study is designed to evaluate the effects of talazoparib on cardiac repolarization in at least 30 patients with advanced solid tumors with no available standard treatment options. Eligible patients will have continuous 12-lead electrocardiogram (ECG) recordings at baseline (day -1); time-matched pharmacokinetic (PK) samples and continuous ECG recordings will be obtained at days 1, 2, and 22; single ECGs will be collected at screening and safety follow-up. Patients will fast for at least 6 hours before and 2 hours after the dose on days 1 and 22.

On day -1, patients will have continuous 12-lead ECG recording, starting at time 0 (baseline, corresponding to the dosing time on day 1) and continuing for 6 hours. On day 1, within 72 hours of time 0, continuous 12-lead ECG recording will start 45 minutes before administration of talazoparib 1 mg at time 0, and continue through 6 hours postdose. Blood samples for PK will be collected predose and at 1, 2, 4, and 6 hours postdose. On day 2 (24 hours after the first dose of study drug), a 30-minute continuous 12-lead ECG recording and a blood sample for PK will be obtained before the day 2 dose of talazoparib. On days 3 to 21, talazoparib at 1 mg/day every day will be self-administered orally. On days 8 and 15, patients will return for general assessments.

On day 22, patients will return for steady-state continuous 12-lead ECG recordings, starting 45 minutes before the dose of talazoparib, and continuing for 6 hours postdose. PK samples will be collected predose and at 1, 2, 4, and 6 hours postdose.

ECG data from continuous 12-lead ECG recordings will be submitted for independent central review. After reviewing for data quality, triplicate 10-second ECGs will be extracted from a 5-minute extraction window at each planned time point, beginning 15 minutes before each

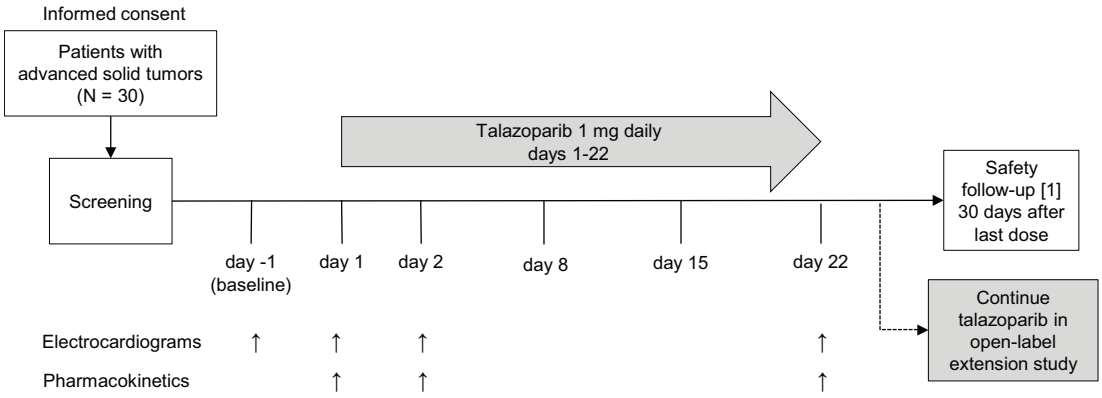
PK collection time point. ECG recordings will be analyzed for measurement of RR, PR, QRS, and QT intervals and evaluation of ECG morphology.

Study periods include screening, baseline (day -1), a 22-day treatment period, and safety follow-up. Safety follow-up will occur approximately 30 days after the last dose of study drug or before initiation of a new antineoplastic therapy, whichever occurs first. Safety follow-up will be omitted for patients who enroll and initiate continued talazoparib treatment within 30 days after the last dose of study drug in a separate open-label extension study; an ECG will be obtained at the time of enrollment in the open-label extension study.

Disease assessments performed at screening will include computed tomography (CT) scans or magnetic resonance imaging (MRI) for assessments of soft tissue disease and other assessments (eg, bone scan, prostate-specific antigen or other tumor markers) as appropriate for the type of cancer and sites of disease. Continuous ECGs will be collected on days -1, 1, 2, and 22; and PK samples will be collected on days 1, 2, and 22. Other general and laboratory assessments will be performed at screening; days -1, 1, 2, 8, 15, and 22; and safety follow-up according to the schedules of activities. Safety will be assessed by adverse events, physical examinations, vital signs, ECGs, and clinical laboratory tests. No efficacy assessments will be performed for this study.

The study design is summarized graphically in Figure 1.

Figure 1. Overall Study Design



[1] Safety follow-up will be omitted for patients who enroll and initiate continued talazoparib treatment within 30 days in the open-label extension study; an ECG will be obtained at the time of enrollment in the open-label extension study.

2.2. Study Objectives

2.2.1. Primary Objectives

- To evaluate the effect of talazoparib on cardiac repolarization in patients with advanced solid tumors by assessing the corrected QT interval (QTc)
- To assess the relationship between plasma talazoparib concentrations and the QTc

2.2.2. Secondary Objectives

- To evaluate the safety and tolerability of talazoparib
- To evaluate the effect of talazoparib on heart rate (HR), RR, PR, QRS intervals, and ECG morphology
- To evaluate the pharmacokinetics (PK) of talazoparib

3. ENDPOINTS AND BASELINE VARIABLES

3.1. Primary Endpoints

- Time-matched change from baseline in QTc corrected for HR based on the Fridericia's correction method (QTcF) method (ΔQTcF)
- Evaluation of the relationship between the plasma concentration of talazoparib and the change from baseline in QTc, corrected for HR based on the Fridericia's correction method (QTcF) method (ΔQTcF)

3.2. ECG Secondary Endpoints

- Time-matched change from baseline in QTc, corrected for HR based on the Bazett's correction method (QTcB) method (ΔQTcB)
- Heart rate
- PR interval
- RR interval
- QRS interval
- QT interval (uncorrected)
- ECG morphology

3.3. Baseline Variables

The baseline characteristics include:

- Age
- Sex
- Race
- Height

- Weight
- Eastern Cooperative Oncology Group (ECOG) performance status
- Primary diagnosis
- Prior surgeries
- Prior systemic anti-cancer therapies
- Prior radiotherapy

3.4. Safety Endpoints

3.4.1. Adverse Events

All adverse events will be graded by the Investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 and coded by system organ class (SOC) and preferred term (PT) based on Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.

3.4.2. Laboratory Data

Laboratory data in this study consist of hematology and blood chemistry values. Laboratory values will be classified by severity using the CTCAE v4.03, as appropriate.

3.4.3. Vital Signs

Temperature, blood pressure (systolic and diastolic), heart rate, respiration rate will be collected at baseline and each subsequent scheduled assessment.

3.4.4. Electrocardiogram

Single safety ECGs will be collected at screening and safety follow-up.

4. ANALYSIS POPULATIONS

4.1. Screened Population

Screened population includes all patients who have signed the informed consent form (ICF) and completed the screening phase.

4.2. Screening Failures

Screening failures include patients who have signed the ICF but failed eligibility criteria in the study.

4.3. Enrolled Population

Enrolled population includes all patients who have met all inclusion/exclusion criteria and enrolled into the study.

4.4. Saftey Population

Safety population consists of all patients who receive any amount of talazoparib.

4.5. Electrocardiographic Analysis Population

The ECG analysis population is defined as all enrolled patients who receive at least 1 dose of talazoparib, and have at least 1 available baseline and one on-treatment ECG data.

4.6. Pharmacokinetic Population

The PK population is defined as all patients who receive at least 1 dose of talazoparib and provide at least 1 reportable concentration.

4.7. Pharmacokinetic Analysis Population

The PK analysis population is defined as all patients who have sufficient concentration data to derive at least 1 PK parameter.

4.8. Pharmacokinetic-Pharmacodynamic Analysis Population

The pharmacokinetic-pharmacodynamic (PK-PD) population analysis is defined as all patients in the ECG Analysis Population who have at least one time-matched pair of plasma concentration and ECG measurement obtained at the same nominal time point and meet the additional requirements as follows:

- The actual time of the ECG must deviate ≤ 0.5 hour from the corresponding time-matched PK measurement (ie, abs[ECG time – PK time] ≤ 0.5 hour)
- A valid date and time must be reported for all PK concentration records
- PK concentrations scheduled as postdose must have actual times confirming that they will be taken on or after the dose time
- PK concentrations scheduled as predose must have actual times showing they will be actually taken on or before the dose time

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Definitions

5.1.1. Study Drug

The study drug is talazoparib (ie, MDV3800), which is administered daily for 22 days as part of the study procedure.

5.1.2. Date of First Dose

Date of first dose is the first date when a non-zero dose of study drug is administered in the treatment phase.

5.1.3. Study Day

Study day will be calculated in reference to the date of first dose.

For assessments conducted on or after the first dose, study day is calculated as (assessment date – first dose date + 1).

For assessments conducted before the first dose date, study day is calculated as (assessment date – first dose date).

The study day will be displayed in all relevant data listings.

5.1.4. Treatment-Emergent Period

The treatment emergent period is defined as the period of time from the date and time of the first dose of study drug treatment through 30 days after the last dose (ie, permanent discontinuation), before initiation of a new antineoplastic therapy, or enrollment in the open-label extension study, whichever occurs first.

5.1.5. Baseline and Post-baseline Values

Unless otherwise specified, the baseline value is defined as the last measurement before the first administration (date and time) of study drug. Post-baseline values are defined as measurements taken after the first administration of study drug. Change from baseline is defined as (post-baseline value – baseline value). Both date and time of study drug administration and measurement will be considered when calculating baseline value. If time is not available, then only the date will be used.

5.2. Study Visits and Time Points

Study visits and time points will be determined from the scheduled times as reported on the electronic case report form (eCRF) for the summarization and analysis of data that are shown by time point unless otherwise specified.

5.2.1. Timing of ECG Holter Extraction

ECGs will be recorded with continuous 12-lead ECG recordings on days -1, 1, 2, and 22. Triplicate ECGs will be extracted at the following time points:

- Day -1: 0, 1, 2, 4, and 6 hours
- Day 1: pre-dose and 1, 2, 4, 6 hours post-dose
- Day 2: pre-dose (24 hours following dose time on day 1)
- Day 22: pre-dose and 1, 2, 4, 6 hours post-dose

5.2.2. Timing of PK Sample Collection

PK samples will be collected at the following time points:

- Day 1: pre-dose and 1, 2, 4, 6 hours post-dose

- Day 2: pre-dose (24 hours following dose time on day 1)
- Day 22: pre-dose and 1, 2, 4, 6 hours post-dose

5.3. ECG Methodology

5.3.1. 12-Lead ECG Acquisition and Analysis

ECGs will be obtained digitally using a Mortara Instrument (Milwaukee, WI, USA) H-12+ ECG continuous 12-lead digital recorder, which will record ECGs on days -1, 1, 2, and 22 of the trial. The ECGs are stored continuously on a flash card and are not available for review until the card is received by ERT and analyzed. However, safety ECGs (standard digital 12-lead) will be immediately available to site staff for assessment. ECGs to be used in the analysis will be selected at predetermined time points as detailed below and will be read centrally using a high-resolution manual on-screen caliper semiautomatic method with annotations.

The 12-lead digital continuous ECG signals for each session for each patient will be recorded on compact flash memory cards provided to the site. The patient's unique identification number and demographic information will be recorded for each card. Without knowledge of patient treatment assignment, ERT will generate triplicate 10-second, 12-lead digital ECGs at each time point specified in the protocol. If targeted ECG time points are artifactual and of poor quality, ERT will capture analyzable 10-second ECGs as close as possible to the targeted time points.

Digital ECGs will be transmitted to ERT's validated data management system, EXPERT. Interval duration measurements will be collected using computer-assisted caliper placements on three consecutive beats. Trained analysts will then review all ECGs for correct lead and beat placement and will adjudicate the pre-placed algorithm calipers as necessary using the proprietary validated electronic caliper system applied on a computer screen. A cardiologist will then verify the interval durations and perform the morphology analysis, noting any T-U wave complex that is compatible with an effect on cardiac repolarization.

The ECG analysis will be conducted in Lead II and when Lead II is not analyzable, then in Lead V5. If Lead V5 is not analyzable, the Lead V2 will be used, followed by the most appropriate lead if necessary. ECG readers will be blinded to patient identifiers, treatment, and visit.

On-screen measurements of the RR, PR, QRS, and QT interval durations will be performed and QTcB, QTcF, and heart rate will be derived by the following processes:

- Three (3) RR: mean RR Interval is reported
- Three (3) PR: mean PR Interval is reported
- Three (3) QRS: mean QRS Width is reported
- Three (3) QT: mean QT Interval is reported

The following calculations will be made from the interval measurements:

Three (3) QTcF measurements - QTc correction by the Fridericia's Formula

- $QTcF1 = QT1/(RR1)^{1/3}$
- $QTcF2 = QT2/(RR2)^{1/3}$
- $QTcF3 = QT3/(RR3)^{1/3}$
- Mean QTcF = (QTcF1 + QTcF2 + QTcF3)/3

Three (3) QTcB measurements - QTc correction by the Bazett's Formula

- $QTcB1 = QT1/(RR1)^{1/2}$
- $QTcB2 = QT2/(RR2)^{1/2}$
- $QTcB3 = QT3/(RR3)^{1/2}$
- Mean QTcB = (QTcB1 + QTcB2 + QTcB3)/3

Three (3) Heart Rate Measurements

- HR1 = 60 / RR1
- HR2 = 60 / RR2
- HR3 = 60 / RR3
- Mean HR = (HR1 + HR2 + HR3)/3

Each fiducial point (onset of P wave, onset of Q wave, offset of S wave, and offset of T wave) will be electronically marked. The original ECG waveform and such annotations will be saved separately in XML format for independent review.

5.3.2. Concept and Criteria for ECG Analysis

The ECG interval durations will be subjected to the following plan: to describe central tendency and outlier effects for each of heart rate, PR, QRS, QT, and QTc (2 types of QTc: Fridericia's correction and Bazett's correction) intervals. The Fridericia's QTc method will be utilized for analysis as the primary endpoint. The Bazett's QTc correction is presented for comparison. New ECG morphological changes will also be defined. "New" is defined as "not present on any baseline ECG but present on any on-treatment ECG."

5.3.3. QT Correction Formulae

The physiologically inverse relationship between heart rate and QT interval requires an adjustment process to 'correct', or 'normalize', the QT interval to the heart rate. Therefore, the corrected QT interval (QTc) allows comparisons of QTc intervals across a range of heart rates.

Where data are available, the following QTc intervals will be computed for each patient.

Correction formulae included are QTcF and QTcB. The corrected QT intervals, QTcB and QTcF, are defined as:

QTcF is the length of the QT interval corrected for heart rate by Fridericia's formula:

- $QTcF = QT/(RR)^{1/3}$

QTcB is the length of the QT interval corrected for heart rate by Bazett's formula:

- $QTcB = QT/(RR)^{1/2}$

5.4. Standard Derivations and Reporting Conventions

Descriptive statistics (the number of patients [n], mean, standard deviation [SD], median, minimum, and maximum) will be used to summarize continuous variables. Means will be presented to 1 more decimal place than the recorded data. Medians will be presented using the same number of decimal places as the recorded data unless the calculated median results in an additional decimal place ending in '5' (ie, 5 and 7 = 6, 5 and 8 = 6.5, etc). Standard deviations will be presented to 2 more decimal places than the recorded data. Minimum and maximum values will be presented using the same number of decimal places as the recorded data.

Frequency distributions (number [n] and percentage of patients [%]) will be used to summarize categorical or qualitative variables. In general, the denominator for the percentage calculation will be based upon the total number of patients in the study population for that particular time point assessment. Records that are missing or not done will not be factored into the percentage calculation, unless otherwise specified.

Percentages will be presented to a maximum of 1 decimal place.

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

- 1 year = 365.25 days. Year is calculated as (days/365.25) rounded up to 1 significant digit
- 1 month = 30.4375 days. Month is calculated as (days/30.4375) rounded up to 1 significant digit
- Age will be calculated as the integer relative to the patient's signed informed consent date and Date of Birth.
- 1 pound = 0.454 kg
- 1 inch = 2.54 cm
- Missing data will not be imputed unless otherwise specified
- For laboratory results collected as < or > for a numeric value, 0.0000000001 will be subtracted or added, respectively, to the value

- For safety analyses, percentages will be calculated based on the number of patients in the safety population

- For by-visit observed data analyses, percentages will be calculated based on the number of patients with non-missing data as the denominator unless otherwise specified

- Medical history and adverse events will be coded using the MedDRA, version 19.1

- Prior therapies and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD), version Q12016.

5.5. Handling of Missing Data

Unless otherwise specified, all data will be evaluated as observed, and no imputation method for missing values will be used.

5.5.1. **Missing Dates**

The imputed dates for adverse events 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 ≠ year of treatment start date, then set to January 1

  - 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 ≠ month and year of treatment start date, then set to first of the month

  - If start date is completely missing, set to treatment start date as long as adverse event end date is not prior to 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 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 1
  - 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 start date or end date of a medication is completely missing, do not impute

Listings will show the original date information without imputation, but derived parameters (treatment-emergent adverse event indicator and duration of adverse events) will be flagged.

5.5.2. Missing ECG Data

No values will be imputed for missing data. If one or two of the triplicate measurements for an ECG parameter are missed, the average of the remaining two measurements or the single measurement can be used in the analyses. If all triplicate measurements are missing at a timepoint for an ECG parameter, no values will be imputed for this timepoint.

6. ANALYSES AND SUMMARIES

6.1. Analyses for the Primary Objectives

6.1.1. Time-Matched Analyses

The change between baseline and post-dose ECG data will be calculated for each patient at each time point on each treatment day (Table 2). The estimate of the change from baseline (delta) will be calculated as the mean across all patients and its confidence interval (CI) will be calculated using PROC MEANS. For this analysis a 90% two-sided confidence interval (CI) will be calculated.

Table 2: Time Matching Schedule for Change from Baseline

Baseline Time Point	Treatment Time Point
Day -1 0 hours	Day 1 45 minutes pre-dose
Day -1 1 hour	Day 1 1 hour post-dose
Day -1 2 hours	Day 1 2 hours post-dose

Baseline Time Point	Treatment Time Point
Day -1 4 hours	Day 1 4 hours post-dose
Day -1 6 hours	Day 1 6 hours post-dose
Day -1 0 hours	Day 2 predose (24 hours after Day 1 dose)
Day -1 0 hours	Day 22 pre-dose
Day -1 1 hour	Day 22 1 hour post-dose
Day -1 2 hours	Day 22 2 hours post-dose
Day -1 4 hours	Day 22 4 hours post-dose
Day -1 6 hours	Day 22 6 hours post-dose

To evaluate the drug effect, the statistical hypotheses will be based upon the Intersection Union Test as specified below:

- H_O: $\cup \{\mu_{CBD(i)} \geq 10, i = 1, 2, \ldots, k$
- H_A: $\cap \{\mu_{CBD(i)}) < 10, i = 1, 2, \ldots, k$

Where $\mu_{CBD(i)}$ are the mean change from baseline of QTc for the drug at time point i for the post dose time points, respectively. Since the Intersection-Union Test can be applied here, no multiple endpoint adjustment is needed. Based on regulatory guidance for oncologic agents, this hypothesis is evaluated by observing if any of the time points have a 2-sided 90% upper confidence bound (ie, 1-sided 95%) which is equal to, or exceeds, 20 msec.

The upper limit of the 2-sided 90% CI on treatment will be compared to the 20 msec bound. If the upper limit of the 2-sided 90% CI for the studied dose falls below 20 msec, it will be concluded that the clinical dose does not prolong the QTc interval to a clinically significant degree.

The analysis also will be presented in a graphical manner: for each comparison of interest all CI's (corresponding to the number of post-baseline time points) will be presented for the clinical dose of talazoparib. All analyses will be separately done for QTc (QTcF and QTcB).

All data collected will be presented in data listings. Unscheduled ECGs and ECG data from patients excluded from an analysis population will be included in the listings but not used in the formal analyses.

6.1.2. **Pharmacokinetic-Pharmacodynamic Analysis**

A pharmacokinetic-pharmacodynamic (PK-PD) analysis will be performed using all patients in the PK-PD Analysis Population. This will be the second primary endpoint for this trial, as the most recent R3 Q&A document updating the ICH E14 Guidance specifies that concentration-response analysis, can serve as an alternative to the by-timepoint analysis or intersection-union test as the primary basis for decisions to classify the risk of a drug.

For this PK-PD analysis, a linear mixed effects modeling approach will be used to examine the relationship between the change from baseline in QTc intervals (QTcF and QTcB) and

the plasma concentration of talazoparib (see Equation 1 below). The model will include plasma concentration, time (categorical), and treatment with random subject effects on plasma concentration and the intercept included in the model. This model will be used to estimate the population slope and the standard error of the slope of the relationship between the change from baseline in QTc intervals and plasma concentrations of talazoparib. If this model does not converge, then plasma concentration will be included as a fixed effect only with intercept and subject included as random effects.

Equation 1: $Y_{lkt} = \mu_l + p_t + \theta C_{lkt} + W_k + D_k C_{kt} + \varepsilon_{lkt}$

Where the dependent variable ΔQTc (Y_{lkt}) for the l^{th} treatment, k^{th} subject and t^{th} timepoint and parameters are: μ_l is the treatment specific intercept, θ is the slope, C is the concentration, W_k is the random subject effect on the intercept, D_k is the random subject effect on the slope, p_t is the time effect on the intercept and ε_{lkt} is the residual error.

If the above model (Equation 1) does not converge, then the same model without the random subject effects on plasma concentration will be refit.

The following plots will be generated using data from individual subjects and mean data:

- Plots of QTc (QTcF and QTcB) changes from baseline versus plasma concentration of talazoparib collected at the corresponding timepoint for the population.

If the p-value of the slope is less than 0.05, then a linear relationship will be declared. The mean maximum effect as well as the upper one-sided 95% confidence interval (CI) will be calculated using the following equation:

Mean maximum effect: $\Delta QTc_{max} = \mu_l + \theta \overline{C_{max}}$

Where the mean C_{max} will be the geometric mean of the C_{max}.

The upper one-sided 95% (i.e., obtained from the upper CI of 2-sided 90%) confidence interval will be obtained from the upper 2-sided 90% C.I. obtained using a nonparametric bootstrap method.

Testing of model assumptions, testing for hysteresis, linearity, and goodness of model fit will be documented.

The modeling will be performed using the SAS procedure PROC MIXED using Satterthwaite degrees of freedom. The bootstrap procedure for calculating 90% 2-sided CIs will be programmed within the same program, using at least 10,000 replicates will also be programmed using SAS.

For talazoparib, the resulting parameters [β, *SE* β, p-value, predicted ΔQTc at average C_{max}, upper one-sided 95% CI of predicted ΔQTc, and overall model fit] will be summarized for QTcF and QTcB.

6.2. Analyses for the ECG Secondary Objective

6.2.1. Central Tendency Analyses

The ECG analysis will be based on defining the central tendency of all ECG interval parameter changes (heart rate, PR, QRS, QT, QTcF, and QTcB) as a change from baseline.

For this analysis, a time-matched baseline will be used. The baseline for comparisons in the time-matched analysis is defined as each patient's individual time point ECG mean measurement (the mean of the 3 replicates at each time point) on day -1. For each patient, this value will be subtracted from the time-matched value on days 1, 2, and 22 in order to calculate the change from baseline for each measurement.

Three ECGs will be collected at each time point to provide a more robust point estimate of that interval's value. The ECG interval values will be obtained by averaging the mean interval duration measurements from these 3 ECGs (or however many ECGs are actually available).

Descriptive statistics (e.g., frequency, percent, mean, standard deviation (SD), median, maximum, and minimum) will be used to summarize the ECG variables and the corresponding changes from the mean baseline to each time point, for each time point analysis. Additionally, data-based (ie, not model-based) 2-sided 90% confidence interval (CI) descriptive statistics will be summarized for the change from baseline data.

This will provide time point analyses which will be detailed in the tables but also demonstrated graphically with the x-axis showing the time (time point) and the y-axis showing the change from baseline for each of the ECG intervals parameters separately (ie, heart rate, PR, QRS, QT, QTcF, and QTcB).

The following central tendency analyses will be performed:

- A time-matched statistical analysis will be performed at each of the post-dose time points on days 1, 2, and 22 to determine if the upper 90% two-sided confidence interval (CI) exceeds 20 msec for ECG secondary endpoints

- Change from mean of all baseline ECGs to the mean of all post-treatment ECG values for a given patient for each ECG interval (traditional time-averaged analysis) for ECG secondary endpoints

- Descriptive analysis on the time-matched and time-averaged means for the ECG interval parameters: heart rate, PR, QRS, QT, and QTc (QTcF, and QTcB) will be listed in the tables

6.2.2. **Time-Averaged Analyses**

A time-averaged analysis for ECG interval data will be made using the endpoint "change from baseline" for each of the ECG interval parameters. In effect, for each patient, the baseline (mean of all ECGs collected on Day -1) will be subtracted from the mean of all post-treatment ECGs across all time points after the start of dosing.

6.2.3. **Outlier Analyses**

An outlier analysis supplements the central tendency analysis by determining if there were patients who had an exaggerated effect on any ECG interval that would not be revealed in a mean change from baseline central tendency analysis. Each patient would be considered having an outlier value based on the most-extreme value across all of the time points.

Therefore, the data will be presented as the frequency and percent of patients with each type of outlier. The following criteria ("study endpoints") are defined for this analysis ("new" means not present at baseline, and becomes present on at least 1 on-treatment ECG time point) where "baseline" is defined as the time-averaged value based on the mean of all ECGs on day -1 and predose from day 1:

Heart rate: A value for a patient is considered to be an outlier at pre-defined post dose time point if the heart rate measurement at that time point is < 50 beats per minute (bpm) and the measure is at least a 25% decrease from the patient's baseline mean heart rate (i.e., a bradycardic event) or if the heart rate measurement at the pre-defined post dose time point is > 100 bpm and the measure is at least a 25% increase from the baseline mean heart rate (i.e., a tachycardic event).

PR interval: A value for a patient is considered to be an outlier at a pre-defined post dose time point if the PR interval at that time point is > 200 msec and it is at least a 25% increase from the patient's baseline mean PR interval.

QRS interval: A value for a patient is considered to be an outlier at a pre-defined post dose time point if the QRS interval at that time point is > 100 msec and it is at least a 25% increase from the patient's baseline mean QRS interval.

QT interval: A value for a patient is considered to be an outlier at a pre-defined post dose time point if the QT interval at that time point is > 500 msec and the patient's baseline mean QT interval is ≤ 500 msec.

QTcB: A value for a patient is considered to be an outlier at a pre-defined post dose time point if the QTcB interval at that time point is > 500 msec and the patient's baseline mean QTcB interval is ≤ 500 msec. A value is also considered an outlier if the QTcB interval at a pre-defined post dose time point is > 480 msec when the patient's baseline mean QTcB interval is ≤ 480 msec and when the QTcB interval at a pre-defined post dose time point is > 450 msec when the patient's baseline mean QTcB interval is ≤ 450 msec. In addition, the number and percentage of patients with changes from baseline of > 30-60 msec and > 60 msec are presented.

QTcF: A value for a patient is considered to be an outlier at a pre-defined post dose time point if the QTcF interval at that time point is > 500 msec and the patient's baseline mean QTcF interval is ≤ 500 msec. A value is also considered an outlier if the QTcF interval at a pre-defined post dose time point is > 480 msec when the patient's baseline mean QTcF interval is ≤ 480 msec and when the QTcF interval at a pre-defined post dose time point is > 450 msec when the patient's baseline mean QTcF interval is ≤ 450 msec. In addition, the number and percentage of patients with changes from baseline of > 30-60 msec and > 60 msec are presented.

A categorical or outlier analysis is considered exploratory since the study is not powered to pick up unusual individual responses to the potential effects of drugs. The categorical analysis is assessed using the time-averaged baseline, comparing this baseline ECG interval value to all post-treatment ECG time points and then choosing the value that is the largest

positive change from baseline to define whether each patient falls into the outlier criterion. For heart rate, both the largest negative and positive value compared to baseline is chosen. Outlier analyses produce data as percentage of all patients that meet the criteria as defined for this analysis. The outlier summary tables include counts of patients. Therefore, if a patient experiences more than 1 episode of a particular outlier event, the patient will be counted only once for that event.

6.2.4. Morphological Analyses

Morphological analyses will be performed with regard to the ECG waveform interpretation as defined by the central ECG laboratory's cardiologist. Changes from baseline (looking at each of the baseline ECGs individually [day -1 and pre-dose on day 1] and each of the ECGs at all on-treatment ECGs) will be evaluated, through the last observation on Day 22.

All findings will be presented in the ECG listings. New onset (presented as percentage of patients meeting the new criteria) for the following variables will be detailed in the tables:

- Atrial fibrillation or flutter
- Second-degree heart block
- Third-degree heart block
- Complete right bundle branch block
- Complete left bundle branch block
- ST segment depression
- ST segment elevation
- T-wave abnormalities (negative T-waves only)
- Myocardial infarction pattern
- Any new abnormal U waves

6.3. Baseline Summaries and Other Analyses

6.3.1. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized for the safety population. The variables to be included in the summary are age, sex, race, ethnicity, baseline body weight, height, and body mass index (BMI). Age in years will be calculated as the whole number of years between the date of birth and the date of informed consent.

Cancer diagnosis, disease characteristics and ECOG performance status will be summarized using frequency counts and percentages.

6.3.2. **Medical History**

Verbatim medical history terms collected will be coded by SOC and PT based on MedDRA version 19.1 coding dictionary.

Medical History will be summarized by SOC and PT for the safety population.

6.3.3. **Prior and Concomitant Medications**

Prior and concomitant medications will be coded using the WHO-DD, and will be classified according to the default Anatomical Therapeutic Chemical (ATC) classification system code, WHO-DD Drug Name, and PT.

Depending on the start and stop dates of the medication, it is possible for a medication to be both prior and concomitant.

Prior and concomitant medications will be summarized by the highest ATC class level and PT for the safety population. Patients may have more than one medication per ATC category and PT. At each level of patient summarization, a patient will be counted once if he/she reports one or more medications at that specific level.

6.3.4. **Enrollment Status**

All inclusion/exclusion criteria met, not met, or not done will be provided in listings. These listings will also provide any eCRF data collected detailing the allowance of patients into a study if at least one inclusion/exclusion criterion is not met.

Additional patient informed consent and eligibility information collected on the eCRF will be also provided in a listing.

6.3.5. **Patient Disposition**

Patients included in the safety populations, who completed the study, discontinued with reasons for treatment discontinuation, and whether continued to the open-label extension (OLE) study, will be summarized and listed as well.

6.3.6. **Protocol Deviations**

Patients with major protocol deviations will be listed and categories of major deviations include at least one of the following:

- Eligibility criteria not met
- Excluded concomitant medication taken
- Informed consent not signed before study-specific procedures were performed

A detailed list of all major protocol deviations will be determined before the database lock and a listing of all major deviations will be provided.

6.3.7. Treatment Exposure and Compliance

Patient exposure and compliance to study drug will be summarized for the safety population, and the variables include duration of exposure in days, cumulative dose, percent of days received the planned dose, number of capsules taken and percent compliance.

Treatment compliance will be assessed based on patients' used and unused study drug containers and their completed study drug diary. Dose administration and treatment compliance will be listed for all patients.

6.4. Safety Summaries and Analyses

6.4.1. Adverse Events

An adverse event will be considered treatment-emergent adverse event (TEAE) if the onset date occurred on or after the administration of study drug. A study drug-related TEAE is defined as any TEAE with at least a possible relationship to the study drug as assessed by the investigator or that is missing the assessment of causal relationship whose relationship to the study drug could not be ruled out.

Summaries including the number of patients and percentages of the following adverse events will be provided:

- Overview of TEAE
- TEAE by SOC and PT
- TEAE by PT
- TEAE related to study drug by PT
- TEAE by SOC, PT, and maximum severity
- Serious TEAE by SOC and PT
- Serious TEAE related to study drug by PT
- TEAE leading to study drug discontinuation by SOC and PT

All AEs will be listed with its relationship to study drug and severity, flagging those which are not events during treatment-emergent period.

A listing of all deaths with date, cause and its relationship to study drug will be also listed.

Additionally, a separate listing of any serious adverse events among screening failures will be provided.

6.4.2. **Laboratory Data**

Quantitative laboratory test results and their change from baseline will be summarized by scheduled visit. The last non-missing value before the first dose of study drug will be used as baseline.

Shift tables using CTCAE v4.03 grades will be provided to compare the baseline with the worst post-baseline toxicity. For tests where CTCAE grades are not defined, results will be graded by the low/normal/high classifications based on laboratory normal ranges.

Liver tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline Phosphatase (ALP), and total bilirubin (TBL) are used to assess possible drug induced liver toxicity. The ratios of test result over the upper limit of normal (ULN) will be calculated and classified for these parameters. The number and percentage of patients with each of the following categories will be summarized:

- ALT ≥ 3xULN
- AST ≥ 3xULN
- ALT or AST ≥ 3xULN
- ALT or AST > 5xULN
- ALT or AST > 10xULN
- ALT or AST > 20xULN
- TBL > 2xULN
- ALT or AST ≥ 3xULN and TBL > 2xULN
- ALT or AST ≥ 3xULN and TBL > 2xULN and ALP < 2xULN
- Concurrent ALT or AST ≥ 3xULN and TBL > 2xULN
- Concurrent ALT or AST ≥ 3xULN and TBL > 2xULN and ALP < 2xULN

Concurrent measurements are those occurring on the same date.

All laboratory data will be provided in data listings.

6.4.3. **Vital Signs**

Change from baseline will be calculated and presented at scheduled postbaseline assessments for each vital sign parameter (ie, temperature, systolic and diastolic blood pressure, heart rate, respiration rate). Baseline results are defined as the last vital sign results taken before the date and time of the first dose of study drug.

Clinically notable changes in vital signs results will be summarized using frequency counts and percentages.

Vital sign data will be provided in a listing.

6.4.4. Electrocardiogram

Change from baseline will be calculated for the ECG parameters: heart rate, PR, QRS, QT, QTc (QTcF and QTcB). Baseline is defined as the measurement taken at screening visit.

Safety ECG data will be provided in a listing.

6.5. Pharmacokinetic Analyses

6.5.1. Pharmacokinetic Concentrations

Plasma talazoparib concentrations will be analyzed to assess the PK profiles. Individual and mean plasma concentrations will be listed and summarized by days. Individual concentrations that are excluded from the PK analyses will be annotated and excluded from summary statistics calculations. Values will be handled as follows:

- All plasma concentrations reported as no result (NR) values will be treated as missing and will appear in the dataset as "."
- For PK parameter calculations, plasma concentration values below the lower limit of quantitation (LLOQ) will be treated as 0 when they occur before the first measurable concentration; all other values below the LLOQ will be treated as missing and set to "."
- For summary statistics of plasma concentration-time data, plasma concentration values below the LLOQ will be set to 0
- Summary statistics will not be calculated if all values are below the LLOQ
- If the actual sample collection time deviates more than ± 15% from the nominal collection time, the corresponding plasma concentration value will be excluded from the descriptive statistics calculations.

Plasma concentrations will be tabulated and summarized descriptively by days. The following descriptive statistics will be calculated for each nominal sampling time: arithmetic mean (mean), SD, coefficient of variation (CV%), geometric mean (geomean), geometric coefficient of variation (geoCV%), minimum, median, maximum, and the number of measurements.

Graphics will be produced for plasma concentrations, including mean (SD) concentration-time profiles (both linear and semilogarithmic), individual concentration-time profiles (both linear and semilogarithmic), and overlay ("spaghetti") plots of individual concentration-time profiles.

6.5.2. Pharmacokinetic Parameters

Plasma PK parameters of talazoparib will be calculated from the plasma concentration-time data using noncompartmental methods (NCA) with Phoenix WinNonlin (Certara, Cary, NC). The calculated elapsed time postdose and actual dose will be used for all calculations.

The PK analyses will include descriptions of the PK by days. Selected PK parameters will be summarized, such as maximum plasma concentration (C_{max}), time to maximum plasma concentration (T_{max}), concentration at 24 hours (C_{24h}), area under the plasma concentration time-curve (AUC_{24h}), AUC accumulation ratio (AR) and apparent plasma clearance (CL/F). AUC_{24h} on Day 22 will be calculated by imputing Day 22 24 hour concentration to be the same as Day 22 predose concentration.

PK parameters of talazoparib will be listed by patient and summarized descriptively by day for the PK population. Exclusion of values from the summary statistics calculations due to dose changes (eg, dose interruptions, dose reductions) will be handled on a case-by-case basis. The following descriptive statistics of individual analytes will be provided for all PK parameters except T_{max}: n, arithmetic mean, SD, CV%, geomean, geoCV%, median, minimum, and maximum. For T_{max}, only n, median, minimum, and maximum will be reported. Descriptive statistics will be calculated only for PK parameters obtained from $n \geq 3$.

7. SAMPLE SIZE CONSIDERATIONS

A sample size of at least 27 evaluable patients will provide 80% power to reject the null hypothesis if the mean change from baseline in QTcF is ≥ 10 msec with one-sided 5% level of significance, assuming a standard deviation of 20 msec. To allow for 10% dropouts, 30 patients will be enrolled.

Patients will be enrolled until 30 patients complete day 22, miss ≤ 5 consecutive doses of study drug, have technically adequate ECG recordings, and have at least 80% of specified PK samples collected representing all 3-days of observation (days 1, 2 and 22).

8. INTERIM ANALYSES

N/A

9. REFERENCES

No literature reference is cited.

10. APPENDICES

Appendix 1. Clinical Study Report Tables, Listings, and Figures

CSR TLF No.	Title	Analysis Population	Analysis Performed by?
Tables			
14.1.1	Patient Disposition	Safety Population	MDVN/PFE
14.1.2	Analysis Populations	Enrolled Population	MDVN/PFE
14.1.3.1	Demographics and Baseline Characteristics	Safety Population	MDVN/PFE
14.1.3.2	Baseline Disease Characteristics	Safety Population	MDVN/PFE
14.1.4	Medical History by System Organ Class and Preferred Term	Safety Population	MDVN/PFE
14.1.5.1	Treatment Exposure and Compliance	Safety Population	MDVN/PFE
14.1.5.2	Concomitant Medications by ATC Class and Preferred Term	Safety Population	MDVN/PFE
14.3.1.1	Overview of Treatment-Emergent Adverse Events	Safety Population	MDVN/PFE
14.3.1.2	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population	MDVN/PFE
14.3.1.3	Treatment-Emergent Adverse Events by Preferred Term	Safety Population	MDVN/PFE
14.3.1.4	Treatment-Emergent Adverse Events Related to Study Drug by Preferred Term	Safety Population	MDVN/PFE
14.3.1.5	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity	Safety Population	MDVN/PFE
14.3.2.1	Serious Adverse Events by System Organ Class and Preferred Term	Safety Population	MDVN/PFE
14.3.2.2	Serious Adverse Events Related to Study Drug by Preferred Term	Safety Population	MDVN/PFE
14.3.2.3	Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term	Safety Population	MDVN/PFE
14.3.4.1	Hematology Shift Table by Worst Postbaseline Toxicity Grade	Safety Population	MDVN/PFE
14.3.4.2	Chemistry Shift Table by Worst Postbaseline Toxicity Grade	Safety Population	MDVN/PFE
14.3.4.3	Hematology Shift Table Based on Normal Range	Safety Population	MDVN/PFE
14.3.4.4	Chemistry Shift Table Based on Normal Range	Safety Population	MDVN/PFE
14.3.4.5	Change from Baseline Hematology Laboratory Result	Safety Population	MDVN/PFE
14.3.4.6	Change from Baseline Chemistry Laboratory Result	Safety Population	MDVN/PFE
14.3.4.7	Treatment-Emergent Liver Test Elevations	Safety Population	MDVN/PFE
14.3.5.1	Change From Baseline Vital Sign Results	Safety Population	MDVN/PFE

CSR TLF No.	Title	Analysis Population	Analysis Performed by?
14.3.5.2	Clinically Notable Changes in Vital Sign Results	Safety Population	MDVN/PFE
14.3.6	Change from Baseline ECG Results	Safety Population	MDVN/PFE
14.3.6.1.1	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - Heart Rate (bpm)	Electrocardiographic Population	ERT
14.3.6.1.2	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - PR Interval (msec)	Electrocardiographic Population	ERT
14.3.6.1.3	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - QRS Interval (msec)	Electrocardiographic Population	ERT
14.3.6.1.4	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - QT Interval (msec)	Electrocardiographic Population	ERT
14.3.6.1.5	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - QTc Fridericia (msec)	Electrocardiographic Population	ERT
14.3.6.1.6	Time-Matched and Time-Averaged ECG Central Tendency and Outlier Analyses - QTc Bazett (msec)	Electrocardiographic Population	ERT
14.3.6.1.7	Timepoint and Time-Averaged ECG Central Tendency and Outlier Analyses QTc Individual (ms)	Electrocardiographic Population	ERT
14.3.6.1.8	Timepoint and Time-Averaged ECG Central Tendency and Outlier Analyses QTc Fridericia (ms)	Electrocardiographic Population	ERT
14.3.6.2.1	Treatment-Emergent Abnormalities – Atrial Fibrillation	Electrocardiographic Population	ERT
14.3.6.2.2	Treatment-Emergent Abnormalities – Atrial Flutter	Electrocardiographic Population	ERT
14.3.6.2.3	Treatment-Emergent Abnormalities - Second Degree Heart Block	Electrocardiographic Population	ERT
14.3.6.2.4	Treatment-Emergent Abnormalities - Third Degree Heart Block	Electrocardiographic Population	ERT
14.3.6.2.5	Treatment-Emergent Abnormalities - Complete Right Bundle Branch Block	Electrocardiographic Population	ERT
14.3.6.2.6	Treatment-Emergent Abnormalities - Complete Left Bundle Branch Block	Electrocardiographic Population	ERT
14.3.6.2.7	Treatment-Emergent Abnormalities - ST Segment Depression	Electrocardiographic Population	ERT
14.3.6.2.8	Treatment-Emergent Abnormalities - ST Segment Elevation	Electrocardiographic Population	ERT
14.3.6.2.9	Treatment-Emergent Abnormalities - Negative (Inverted) T Waves	Electrocardiographic Population	ERT
14.3.6.2.10	Treatment-Emergent Abnormalities - Myocardial Infarction Pattern	Electrocardiographic Population	ERT
14.3.6.2.11	Treatment-Emergent Abnormalities - Abnormal U Waves	Electrocardiographic Population	ERT
14.3.6.3.1	Change from Baseline with 90% Two-Sided Confidence Interval - QTc Fridericia (msec)	Electrocardiographic Population	ERT
14.3.6.3.2	Change from Baseline with 90% Two-Sided Confidence Interval - QTc Bazett (msec)	Electrocardiographic Population	ERT

CSR TLF No.	Title	Analysis Population	Analysis Performed by?
14.4.1.1	Concentration-ECG Interval Effect Analysis- Change from Baseline versus the Talazoparib Plasma Concentration – Estimates from Linear Mixed Model -QTc Fridericia, QTc Bazett Interval (msec)	Safety Population	ERT
14.4.1.2	Individual and Summary of Plasma Talazoparib Concentrations	PK Population	MDVN/PFE
14.4.1.3	Individual and Summary of Plasma Talazoparib PK Parameters on Day 1	PK Analysis Population	MDVN/PFE
14.4.1.4	Individual and Summary of Plasma Talazoparib PK Parameters on Day 22	PK Analysis Population	MDVN/PFE
14.4.1.5	Overall Summary of Plasma Talazoparib PK Parameters	PK Analysis Population	MDVN/PFE
Figures			
14.3.6.1.1	Mean Change from Baseline- Heart Rate (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.3.6.1.2	Mean Change from Baseline- PR Interval (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.3.6.1.3	Mean Change from Baseline- QRS Duration (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.3.6.1.4	Mean Change from Baseline- QT Interval (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.3.6.1.5	Mean Change from Baseline- QTcF Interval (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.3.6.1.6	Mean Change from Baseline- QTcB Interval (Values with Means ± 90% CIs - Estimates and CI are model based)	Electrocardiographic Population	ERT
14.4.1.1	Change from Baseline QTcF Versus Mean Talazoparib Plasma Concentration Estimates from the Mixed Effects Model Regression	Pharmacokinetic-Pharmacodynamic Population	ERT
14.4.1.2	Change from Baseline QTcB Versus Mean Talazoparib Plasma Concentration Estimates from the Mixed Effects Model Regression	Pharmacokinetic-Pharmacodynamic Population	ERT
14.4.1.3	Mean (SD) Plasma Talazoparib Concentration-Time Profiles	PK Population	MDVN/PFE
14.4.1.4	Individual Plasma Talazoparib Concentration-Time Profiles for Day 1	PK Population	MDVN/PFE
14.4.1.5	Individual Plasma Talazoparib Concentration-Time Profiles for Day 22	PK Population	MDVN/PFE
14.4.2.1	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT
14.4.2.2	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT
14.4.2.3	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT
14.4.2.4	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT
14.4.2.5	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT
14.4.2.6	Subject Profiles: Change from Baseline vs Talazoparib Plasma Conc.	Individual (PK-PD Population)	ERT

CSR TLF No.	Title	Analysis Population	Analysis Performed by?
Listings			
16.2.1.1	Inclusion and Exclusion Criteria	Screened Population	MDVN/PFE
16.2.1.2	Patient Disposition	Safety Population	MDVN/PFE
16.2.2	Protocol Deviations	Safety Population	MDVN/PFE
16.2.3	Analysis Populations	Enrolled Population	MDVN/PFE
16.2.4.1	Baseline Demographics	Safety Population	MDVN/PFE
16.2.4.2	Baseline Disease Characteristics	Safety Population	MDVN/PFE
16.2.4.3	Medical History	Safety Population	MDVN/PFE
16.2.4.4	Prior Systemic Anti-Cancer Therapy	Safety Population	MDVN/PFE
16.2.4.5	Prior Radiation Therapy	Safety Population	MDVN/PFE
16.2.4.6	Prior Surgery for Cancer	Safety Population	MDVN/PFE
16.2.5.1	Dose Administration Record	Safety Population	MDVN/PFE
16.2.5.2	Drug Accountability	Safety Population	MDVN/PFE
16.2.5.3	Concomitant Medication	Safety Population	MDVN/PFE
16.2.5.4	Other Procedures	Safety Population	MDVN/PFE
16.2.7.1	Treatment-Emergent Adverse Events	Safety Population	MDVN/PFE
16.2.7.2	Serious Adverse Events	Screening Failures	MDVN/PFE
16.2.7.3	Deaths	Enrolled Population	MDVN/PFE
16.2.8.1	Hematology Laboratory Results	Safety Population	MDVN/PFE
16.2.8.2	Chemistry Laboratory Results	Safety Population	MDVN/PFE
16.2.8.3	Vital Sign Results	Safety Population	MDVN/PFE
16.2.8.4.1	ECG Results	Safety Population	MDVN/PFE
16.2.8.4.2	Listing of ECG Parameters -- Holter Extraction	Safety Population	ERT
16.2.8.4.3	Listing of ECG Morphology Interpretations -- Holter Extraction	Safety Population	ERT
16.2.8.5	Pregnancy Test Results	Safety Population	MDVN/PFE
16.2.8.6	Other Laboratory Results	Safety Population	MDVN/PFE
16.2.8.7	Individual Plasma Talazoparib Concentrations	PK Population	MDVN/PFE

Appendix 2. Shells and Specifications

Appendix 2.1. Section 14 Tables

Table 14.1.1: Patient Disposition (Safety Population)

Disposition Reason	Talazoparib 1 mg (N = xx)
Patients treated	xx (xx.x%)
Completed	xx (xx.x%)
Discontinued	xx (xx.x%)
Primary reason for treatment discontinuation	
Reason 1	xx (xx.x%)
Reason 2	xx (xx.x%)
Reason 3	xx (xx.x%)
Is patient continuing open-label extension study?	
Yes	xx (xx.x%)
No	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
Data source: Listing 16.2.1.2.

Table 14.1.2: Analysis Populations (All Enrolled)

Analysis Set	Talazoparib 1 mg (N = xx)
Safety population	xx (xx.x%)
ECG analysis population	xx (xx.x%)
PK population	xx (xx.x%)
PK analysis population	xx (xx.x%)
PK-PD analysis population	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
ECG: electrocardiogram, PD: pharmacodynamics, PK: pharmacokinetics
The safety population includes all patients who receive any amount of talazoparib.
The ECG analysis population consists of all enrolled patients who receive at least 1 dose of talazoparib, and have at least 1 available baseline and 1 on-treatment ECG data.
The PK population is defined as all patients who receive at least 1 dose of talazoparib and provide at least 1 reportable concentration.
The PK analysis population is defined as all patients who have sufficient concentration data to derive at least 1 PK parameter.
The PK-PD analysis population is defined as all patients in the ECG analysis population who have at least 1 time-matched pair of plasma concentration and ECG measurements obtained at the same nominal time point.
Percentage is based on N.
Data source: Listing 16.2.3.

Table 14.1.3.1: Demographics and Baseline Characteristics (Safety Population)

Demographic Variable	Talazoparib 1 mg (N = xx)
Age (years)	
n	xxx
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	xx.x, xx.x
Sex	
Female	xx (xx.x%)
Male	xx (xx.x%)
Missing	xx (xx.x%)
Race	
American Indian or Alaska Native	xx (xx.x%)
Asian	xx (xx.x%)
Black or African American	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)
White	xx (xx.x%)
Other	xx (xx.x%)
Missing	xx (xx.x%)
Ethnicity	
Hispanic or Latino	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)
Other	xx (xx.x%)
Unknown	xx (xx.x%)
Weight (kg)	
n	xxx
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	xx.x, xx.x
Height (cm)	

Demographic Variable	Talazoparib 1 mg (N = xx)
n	xxx
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	xx.x, xx.x
Body mass index [BMI] (kg/m^2)	
n	xxx
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, Min: minimum, Max: maximum, n: counts of non-missing values.
Percentage is based on N.
Data source: Listing 16.2.4.1.

Programming Specification:

- 'Missing' is shown only if the count is not zero.

Table 14.1.3.2: Baseline Disease Characteristics (Safety Population)

Disease Characteristics	Talazoparib 1 mg (N = xx)
Primary Cancer Site	
Breast	xx (xx.x%)
Colorectal	xx (xx.x%)
Liver	xx (xx.x%)
Lung	xx (xx.x%)
Kidney	xx (xx.x%)
Ovary	xx (xx.x%)
Prostate	xx (xx.x%)
Melanoma	xx (xx.x%)
Other	xx (xx.x%)
Staging at Initial Diagnosis [1]	
Primary Tumor:	xx (xx.x%)
T0	xx (xx.x%)
T1	xx (xx.x%)
T2	xx (xx.x%)
T3	xx (xx.x%)
T4	xx (xx.x%)
TX	xx (xx.x%)
Regional Lymph Nodes:	
N0	xx (xx.x%)
N1	xx (xx.x%)
N2	xx (xx.x%)
N3	xx (xx.x%)
NX	xx (xx.x%)
Distant Metastases:	
M0	xx (xx.x%)
M1	xx (xx.x%)

Disease Characteristics	Talazoparib 1 mg (N = xx)
MX	xx (xx.x%)
Histopathological Type at Initial Diagnosis	
Adenocarcinoma	xx (xx.x%)
Squamous Cell Carcinoma	xx (xx.x%)
Other	xx (xx.x%)
ECOG performance status	
0	xx (xx.x%)
1	xx (xx.x%)
2	xx (xx.x%)
3	xx (xx.x%)
4	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
AJCC: American Joint Committee on Cancer, ECOG: Eastern Cooperative Oncology Group.
[1] The Classification of Staging at Initial Diagnosis are as per AJCC Staging Manual Sixth Edition.
Data source: Listing 16.2.4.2.

Table 14.1.4: Medical History by System Organ Class and Preferred Term (Safety Population)

System Organ Class Preferred Term	Talazoparib 1 mg (N = xx)
Number of Patients Who Had at Least One Medical History	xx (xx.x%)
SOC 1 <- total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
preferred term 3	xx (xx.x%)
SOC 2 <- total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
preferred term 3	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
A patient with multiple occurrences of a given preferred term within a system organ class is counted once only in the total row.
Preferred terms are sorted within system organ class in descending frequency and then alphabetically.
Percentage is based on N.
Data source: Listing 16.2.4.3.

Programming Specification:

- System organ classes are presented in descending frequency and then alphabetically.
- Preferred terms are sorted within system organ class in descending frequency and then alphabetically.

Table 14.1.5.1: Treatment Exposure and Compliance (Safety Population)

Category	Talazoparib 1 mg (N = xx)
Duration of Exposure (Days)	
= 22	xx (xx.x%)
< 22	xx (xx.x%)
Cumulative Dose (mg)	
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	xx.x, xx.x
Percent of Days Received Planned Dose [1]	
= 100%	xx (xx.x%)
80% -< 100%	xx (xx.x%)
< 80%	xx (xx.x%)
Number of Capsules Taken [2]	
Mean (SD)	xx.x (x.xx)
Median	xx.x
Min, Max	xx.x, xx.x
Percent of Compliance [3]	
= 100%	xx (xx.x%)
80% -< 100%	xx (xx.x%)
< 80%	xx (xx.x%)

Category	Talazoparib 1 mg (N = xx)
The date of analysis data transfer is DDMONYYYY. A patient is counted in one duration range only. SD: standard deviation, Min: minimum, Max: maximum. Percentage is based on N. [1] Denominator is defined as number of scheduled days of full dosing as per protocol. [2] Total number of capsules taken is calculated as the number of capsules dispensed at all visits minus the number of capsules returned. [3] Percent compliance is calculated as the number of capsules taken divided by the expected number of capsules taken, multiplied by 100. Data source: Listing 16.2.5.1 and Listing 16.2.5.2.	

Programming Specification:

- Duration of exposure in days = Last dosing date – First dosing date + 1 excluding dose interruptions.

Table 14.1.5.2: Concomitant Medications by ATC Class and Preferred Term (Safety Population)

ATC Class Preferred Term	Talazoparib 1 mg (N = xx)
Number of Patients Who Had at Least One Concomitant Medication	xx (xx.x%)
ATC 1 <-total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
ATC 2 <-total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
ATC: anatomical therapeutic chemical classification system using the World Health Organization Drug Dictionary (WHO-DD).
Medications are considered concomitant if taken during the treatment period.
A medication can appear with more than one ATC class.
A patient with multiple generic medication names within an ATC class is counted once only in the total row.
ATC classes are presented in descending frequency and then alphabetically. Preferred terms are sorted within ATC class in descending frequency and then alphabetically.
Percentage is based on N.
Data source: Listing 16.2.5.3.

Programming Specification:

- ATC classes are presented in descending frequency and then alphabetically.
- Preferred terms are sorted within ATC class in descending frequency and then alphabetically.

Table 14.3.1.2: Overview of Treatment-Emergent Adverse Events (Safety Population)

Category	Talazoparib 1 mg (N = xx)
Patients with at Least One AE	xx (xx.x%)
Patients with at Least One AE Related to Study Drug	xx (xx.x%)
Patients with at Least One AE of Grade 3 or Higher	xx (xx.x%)
Patients with at Least One AE of Grade 3 or Higher Related to Study Drug	xx (xx.x%)
Patients with at Least One SAE	xx (xx.x%)
Patients with at Least One SAE Related to Study Drug	xx (xx.x%)
Patients who died	xx (xx.x%)
Patients who Discontinued from Study Treatment due to AEs	xx (xx.x%)
Patients who Discontinued from Study Treatment due to SAEs	xx (xx.x%)
Patients who had Study Treatment Interrupted due to AEs	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
AE: adverse event, SAE: serious adverse event.
A patient with multiple occurrences of an event is counted once only in the AE category.
Percentage is based on N.
AE grades are evaluated per NCI-CTCAE version 4.03.
Data source: Listing 16.2.7.1.

Table 14.3.1.2: Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class Preferred Term	Talazoparib 1 mg (N = xx)
Number of Patients with at Least One AE	xx (xx.x%)
Vascular disorders <-total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
preferred term 3	xx (xx.x%)
SOC 2 <-total>	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
preferred term 3	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
Patients with multiple events for a given preferred term or system organ class are counted once only for each preferred term or system organ class, respectively.
Preferred terms are sorted within system organ class in descending frequency and then alphabetically.
Percentage is based on N.
MedDRA version 19.1.
Data source: Listing 16.2.7.1.

Programming Specification:

- System organ classes are presented in descending frequency and then alphabetically.
- Preferred terms are sorted within system organ class in descending frequency and then alphabetically.

Table 14.3.1.3: Treatment-Emergent Adverse Events by Preferred Term (Safety Population)

Preferred Term	Talazoparib 1 mg (N = xx)
Number of Patients with at Least One AE	xx (xx.x%)
preferred term 1	xx (xx.x%)
preferred term 2	xx (xx.x%)
preferred term 3	xx (xx.x%)
preferred term 4	xx (xx.x%)
preferred term 5	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
A patient with multiple occurrences of a given preferred term is counted once only.
Preferred terms are sorted in descending frequency and then alphabetically.
Percentage is based on N.
MedDRA version 19.1.
Data source: Listing 16.2.7.1.

Programming Specification:

- Preferred terms are presented in descending frequency and then alphabetically.

Table 14.3.1.4: Treatment-Emergent Adverse Events Related to Study Drug by Preferred Term (Safety Population)

Preferred Term	Talazoparib 1 mg (N = xx)
Number of Patients with at Least One AE	x (xx.x%)
preferred term 1	x (xx.x%)
preferred term 2	x (xx.x%)
preferred term 3	x (xx.x%)
preferred term 4	x (xx.x%)
preferred term 5	x (xx.x%)

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
A patient with multiple occurrences of a given preferred term is counted once only.
Preferred terms are sorted in descending frequency and then alphabetically.
Percentage is based on N.
MedDRA version 19.1.
Data source: Listing 16.2.7.1.

Programming Specification:
- Preferred terms are sorted in descending frequency and then alphabetically.

Table 14.3.1.5: Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Safety Population)

System Organ Class Preferred Term	Talazoparib 1 mg (N = xx) Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Number of Patients with at Least One AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vascular disorders <-total>	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 2 <-total>	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
Patients with multiple events for a given preferred term or system organ class are counted once only for each preferred term or system organ class, respectively.
System organ classes are presented in descending frequency of 'Grade 1' column, as reported in the 'Total' and then alphabetically. Preferred terms are sorted within system organ class in descending frequency of 'Grade 1' column, as reported in the "Total" and then alphabetically.
Percentage is based on N.
MedDRA version 19.1.
AE grades are evaluated per NCI-CTCAE version 4.03.
Data source: Listing 16.2.7.1.

Programming Specification:

- System organ classes are presented in descending frequency of 'Grade 1' column, as reported in the 'Total' and then alphabetically.
- Preferred terms are sorted within system organ class in descending frequency of 'Grade 1' column, as reported in the 'Total' and then alphabetically.

Table 14.3.2.1: Serious Adverse Events by System Organ Class and Preferred Term (Safety Population)

Table 14.3.2.2: Serious Adverse Events Related to Study Drug by Preferred Term (Safety Population)

Table 14.3.2.3: Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Safety Population)

Programming Specification:
For Table 14.3.2.1 and Table 14.3.2.3: Follow similar structure to Table 14.3.1.2.
For Table 14.3.2.2: Follow similar structure to Table 14.3.1.4.

Table 14.3.4.1: Hematology Shift Table by Worst Postbaseline Toxicity Grade (Safety Population)

	Baseline [1]	Worst Post-baseline Toxicity Grade [2]					
Category		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Missing
Talazoparib 1 mg (N = xx)							
Grade 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
Toxicity grading is per NCI-CTCAE version 4.03.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] Based on all test results collected in the treatment-emergent period. For each parameter, patients are counted once only at the worst grade.
Data source: Listing 16.2.8.1.

Programming Specification:

- Include all hematology parameters specified in the protocol without CTC grades (where applicable), output one parameter for each file.
- Post-baseline laboratory assessments include both scheduled and unscheduled visits.

Table 14.3.4.2: Chemistry Shift Table by Worst Postbaseline Toxicity Grade (Safety Population)

	Baseline [1]	Worst Post-baseline Toxicity Grade [2]					
Category		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Missing
Talazoparib 1 mg (N = xx)							
Grade 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
Toxicity grading is per NCI-CTCAE version 4.03.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] Based on all test results collected in the treatment-emergent period. For each parameter, patients are counted once only at the worst grade.
Data source: Listing 16.2.8.2.

Programming Specification:

- Include all chemistry parameters specified in the protocol without CTC grades (where applicable), output one parameter for each file.
- Post-baseline laboratory assessments include both scheduled and unscheduled visits.

Table 14.3.4.3: Hematology Shift Table Based on Normal Range (Safety Population)

	Baseline [1]	Worst Post-baseline Value [2]				
Category		Low	Normal	High	Low and High	Missing
Talazoparib 1 mg (N = xx)						
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] The categories of Low and High are defined by normal ranges. If the patient has laboratory values that are both Low and High, then the patient will be counted in the category “Low and High”. Patients will be counted once only.
Data source: Listing 16.2.8.1.

Programming Specification:

- Include all hematology parameters specified in the protocol without CTC grades (where applicable), output one parameter for each file.
- Parameters that have criteria available for both low and high values are summarized for both criteria (low and high). Patients will only be counted once for each criterion. The same patient can be counted for both criteria if the patient has laboratory values meeting each criterion (low and high).
- Post-baseline laboratory assessments include both scheduled and unscheduled visits.

Table 14.3.4.4: Chemistry Shift Table Based on Normal Range (Safety Population)

	Baseline [1]	Worst Post-baseline Value [2]				
Category		Low	Normal	High	Low and High	Missing
Talazoparib 1 mg (N = xx)						
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Percentage is based on N.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] The categories of Low and High are defined by normal ranges. If the patient has laboratory values that are both Low and High, then the patient will be counted in the category "Low and High". Patients will be counted once only.
Data source: Listing 16.2.8.2.

Programming Specification:

- Include all chemistry parameters specified in the protocol without CTC grades (where applicable), output one parameter for each file.
- Parameters that have criteria available for both low and high values are summarized for both criteria (low and high). Patients will only be counted once for each criterion. The same patient can be counted for both criteria if the patient has laboratory values meeting each criterion (low and high).
- Post-baseline laboratory assessments include both scheduled and unscheduled visits.

Table 14.3.4.5: Change from Baseline Hematology Laboratory Result (Safety Population)

Visit/Time Point Statistics	Talazoparib 1 mg (N = xx) Lab Results	Change from Baseline[2]
Baseline [1]		
n	xxx	
Mean (SD)	xx.x (xx.x)	
Median	xx.x	
Min, Max	xx.x, xx.x	
Visit name 1		
n	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, Min: minimum, Max: maximum, n: counts of non-missing values.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] Only patients with a value at both baseline and during study treatment are included.
Data source: Listing 16.2.8.1.

Programming Specification:

- For each laboratory test, only patients with a value at both baseline and during study treatment are included.
- Post-baseline laboratory assessments include only scheduled visits.
- Output one parameter for each file.

Table 14.3.4.6: Change from Baseline Chemistry Laboratory Result (Safety Population)

Visit/Time Point Statistics	Talazoparib 1 mg (N = xx) Lab Results	Change from Baseline[2]
Baseline [1]		
n	xxx	
Mean (SD)	xx.x (xx.x)	
Median	xx.x	
Min, Max	xx.x, xx.x	
Visit name 1		
n	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, Min: minimum, Max: maximum, n: counts of non-missing values.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] Only patients with a value at both baseline and during study treatment are included.
Data source: Listing 16.2.8.2.

Programming Specification:

- For each laboratory test, only patients with a value at both baseline and during study treatment are included.
- Post-baseline laboratory assessments include only scheduled visits.
- Output one parameter for each file.

Table 14.3.4.7: Treatment-Emergent Liver Function Test Elevations (Safety Population)

Test Criteria	Talazoparib 1 mg (N = xx)
Number of Patients Who Met at Least One Criteria [1]	xx (xx.x%)
ALT >= 3xULN	xx (xx.x%)
AST >= 3xULN	xx (xx.x%)
ALT or AST >= 3xULN	xx (xx.x%)
ALT or AST > 5xULN	xx (xx.x%)
ALT or AST > 10xULN	xx (xx.x%)
ALT or AST > 20xULN	xx (xx.x%)
TBL > 2xULN	xx (xx.x%)
ALT or AST >= 3xULN and TBL > 2xULN	xx (xx.x%)
Concurrent ALT or AST >= 3xULN and TBL > 2xULN	xx (xx.x%)
ALT or AST >= 3xULN and TBL > 2xULN and ALP < 2xULN	xx (xx.x%)
Concurrent ALT or AST >= 3xULN and TBL > 2xULN and ALP < 2xULN [2]	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, TBL: total bilirubin, ULN: upper limit of normal.
Percentage is based on N.
[1] Criteria are based on worst postbaseline value for any specific parameter. Criteria with multiple parameters are based on worst postbaseline value for each parameter taken at any visit except that concurrent measurements are those occurring on the same date.
[2] Hy's Law according to FDA Guidance for Industry - Drug-Induced Liver Injury: Premarketing Clinical Evaluation (2009).
Data source: Listing 16.2.8.2.

Programming Specification:

- Only count the number of patients who satisfied the criteria. If count=0 for "ALT or AST >= 3xULN", more stringent criteria (eg, "ALT or AST > 5xULN") is not shown.
- Post-baseline laboratory assessments include both scheduled and unscheduled visits.

Table 14.3.5.1: Change from Baseline Vital Sign Results (Safety Population)

Visit/Time Point Statistics	Vital Sign Results Talazoparib 1 mg (N = xx)	Change from Baseline[2]
Baseline [1]		
n	xxx	
Mean (SD)	xx.x (xx.x)	
Median	xx.x	
Min, Max	xx.x, xx.x	
Visit name 1		
n	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, Min: minimum, Max: maximum, n: counts of non-missing values.
[1] Baseline is defined as the last non-missing value prior to the first dose.
[2] Only patients with a value at both baseline and during study treatment are included.
Data source: Listing 16.2.8.3.

Programming Specification:

- For each parameter, only patients with a value at both baseline and during study treatment are included.
- Vital sign parameters include blood pressure (systolic/diastolic,), heart rate, respiratory rate, and body temperature.
- Post-baseline assessments include only scheduled visits.
- Output one parameter for each file.

Table 14.3.5.2: Clinically Notable Changes in Vital Sign Results (Safety Population)

Parameter [unit] Category	Talazoparib 1 mg (N = xx)
Number of Patients Who Met at Least One Criteria	xx (xx.x%)
Systolic Blood Pressure [mmHg] <-total>	xx (xx.x%)
High Only (≥155 with Increase from Baseline of ≥30)	xx (xx.x%)
Low Only (≤90 with Decrease from Baseline of ≥20)	xx (xx.x%)
Both High and Low	xx (xx.x%)
Diastolic Blood Pressure [mmHg] <-total>	xx (xx.x%)
High Only (≥100 with Increase from Baseline of ≥15)	xx (xx.x%)
Low Only (≤50 with Decrease from Baseline of ≥15)	xx (xx.x%)
Both High and Low	xx (xx.x%)
Heart rate [bpm] <-total>	xx (xx.x%)
High Only (≥100 with Increase from Baseline of ≥30)	xx (xx.x%)
Low Only (≤50 with Decrease from Baseline of ≥15)	xx (xx.x%)
Both High and Low	xx (xx.x%)
Respiratory Rate [bpm] <-total>	xx (xx.x%)
High Only (≥25)	xx (xx.x%)
Low Only (<10)	xx (xx.x%)
Both High and Low	xx (xx.x%)
Oral Body Temperature [°C] <-total>	xx (xx.x%)
High Only (>39)	xx (xx.x%)
Low Only (≤ 35)	xx (xx.x%)
Both High and Low	xx (xx.x%)

The date of analysis data transfer is DDMONYYYY.
Baseline is defined as the last non-missing value prior to the first dose.
mmHg: millimeters of mercury, bpm: beats per minute.

Parameter [unit] Category	Talazoparib 1 mg (N = xx)
If a patient has both High and Low post baseline values then count in High and Low. A patient with multiple occurrences for a given abnormality category is counted only once. Percentage is based on N. Data source: Listing 16.2.8.3.	

Programming Specification:

- Only count the number of patients who satisfied the criteria. If count=0 for "High/Low only", criteria "Both High and Low" is not shown
- If no abnormality for a given category, display only *parameter [unit]* <-total> row.
- Post-baseline assessments include both scheduled and unscheduled visits.

Table 14.3.6: Change from Baseline ECG Results (Safety Population)

Visit/Time Point Statistics	Talazoparib 1 mg (N = xx) ECG Results	Change from Baseline
Screening / Baseline [1]		
n	xxx	
Mean (SD)	xx.x (xx.x)	
Median	xx.x	
Min, Max	xx.x, xx.x	
Safety Follow-up		
n	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, Min: minimum, Max: maximum, n: counts of non-missing values.
[1] Baseline is the measurement at screening visit.
Data source: Listing 16.2.8.4.1.

Programming Specification:

- For each parameter, only patients with a value at both screening and Safety follow-up are included.
- ECG parameters include QT, QTcF, QTcB, HR, PR, and QRS.
- Post-baseline assessments include only scheduled visits.
- Output one parameter for each file.

Table 14.4.1.2: Individual and Summary of Plasma Talazoparib Concentrations (PK Population)

Patient ID	Day 1 predose (pg/mL)	Day 1 xhr (pg/mL)	Day 1 xhr (pg/mL)	Day 1 xhr (pg/mL)	Day y predose (pg/mL)	Day y predose (pg/mL)	Day y xhr (pg/mL)	Day y xhr (pg/mL)
PPD	BLQ	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	BLQ
PPD	BLQ	xx.x	xx.x	xx.x	xx.x	xx.x	NS	BLQ
PPD	BLQ	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
PPD	BLQ	xx.x	xx.x	xx.x[1]	xx.x	xx.x	BLQ	BLQ
PPD	BLQ	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	BLQ
PPD	BLQ	xx.x	xx.x	xx.x	NR	xx.x	xx.x	BLQ
Statistics								
n	xx	xx	xx	xx	xx	xx	xx	xx
nBLQ	6	xx	xx	xx	xx	xx	xx	5
Mean (SD)	0 (0)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	NC
CV% mean	na	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	na
GeoMean	na	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	na
CV% GeoMean	na	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	na
Median	na	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	na
Min, Max	na	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	na

The date of analysis data transfer is DDMONYYYY.
NS: no sample, NR: not reported, BLQ: below the lower limit of quantitation, na: not applicable.
n: number of non-missing concentrations, nBLQ: number of BLQ values.
SD: standard deviation, CV%: coefficient of variation (%), GeoMean: geometric mean, Min: minimum, Max: maximum.
Concentrations below BLQ (< 25.0 pg/mL) are set as zero. NC: not calculated due to post-dose mean < BLQ
Zero concentrations are considered as missing in geometric mean calculations.
CV% = SD/Mean*100, CV% GeoMean = sqrt (exp (variance for log transformed data)-1)*100.
[1] The sample collected outside the accepted window of ± 15% from the nominal sampling time has been excluded from the analysis.

Table 14.4.1.3: Individual and Summary of Plasma Talazoparib PK Parameters on Day 1 (PK Analysis Population)

Patient ID	AUC_{24h}(h*ng/mL)	R_{AUC}	C_{max}(ng/mL/L)	t_{max}(h)	CL/F(L/h)
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	NE	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
Statistics					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	na	xx.x (xx.x)
CV% mean	xx.x	xx.x	xx.x	na	xx.x
GeoMean	xx.x	xx.x	xx.x	na	xx.x
CV% GeoMean	xx.x	xx.x	xx.x	na	xx.x
Median	xx.x	xx.x	xx.x	x.xx	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, CV%: coefficient of variation (%), GeoMean: geometric mean, Min: minimum, Max: maximum, n: number of non-missing values.
NE: not evaluable, na: not applicable.
CV% = SD/Mean*100, CV% GeoMean = sqrt (exp (variance for log transformed data)-1)*100.

Table 14.4.1.4: Individual and Summary of Plasma Talazoparib PK Parameters on Day 22 (PK Analysis Population)

Patient ID	AUC_{24h}(h*ng/mL)	R_{AUC}	C_{max}(ng/mL)	t_{max}(h)	CL/F(L/h)
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	NE	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
PPD	xx.x	xx.x	xx.x	x.xx	x.xx
Statistics					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	na	xx.x (xx.x)
CV% mean	xx.x	xx.x	xx.x	na	xx.x
GeoMean	xx.x	xx.x	xx.x	na	xx.x
CV% GeoMean	xx.x	xx.x	xx.x	na	xx.x
Median	xx.x	xx.x	xx.x	x.xx	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx	xx.x, xx.x

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, CV%: coefficient of variation (%), GeoMean:geometric mean, Min: minimum, Max: maximum, n: number of non-missing values.
NE: not evaluable, na: not applicable.
CV% = SD/Mean*100, CV% GeoMean = sqrt (exp (variance for log transformed data)-1)*100.

Table 14.4.1.5: Overall Summary of Plasma Talazoparib PK Parameters (PK Analysis Population)

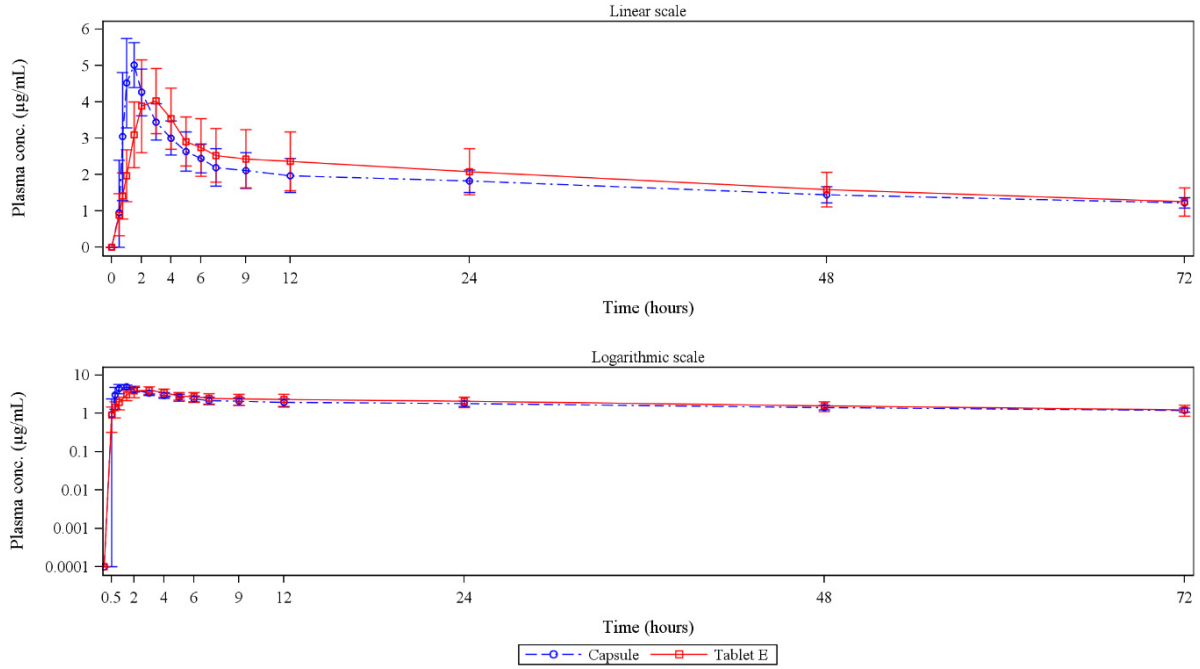
Parameter (unit) Statistics	Day 1	Day 22
n	xx	xx
C_{max} (ng/mL)	xx.x ± x.xx (xx.x)	xx.x ± x.xx (xx.x)
t_{max} (h)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
AUC_{24h} (h*ng/mL)	xx.x ± x.xx (xx.x)	xx.x ± x.xx (xx.x)
CL/F (L/h)	xx.x ± x.xx (xx.x)	xx.x ± x.xx (xx.x)
R_{AUC}	x.xx ± x.xxx (xx.x)	x.xx ± x.xxx (xx.x)

The date of analysis data transfer is DDMONYYYY.
SD: standard deviation, CV%: coefficient of variation (%), n: number of non-missing values.
Statistics are reported as the arithmetic mean ± SD (%CV) with the following exception: for t_{max}, the median (min, max) is reported.
Data source: Table 14.4.1.3 and Table 14.4.1.4.

Appendix 2.2. Section 14 Figures

Figure 14.4.1.3: Mean (SD) Plasma Talazoparib Concentration-Time Profiles (PK Population)

Day x

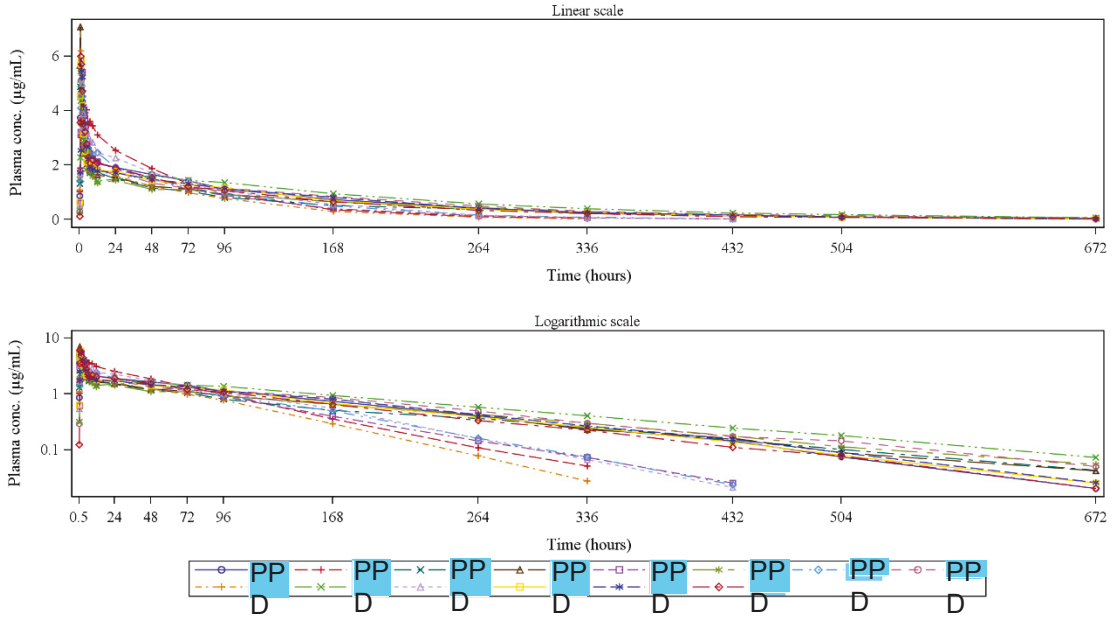


The date of analysis data transfer is DDMONYYYY.
Predose concentrations below the lower limit of quantitation (BLQ) values (< 25.0 pg/mL) are set as zero in the linear scale plot and set as missing in the semi-logarithmic scale plot.
SD: standard deviation.
Data source: Table 14.4.1.2.

Programming Specification:

- Plot Separately for Day 1 and Day 22.
- Y-axis label: Plasma Concentration (pg/mL).

Figure 14.4.1.4: Individual Plasma Talazoparib Concentration-Time Profiles for Day 1 (PK Population)

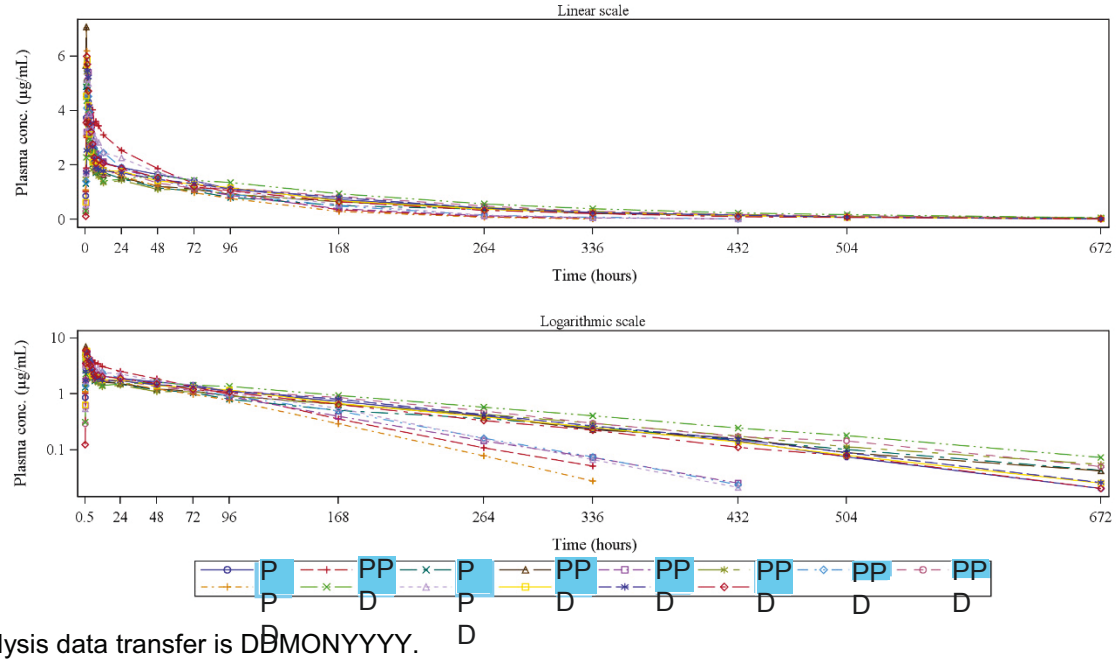


The date of analysis data transfer is DDMONYYYY.
Post-dose concentrations below the lower limit of quantitation (BLQ) values (< 25.0 pg/mL) are set as missing.
Predose concentrations < BLQ are set as zero in the linear scale plot and set as missing in the semi-logarithmic scale plot.
Data source: Table 14.4.1.2.

Programming Specification:

- Y-axis label: Plasma Concentration (pg/mL).

Figure 14.4.1.5: Individual Plasma Talazoparib Concentration-Time Profiles for Day 22 (PK Population)



The date of analysis data transfer is DDMONYYYY.
Post-dose concentrations below the lower limit of quantitation (BLQ) values (< 25.0 pg/mL) are set as missing.
Predose concentrations < BLQ are set as zero in the linear scale plot and set as missing in the semi-logarithmic scale plot.
Data source: Table 14.4.1.2.

Programming Specification:

- Y-axis label: Plasma Concentration (pg/mL).

Appendix 2.3. Section 16 Listings

Listing 16.2.1.1: Inclusion and Exclusion Criteria (All Screened)

Patient ID	Protocol Version at Enrollment	Informed Consent Date	Date of Screen Visit	Screening Eligibility Satisfied?	Inclusion Criteria Number Not Met	Exclusion Criteria Number Met	Other Screening Failure Reason
PPD	1	PPD	PPD	No	02	03	Withdrawal by subject

The date of analysis data transfer is DDMONYYYY.

Listing 16.2.1.2: Patient Disposition (Safety Population)

Patient ID	Enrollment Date	Last Dose Date (Study Day)	Did Patient Complete the Treatment?	Primary Reason for Treatment Discontinuation	Last Date of Safety Follow-up (Study Day)	Patient continuing Open-Label Extension study?
PPD	PPD	PPD	Yes		PPD	Yes
PPD		PPD	No	Adverse Event	PPD	

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.2: Protocol Deviations (Safety Population)

Patient ID	Type of Violation	Description of Violation
PPD	Exclusion #2	*(Full text description from protocol)*

The date of analysis data transfer is DDMONYYYY.

Listing 16.2.3: Analysis Populations (All Enrolled)

Patient ID	Safety Population	ECG Analysis Population	PK Population	PK Analysis Population	PK –PD Analysis Population
PPD	Yes	No	Yes	Yes	Yes

The date of analysis data transfer is DDMONYYYY.
The safety population includes all patients who receive any amount of talazoparib.
The ECG analysis population consists of all enrolled patients who receive at least 1 dose of talazoparib, and have at least 1 available baseline and 1 on-treatment ECG data.
The PK population is defined as patients who receive at least 1 dose of talazoparib and provide at least 1 reportable concentration.
The PK analysis population is defined as patients who have sufficient concentration data to derive at least one PK parameter.
The PK-PD analysis population is defined as all patients in the ECG analysis population who have at least 1 time-matched pair of plasma concentration and ECG measurements obtained at the same nominal time point.

Listing 16.2.4.1: Baseline Demographics (Safety Population)

Patient ID	Age (year)	Sex	Race	Ethnicity	Weight (kg)	Height (cm)	BMI (kg/m^2)
PPD	xx	xxx	xxx	xxx	xx	xx	xx

The date of analysis data transfer is DDMONYYYY.
BMI: Body mass index.

Listing 16.2.4.2: Baseline Disease Characteristics (Safety Population)

Patient ID	Initial Diagnosis Date (Study Day)	Primary Cancer Site	Staging at Initial Diagnosis [1]	Histopathological Type at Initial Diagnosis	Advance Disease Diagnosis Date (Study Day)	ECOG Grade (Score)
PPD	PPD	Breast	M1	Other	PPD	0

The date of analysis data transfer is DDMONYYYY.
AJCC: American Joint Committee on Cancer, ECOG: Eastern Cooperative Oncology Group.
[1] The Classification of Staging at Initial Diagnosis are as per AJCC Staging Manual Sixth Edition.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.4.3: Medical History (Safety Population)

Patient ID	MH No.	Condition/Diagnosis	MedDRA System Organ Class Preferred Term Verbatim Term	Start Date	Stop Date	Ongoing	If Ongoing, currently being treated?
PPD	xxxxxx	xxxxxx	Gastrointestinal disorders Constipation Constipation	2010		Yes	Yes

The date of analysis data transfer is DDMONYYYY.
MH: medical history.
MedDRA version 19.1.

Listing 16.2.4.4: Prior Systemic Anti-Cancer Therapy (Safety Population)

Patient ID	Regimen Number	Start Date (Study Day)	End Date (Study Day)	Drug Name	Indication	Reason for Discontinuation	Other Reason for Discontinuation
PPD	1	PPD	PPD	xxxx	ADVANCED DISEASE	DISEASE PROGRESSION	xxxxx

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.4.5: Prior Radiation Therapy (Safety Population)

Patient ID	Start Date (Study Day)	End Date (Study Day)	Total Dose (Gy)	Radiotherapy Site	Indication
PPD	PPD	PPD	xx	xxxxx	NEOADJUVANT/ADJUVANT

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.4.6: Prior Surgery for Cancer (Safety Population)

Patient ID	Surgery (Type/Specification)	Date of Surgery (Study Day)
PPD	xxxxxxx	PPD

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.5.3: Dose Administration Record (Safety Population)

Patient ID	Visit	Start Date (Study Day)	End date (Study Day)	Prescribed Daily Dose (unit)	Actual Daily Dose (unit)	Duration (days)	Dose Interrupted?	Dose Reduced?	Reason	AE No	Study Drug Discontinued?	Last Dose?
PPD	Day x	PPD	PPD	1 mg	0.50 mg	22	NO	Yes	Adverse Event	2	No	No

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.5.4: Drug Accountability (Safety Population)

Patient ID	Date Dispensed (Study Day)	Bottle Number	Dosage	Date Returned (Study Day)	Number of Capsules Returned	Bottle Not Returned?
PPD	PPD		1 mg	PPD		Yes

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.5.3: Concomitant Medication (Safety Population)

Patient ID	CM No.	ATC Description Preferred Term Verbatim Term	Start Date (Study Day)	Stop Date (Study Day)	Ongoing	Indication	AE No.	MH No.	Route	Daily Dose/ Unit/ Frequency
PPD	xx	ANALGESICS Tramadol xxx	PPD	PPD	No	Adverse Event Pre-Existing Condition	2	 1	Oral	20 mg QD

The date of analysis data transfer is DDMONYYYY.
ATC: anatomical therapeutic chemical classification system using the World Health Organization drug dictionary (WHO-DD),
CM: concomitant medication, AE: adverse event, MH: medical history.
Medications are considered concomitant if taken during the treatment period.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.5.4: Other Procedures (Safety Population)

Patient ID	Category	Procedure	Assessment Date (Study Day)	Indication	AE No.
PPD	CYTOLOGY	xxxxx	PPD	ADVERSE EVENT	2

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.7.1: Treatment-Emergent Adverse Events (Safety Population)

Patient ID	System Organ Class/ Preferred Term/ Verbatim Term/ AE.No.	SAE	Seriousness Criteria [1]	Start Date (Study Day)	End date (Study Day)	Duration (days)	CTCAE Severity Grade	Related to Study Drug	Outcome [2] / Action Taken [3]
PPD	General disorders and administration site conditions / Fatigue / Fatigue / 2	Yes	2 / 3	PPD	PPD	8	1	Yes	1 / 2

The date of analysis data transfer is DDMONYYYY.
AE: adverse event, SAE: serious adverse event.
Study day is relative to the first day of treatment (day 1).
MedDRA version 19.1.
AE grades are evaluated per NCI-CTCAE version 4.03.
[1] Seriousness Criteria: 1= Death, 2=Life Threatening, 3=Hospitalization (Initial or Prolonged), 4=Persistent or Significant Disability or Incapacity, 5=Congenital Anomaly or Birth Defect, 6=Other Medically Important Event.
[2] Outcome: 1 = Recovered/Resolved, 2 = Recovered/Resolved with Sequelae, 3 = Not Recovered/Not Resolved, 4 = Fatal.
[3] Action Taken: 1 = Dose Not Changed, 2 = Dose Reduced, 3 = Drug Interrupted, 4 = Drug Withdrawn.

Listing 16.2.7.2: Serious Adverse Events (Screening Failures)

Patient ID	System Organ Class/ Preferred Term/ Verbatim Term/ AE.No.	Seriousness Criteria [1]	Start Date (Study Day)	End date (Study Day)	Duration (days)	CTCAE Severity Grade	Related to Study Drug	Outcome [2] / Action Taken [3]
PPD	General disorders and administration site conditions / Fatigue / Fatigue / 2	2 / 3	PPD	PPD)	8	1	Yes	1 / 2

The date of analysis data transfer is DDMONYYYY.
AE: adverse event.
Study day is relative to the first day of treatment (day 1).
MedDRA version 19.1.
AE grades are evaluated based on NCI-CTCAE version 4.03.
[1] Seriousness Criteria: 1= Death, 2=Life Threatening, 3=Hospitalization (Initial or Prolonged), 4=Persistent or Significant Disability or Incapacity, 5=Congenital Anomaly or Birth Defect, 6=Other Medically Important Event.
[2] Outcome: 1 = Recovered/Resolved, 2 = Recovered/Resolved with Sequelae, 3 = Not Recovered/Not Resolved, 4 = Fatal.
[3] Action Taken: 1 = Dose Not Changed, 2 = Dose Reduced, 3 = Drug Interrupted, 4 = Drug Withdrawn.

Listing 16.2.7.3: Deaths (All Enrolled)

Patient ID	Date of Death (Study Day)	Primary Cause of Death	Related to Study Drug
PPD	PPD	ADVERSE EVENT RELATED TO TALAZOPARIB	Yes

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.1: Hematology Laboratory Results (Safety Population)

Patient ID	Lab Test	Visit	Sample Date (Study Day)	Result	Unit	Reference Range	Alert Flag
PPD	Basophils	SCR	PPD	xx.x	10^9/L	xx.x-xx.x	
		Day 1		xx.x	10^9/L	xx.x-xx.x	H/G3

The date of analysis data transfer is DDMONYYYY.
L/H denotes a value below/above normal range, Gx denotes a value meeting criteria for CTC Grade x per NCI-CTCAE version 4.03.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.2: Chemistry Laboratory Results (Safety Population)

Patient ID	Lab Test	Visit	Sample Date (Study Day)	Result	Unit	Reference Range	Alert Flag
PPD	AST	SCR	PPD	xx.x	U/L	xx.x-xx.x	
		Day 1		xx.x	U/L	xx.x-xx.x	H/G3

The date of analysis data transfer is DDMONYYYY.
L/H denotes a value below/above normal range, Gx denotes a value meeting criteria for CTC Grade x per NCI-CTCAE version 4.03.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.3: Vital Sign Results (Safety Population)

Patient ID	Visit	Time Point	Date / Time (Study Day)	Weight (kg)	Blood Pressure Systolic / Diastolic (mmHg)	Heart rate (bpm)	Respiratory Rate (bpm)	Body Temp. (°C)
PPD	SCR	PREDOSE	PPD	xx.x	xxx / xxx	xxx	xx.x	xx.x
	Day -1	1HR		xx.x	xxx / xxx	xxx L	xx.x	xx.x L

The date of analysis data transfer is DDMONYYYY.
mmHg: millimeters of mercury, bpm: beats per minute.
H/L: clinically notable high and low values.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.4.1: ECG Results (Safety Population)

Patient ID	Visit	Date / Time (Study Day)	Category	Parameter (unit)	Value	Overall Interpretation	Abnormal Finding
PPD	SCR	PPD	Intervals Measurement	QTcF Interval (msec)	xx	Normal	
				PR Interval (msec)			
			Morphology Finding	Chamber Hypertrophy or Enlargement	LOW VOLTAGE		
	SFU	PPD	Intervals Measurement	QTcF Interval (msec)	xx [1]	Abnormal	xxxxx
				PR Interval (msec)			
			Morphology Finding	Chamber Hypertrophy or Enlargement	LOW VOLTAGE		

The date of analysis data transfer is DDMONYYYY.
HR: heart rate, bpm: beats per minute.
Study day is relative to the first day of treatment (day 1).
[1] Clinically notable change.

Listing 16.2.8.5: Pregnancy Test Results (Safety Population)

Patient ID	Visit	Test Performed Locally or Centrally	Specimen Type	Sample Date (Study Day)	Result
PPD	SCR	Local	Serum	PPD	Negative
	SFU	Central	Urine	PPD	Negative

The date of analysis data transfer is DDMONYYYY.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.6: Other Laboratory Results (Safety Population)

Patient ID	Visit	Date (Study Day)	Lab Test	Result	Unit	Reference Range	Alert Flag
PPD	SCR	PPD	xxx	xx.x	xx	xx.x-xx.x	
			xxx	xx.x	xx	xx.x-xx.x	H

The date of analysis data transfer is DDMONYYYY.
L/H denotes a value below/above normal range.
Study day is relative to the first day of treatment (day 1).

Listing 16.2.8.7: Individual Plasma Talazoparib Concentrations (PK Population)

Patient ID	Visit	Scheduled Time Point	Actual Date/Time of Collection	Concentration (pg/mL)	Excluded From PK Analysis [1]	Reason for Exclusion
PPD	Day 1	predose	ddmmmyyyy/hh:mm	BLQ		
		1.0 hour	ddmmmyyyy/hh:mm	xx.x	Yes	xxxxxx

The date of analysis data transfer is DDMONYYYY.
Predose concentrations below the lower limit of quantitation (BLQ) values (< 25.0 pg/mL) have been set to zero; post-dose concentrations < BLQ are set to missing in the PK analysis.
Concentration values for “No Result (NR)” or “No Sample (NS)” have been set to missing in the PK analysis.
[1] Excluded from summaries, figures, and PK parameter calculations.