STATISTICAL ANALYSIS PLAN

An Open-Label, Non-Randomized, Multicenter Study to Determine the Pharmacokinetics and Safety of Niraparib Following a Single Oral Dose in Patients with Advanced Solid Tumors and Either Normal Hepatic Function or Moderate Hepatic Impairment

Protocol Number:	3000-01-003
Protocol Version and Date:	V3.0 January 15, 2018 (Amendment 2) v2.0 October 04, 2017 (Amendment 1) v1.0 June 16, 2017 (Original)
Study Drug Name:	Niraparib Capsules
Phase:	Phase 1
Sponsor:	TESARO, a GSK Company
Analysis Plan Date:	March 31, 2020
Analysis Plan Version:	Version 1.1

SPONSOR SIGNATURE PAGE

Protocol Title:	An Open-Label, Non-Randomized, Multicenter Study to Determine the Pharmacokinetics and Safety of Niraparib Following a Single Oral Dose in Patients with Advanced Solid Tumors and Either Normal Hepatic Function or Moderate Hepatic Impairment
Protocol Number:	3000-01-003
Sponsor:	TESARO, a GSK Company 1000 Winter Street Waltham MA 02451

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

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ABBREVIATIONS

ABBREVIATION	DEFINITION
AE	adverse event
AESI	adverse event of special interest
aPTT	activated partial thromboplastin time
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BILI	bilirubin
BMI	body mass index
CBC	complete blood count
CI	confidence interval
CLcr	creatinine clearance
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
ECOG	Easter Cooperative Oncology Group
eCRF	electronic Case Report Form
EOS	end of study
FDA	US Food and Drug Administration
ICF	informed consent form
INR	international normalized ratio
M1	major metabolite
MedDRA	Medical Dictionary for Regulatory Activities
MRI	magnetic resonance imaging
PD	protocol deviation
PK	pharmacokinetics
PT	preferred term
Q_1	first quartile
Q_3	third quartile
RECIST	Response Evaluation Criteria in Solid Tumors
Rel Days	relative study days
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOC	system organ class
TEAE	treatment-emergent adverse event
ULN	upper limit of normal
WHO	World Health Organization

1 INTRODUCTION

This statistical analysis plan (SAP) is designed to outline the statistical methods for safety analyses and data presentation of investigational drug niraparib for study protocol 3000-01-003. Pharmacokinetics (PK) analysis will be described in a separate pharmacokinetic analysis plan.

This document has been prepared based on Study Protocol Amendment 3 dated 15 January 2018. Patient populations to be used for analyses, data handling rules, statistical methods, and formats for data presentation and summary are identified and provided.

2 STUDY DESIGN OVERVIEW

2.1 Overall Study Design

This is a Phase 1, open-label, parallel-group, single-dose study in patients with advanced solid tumors and with either normal hepatic function or moderate hepatic impairment.

Patients with solid tumors will be recruited and enrolled within the following groups:

- Group 1: normal hepatic function (total bilirubin [BILI] and aspartate aminotransferase [AST] ≤ upper limit of normal [ULN])
- Group 2: moderate hepatic impairment (BILI >1.5 × to 3 × ULN) and any degree of AST elevation

All patients will receive niraparib. Approximately 16 patients will be enrolled. Patients may be replaced so that there are 8 PK-evaluable patients per group.

2.1.1 Pharmacokinetic Phase

All patients will receive a single dose of 300 mg niraparib administered as 3 × 100 mg capsules on Day 1. Patients will undergo PK sampling up to 168 hours (7 days) following niraparib administration. Pharmacokinetic parameters to be calculated include area under the concentration × time curve calculated to last measured concentration, area under the concentration × time curve calculated to infinity, maximum concentration, time to maximum concentration, terminal half-life, and apparent total clearance. Protein binding parameters to be calculated include fraction of unbound drug and clearance of free drug. The study will be considered complete when the final PK evaluable patient completes all assessments in the PK phase of the study.

Safety will be assessed through adverse event assessment, physical examination, vital sign measurements, clinical laboratory tests, and monitoring of concomitant medications.

2.1.2 Extension Phase

On the same day that patients complete the final study assessments for the PK phase, patients may be eligible to continue receiving niraparib in the extension phase of the study, if the investigator believes it is in the best clinical interest of the patient. Patients will receive their first therapeutic dose of niraparib on Cycle 1/Day 1 of the extension phase. Patients with normal hepatic function will receive an oral daily dose of 300 mg (3 x 100 mg capsules), and patients with moderately impaired hepatic function will receive an oral daily dose of niraparib 200 mg (2× 100 mg capsules). Patients will return to the study center during Cycle 1 on Days 8, 15, and 21 to undergo safety assessments (including complete blood counts [CBCs]). Thereafter, patients will return on the first day of every treatment cycle (28 ±3 days) to receive study drug and for safety assessments (including CBCs). Dose modification (dose interruption and/or reduction) may be implemented for any grade toxicity considered intolerable by the patient, and must be implemented for any Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4

non-hematologic adverse event considered by the Investigator related to study treatment or for hematologic toxicity as outlined in the protocol. Patients may continue in the extension phase until disease progression (assessed by Response Evaluation Criteria in Solid Tumors [RECIST] v1.1 and clinical signs and symptoms), unacceptable toxicity, death or discontinuation from the study treatment for any other reason. At end of study (EOS), safety assessments will be completed. No new capsules will be dispensed at EOS.

The schedule of assessments for each phase is presented in **Table 1** and **Table 2** respectively.

Table 1: Pharmacokinetic Phase Schedule of Assessments

Assessment	Screening	PK Phase							
Day of Procedure	**-28 to -1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Informed consent	X								
Inclusion/ exclusion criteria review	X								
Demographics	X								
Medical, surgical, cancer, and medication history	X								
Investigator-assessed tumor assessment[a]	X								
Vital signs	X	X[b]	X						X
Height and weight	X								
ECOG performance status	X								
Clinical laboratory assessments									
CBC[c]	X								X
Serum chemistry	X								X
Coagulation	X								
Pregnancy test	X[d]								X
Urinalysis	X								
Physical exam	X								X
CL_{cr} calculation or Creatinine clearance	X								
Blood sample for PK analysis		X	X	X	X		X		X
Blood sample for plasma protein binding analysis		X							X
Concomitant medications/ procedures		Recorded from first dose of study drug through Safety follow-up							
AE monitoring[e]	X	X	X	X	X	X[e]	X	X[e]	X
Niraparib treatment dispensed		X							

Abbreviations: AE = adverse event; AESI = adverse event of special interest; CBC = complete blood count; CLcr = creatinine clearance; CT = computed tomography; ECOG= Eastern Cooperative Oncology Group; EOS = end of study; ICF = informed consent form; MRI = magnetic resonance imaging; PK = pharmacokinetic; SAE = serious adverse event.

[a] RECIST (v1.1) tumor assessment via a CT or MRI scan of clinically indicated areas and evaluation of clinical signs and symptoms should be performed at minimum at screening in the PK Phase and as described in Table 2 for the Extension Phase.

[b] To be collected prior to niraparib dosing

[c] During the extension phase, test complete blood counts weekly for the first month, monthly for the next 11 months of treatment and periodically after this time.
Medical and supportive therapy should be optimized for management of toxicities.

[d] Serum or urine pregnancy test within 72 hours prior to first dose of niraparib

[e] Collection of AEs begins when ICF is signed. AE monitoring on PK Phase Days 5 and 7 may be performed by telephone.

Table 2: Extension Phase Schedule of Assessments

Assessment	Extension Phase Cycle 1				Cycle n /Day 1	EOS	Safety Follow-up
Day of Procedure (window)	**1[a]**	**8**	**15**	**21**	**1**	**(+ 7 Days post-treatment)**	**30 (+ 7 Days)**
Investigator assessed tumor assessment[b]					X	X	
Vital signs	X				X	X	X
ECOG	X					X	X
Weight							X
CBC[c]	X	X	X	X	X	X	X
Serum chemistry					X	X	X
Pregnancy test					X	X	X
Urinalysis							X
Physical exam	X				X	X	X
Concomitant medications/ procedures		Recorded from first dose of study drug through Safety follow-up					
AE monitoring[d]	X	X	X	X	X	X	X
Niraparib treatment dispensed	X[e]				X		

[a] May be the same as PK Day 8/End of PK Phase

Abbreviations: AE = adverse event; AESI = adverse event of special interest; CBC = complete blood count; CLcr = creatinine clearance; CT = computed tomography; ECOG= Eastern Cooperative Oncology Group; EOS = end of study; ICF = informed consent form; MRI = magnetic resonance imaging; PK = pharmacokinetic; SAE = serious adverse event.

[b] Tumor assessment via a CT or MRI scan of clinically indicated areas and evaluation of clinical signs and symptoms should be performed at a minimum at screening and, during the extension phase, every three cycles or per the Institution's standard practice. The Investigator will evaluate the patient scans and clinical symptoms to evaluate disease status and progression, discontinue niraparib and initiate subsequent anticancer treatment as necessary.

[c] During the extension phase, test complete blood counts weekly for the first month, monthly for the next 11 months of treatment and periodically after this time.

Medical and supportive therapy should be optimized for management of toxicities.

[d] AEs are required to be captured through 30 days after cessation of study treatment; SAEs are required to be captured through 90 days after cessation of study treatment (or to a minimum of 30 days post-treatment if the patient starts alternative anticancer therapy); and any pregnancies that occur within 180 days post-treatment are to be captured. Study drug-related SAEs and adverse events of special interest (AESIs) will continue to be monitored via telephone every 90 ± 14 days after the last dose of study drug.

[e] If Cycle 1/Day 1 is the same day as Day 8 of the PK phase, then niraparib treatment must be dispensed after all other assessments (including PK) have been completed.

2.2 Sample Size

16 PK-evaluable patients will be enrolled in the study, in which 8 patients are with normal hepatic function and 8 patients are with moderate hepatic impairment.

This is a descriptive study and no formal sample size calculations were performed. The proposed sample size is consistent with the recommendations in the FDA document (at least 8 subjects), Guidance for Industry for Hepatic Function studies (Guidance for Industry 2003).

2.3 Randomization and Blinding

This is an open-label study, and patients will not be randomized.

3 STUDY OBJECTIVES

3.1 Primary Objective

- To characterize the pharmacokinetics (PK) of niraparib and its major metabolite (M1) when administered as a single dose in cancer patients with normal hepatic function compared to patients with moderate hepatic impairment.

3.2 Secondary Objective

- To evaluate the safety of niraparib when administered as a single dose in patients with moderate hepatic impairment.
- To obtain additional safety data through the extension phase, in which patients have the option to continue receiving niraparib.

4 STUDY ENDPOINTS AND EVALUATIONS

4.1 Safety Evaluations

The safety evaluations include:

- Treatment emergent adverse events (TEAEs)
- Clinical laboratory assessments (including CBC, serum chemistry, and urinalysis)
- Serum or urine pregnancy testing
- Vital signs (including weight)
- Physical examination findings
- ECOG performance status

4.2 Other Evaluations

Other evaluations include:

- Demographics and baseline characteristics
- Medical history
  - General medical history
  - Surgical history
  - Primary cancer history
- Prior anticancer treatment
  - Prior anticancer treatment for primary cancer
  - Previous radiotherapy
  - Previous cancer related surgery
- Medication history (prior medications) and concomitant medications/Procedures
- Growth factors
- Transfusion
- Tumor lesion assessment

5 PLANNED ANALYSIS

5.1 Changes from Planned Analyses in the Protocol

There are no changes from planned analyses in the Protocol.

5.2 Final Analyses and Reporting

All final planned analyses per protocol and this SAP will be performed after database lock.

6 ANALYSIS POPULATIONS AND APPLICATIONS

6.1 All Patients Population

This population includes all patients who sign an informed consent form (ICF).

6.2 Safety Population

Safety Population for PK phase includes patients who receive at least one dose of the investigational drug niraparib during the PK Phase.

Safety Population for extension phase includes patients who receive at least one dose of the investigational drug niraparib during the extension Phase.

6.3 Application of Analysis Populations

Safety Population that will be used for creating the summary table(s) of each type is provided in Table 3. All data will be presented in listings either for All Patients Population or for Safety Population.

Table 3: Application of Safety Population for Tables

Type	PK Phase	Extension Phase
Disposition	X	X
Demographics and baseline characteristics	X	
Protocol deviations	X	
Prior and concomitant medications	X	X
Safety evaluations	X	X
Extent of Exposure		X

7 STATISTICAL CONSIDERATIONS

All analyses described in this plan are considered a priori analyses in that they have been defined prior to locking the database. All other analyses, if any, designed subsequently to locking the database, will be considered post hoc analyses and will be described as exploratory analyses in the Clinical Study Report.

All summaries and statistical analysis will be performed by SAS v9.3 or later.

7.1 General Statistical Procedures

Frequency distributions for categorical variables will be provided as counts of patients and percentages. Percentages will be based on the number of patients with a non-missing parameter unless missing category is presented or based on number of population as indicated below. Percentages will be reported to one decimal place.

The descriptive statistics for continuous variables will be number of patients, mean, standard deviation (SD), median, quartiles (Q1, Q3), minimum and maximum. Mean, median, Q1, and Q3 will be reported to 1 more decimal place than the raw data, while the SD will be reported to 2 more decimal places than the raw data.

All data listings that contain an evaluation date will also contain relative study day (Rel days) which is defined as number of days relative to the first dose date of study drug (see Section 8.2 for details).

7.2 Enrollment and Disposition

7.2.1 Patients Enrollment

Patients enrollment will be summarized for each analysis population. The number of patients in each analysis population will be presented by hepatic function group and overall.

Enrollment information will be provided in a data listing for All Patients Population.

7.2.2 Patients Disposition

Study completion status will be summarized for each hepatic function group. Number and percentage of patients who complete the study, number and percentage of patients discontinued the study early by primary reasons will be presented. The denominators for calculating the percentages will be based on number of patients in Safety Population for each hepatic function group.

Discontinued patients will be provided in a data listing for Safety Population.

7.3 Protocol Deviations

Important or significant protocol deviations (PDs) will be assessed by sponsor personnel following Protocol Deviation Guideline outlined in Clinical Management Plan.

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

All PDs will be identified and finalized prior to database lock and documented in a separate Medical Data Review Plan (MDRP).

Number and percentage of patients with a significant or important PD will be tabulated by type of deviation. The denominators for calculating the percentages will be based on number of patients in Safety Population for each hepatic function group.

All protocol deviations will be listed for Safety Population.

7.4 Demographics and Baseline Characteristics

Demographic and baseline (see Section 8.1 for definition) characteristics will be tabulated using descriptive statistics for all patients and by hepatic function group. The following variables will be included in the tables:

- The demographic data are:
  - Age
  - Sex
  - Race
  - Ethnicity
- Baseline characteristics include:
  - Baseline weight (kg)
  - Baseline height (cm)
  - BMI (Body mass index, kg/m^2, calculated as weight (kg) / height $(m)^2$)
  - ECOG performance status at baseline

Conversions for height and weight are as follows:

height (cm) = height (inches) x 2.54
weight (kg) = weight (lb) x 0.4536

Demographics and baseline characteristics will be listed for Safety Population.

7.5 Prior Anticancer Treatment

Prior anticancer treatment will be tabulated using descriptive statistics for all patients and by hepatic function group. The following variables will be included in the tables:

- Primary tumor site at first and most recent diagnosis
- Cancer stage at first and most recent diagnosis
- Best response during last treatment

- Number of prior treatments, any surgeries/procedures related to cancer

A data listing of prior anticancer treatment including surgical/procedures, primary cancer history and previous radiotherapy will be provided for Safety Population.

7.6 Medical History

The medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary, v22.0. The frequency count and percentage of patients experiencing any medical conditions will be tabulated by system organ classifications (SOC) and preferred term (PT) of MedDRA for all patients and by hepatic function group for each phase. The denominators for calculating the percentages will be based on number of patients in Safety Population for each phase for each hepatic function group.

A data listing of medical history including general medical, surgical and primary cancer history will be provided for Safety Population.

7.7 Prior and Concomitant Medication /Therapy

All medications as documented by the investigator will be coded using the World Health Organization (WHO) Drug Dictionary (WHO-DD Sept 2018). The count and percentage of patients who took prior and concomitant medications will be provided by hepatic function group, ATC level 3 and WHO Drug preferred term (PT) for each phase. The denominators for calculating percentages will be based on the number of patients in Safety Population for each hepatic group. For the summary tables, if a patient has taken a prior or concomitant medication more than once, the patient will be counted only once for the medication.

Prior non-anticancer medications are defined as any medications, other than study treatment, medications for cancer treatment and pre-medications for study treatment, which ended prior to the first dose date of study treatment.

Concomitant medications are medications other than study treatments, being taken on or after the initial study treatment dosing date through 30 days after the last dose or until the start of subsequent antitumor therapy, specifically

- PK Phase:
    - If patient discontinued study during PK phase, concomitant medications are medications being taken on or after first dose date in PK Phase through 30 days after the first dose date in PK Phase
    - If patient **did not** discontinued study during PK phase, concomitant medications are medications being taken on or after first dose date in PK phase but prior to the first dose date in Extension phase.

- Extension Phase:
    - Concomitant medications are medications being taken on or after first dose date in Extension Phase through 30 days after the last dose date in Extension Phase + 30

days (including those medications that started from PK Phase, but not stopped prior to Extension Phase)

The use of prior medications (including non-anticancer and anticancer) and concomitant medications will be provided in a by-patient data listing for Safety Population.

7.8 Analysis of Safety Data

7.8.1 Adverse Events

AEs will be coded using MedDRA and will be classified by SOC and PT of MedDRA v 22.0. Severity of AEs will be assessed by investigators according to CTCAE (v4.03).

A treatment-emergent AE (TEAE) will be defined as any new AE that begins, or any preexisting condition that worsens in severity during the treatment period. For the determination of the TEAEs during the treatment period, AEs with the greatest severity before the baseline will be used as the benchmark for the comparison of the AEs occurring within 30 days after last dose date or until the start of subsequent antitumor treatment, or 90 days after last dose date for serious AEs. Specifically:

- PK Phase:
  - If patient discontinued study during PK phase, TEAE period is from first dose date in PK Phase to first dose date in PK Phase + 30 days
  - If patient **did not** discontinued study during PK phase, TEAE period is first dose date in PK phase to first dose date in Extension phase.

- Extension Phase:
  - TEAE period is from first dose date in Extension Phase to last dose date in Extension Phase + 30 days

AEs that have a possible or definite relationship to study drug niraparib will be defined to be related to the drug niraparib while others will be defined as "not related". Any AEs for which the relationship to study drug niraparib is missing will be considered as related to study drug. AEs with the closest relationship to drug niraparib will be used for summary.

The number and percentage of patients who experienced an AE will be summarized by hepatic function group for each phase. The denominator for calculating the percentages will be based on the number of patients for each hepatic function group in the Safety Population of each phase.

The following types of summaries will be provided for each phase of the study:

- Overview of TEAEs
- TEAEs by SOC and PT
- TEAEs by SOC, PT, and Maximum CTCAE toxicity grade
- TEAEs by SOC, PT, and Maximum CTCAE toxicity grade ≥ 3

- TEAEs by PT in decreasing frequency
- Drug-related TEAEs by SOC and PT
- Drug-related TEAEs by PT in decreasing frequency
- Serious TEAEs by SOC and PT
- TEAEs leading to treatment discontinuation by SOC and PT
- TEAEs leading to dose interruption by SOC and PT
- TEAEs leading to dose reduction by SOC and PT
- TEAEs of special interest by special interest category, SOC, and PT.

If a preferred term or system organ class was reported more than once for a patient, the patient would only be counted once in the incidence for that preferred term or system organ class.

In tabulation by severity (i.e., CTCAE v 4.03 toxicity grade),

- For a given preferred term, only the most severe preferred term for each patient will be included.
- For a given system organ class, only the most severe system organ class for each patient will be included.

Similarly, in tabulation by relationship,

- For a given preferred term, the most closely related preferred term to the study drug for each patient will be included.
- For a given system organ class, the most closely related system organ class to the study drug for each patient will be included.

Adverse events, serious adverse events, and adverse events leading to discontinuation from the study will be provided in separate data listings.

7.8.2 Adverse Events of Special Interests (AESI)

Analyses of AESIs are based on pre-defined MedDRA PTs below in Table 4.

Table 4: Adverse Events of Special Interest

AESI	Preferred Term
Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML)	• 5q minus syndrome • Bone marrow infiltration • Chronic myelomonocytic leukaemia • Chronic myelomonocytic leukaemia (in remission) • Granulocytes maturation arrest • Myelodysplastic syndrome • Myelodysplastic syndrome transformation • Myelodysplastic syndrome unclassifiable

AESI	Preferred Term
	• Myeloid maturation arrest • Myeloid metaplasia • Platelet maturation arrest • Platelet production decreased • Proerythroblast count increased • Refractory anaemia with an excess of blasts • Refractory anaemia with ringed sideroblasts • Refractory cytopenia with multilineage dysplasia • Refractory cytopenia with unilineage dysplasia • Acute myeloid leukaemia • Acute myeloid leukaemia (in remission) • Acute myeloid leukaemia recurrent • Acute myeloid leukaemia refractory • Transformation to acute myeloid leukaemia
Secondary cancers (new malignancies [other than MDS or AML])	Malignant tumors (Narrow) SMQ, see Hepatic SAP AESI_MedDRA22.pdf for details
Pneumonitis	• Interstitial lung disease • Pulmonary fibrosis • Acute interstitial pneumonitis • Alveolitis • Alveolitis necrotizing • Hypersensitivity pneumonitis • Pulmonary toxicity • Non-infectious pneumonitis
Embryo-fetal toxicity	Pregnancy and neonatal topics (SMQ) , see Hepatic SAP AESI_MedDRA22.pdf for details

Lists will be finalized based on most recent MedDRA version prior to the data cutoff.

7.8.3 Extent of Exposure

The number and percentages of patients exposed to study drug in each phase will be provided for each hepatic function group. The denominators for percentages will be based on the number of patients exposed to study drug in each hepatic function group.

Additionally, study drug exposure and dose intensity will be summarized by hepatic function group using descriptive statistics for extension phase including:

- Number of exposure cycles (start from first cycle in extension phase) as a continuous variable
- Number and percentage of patients treated by maximum cycles (1, 2, 3 … and ≥12, start from first cycle in extension phase).
- Duration of exposure (days), defined as
  - last dose date – firs dose date in extension phase + 1
- Number of patients with dose interruptions or dose reduction
- Actual cumulative dose (mg), defined as
  - Sum of all doses actually administered in extension phase

- Actual dose intensity (mg/day), defined as
  - Actual cumulative dose (mg) divided by the duration of exposure (days)
- Relative dose intensity (%), defined as
  - Actual dose intensity (mg/cycle) divided by the intended dose intensity (mg/day), expressed in percentage

Details of study drug exposure and dose intensity for extension phase will be listed for Safety Population.

7.8.4 Clinical Laboratory Tests

All laboratory parameters collected at each center's local laboratory will be normalized by converting values in original units to values in SI units and classified as normal, low, or high based on normal ranges supplied by the local laboratories and upon employing standardization. Both laboratory parameters' values in the original unit collected and corresponding converted values in SI units will be listed for Safety Population.

Clinical laboratory tests (each normalized continuous laboratory parameter's values in SI unit and changes from baseline) will be summarized by visit and hepatic function group using descriptive statistics.

Laboratory test results will be categorized by CTCAE v 4.03 toxicity grades based on the values and normal ranges reported by the local laboratories. Within each hepatic function group, comparisons of CTCAE grades at baseline to grades at each post-baseline visit for each laboratory parameter will be summarized in 5-by-5 shift tables (grade 1 to grade 5). Denominators for calculating the percentages will be based on be number of patients with evaluable shifts at each post-baseline visit for Safety Population for each hepatic function group. Laboratory results with toxicity grades missing at either baseline or at post-baseline will not be used for summary in shift tables.

Coagulation parameters international normalized ratio (INR) and activated partial thromboplastin time (aPTT) will be tabulated by each hepatic function group.

In general, all by visit summaries of clinical laboratory parameters will only be summarized up to and including month 6 and at the treatment discontinuation visit. The maximum and minimum calculations will use all post-baseline data, including any unscheduled assessments.

Unscheduled measurements will not be used in computing the descriptive statistics for change from baseline at each post-baseline time point. However, they will be used in assessing the minimum and maximum of all visits and in the analysis of notable post-baseline results (for example shift tables).

7.8.5 Vital Signs

Observed vital signs and changes from baseline will be summarized by visit for each hepatic function group for each parameter.

A patient-detailed listing of vital signs will be provided for Safety Population.

7.9 Additional Data Presentation as Listing

- Inclusion/exclusion criteria not met
- Serum or urine pregnancy testing
- Physical examination findings including abnormal findings
- CLcr calculation or Creatinine clearance
- Growth factors
- Transfusion
- Tumor lesion assessment
- Tumor response per RECIST 1.1
- Malignancy reported in long term safety follow-up

8 DEFINITIONS AND CONVENTIONS FOR DATA HANDLING

8.1 Definition of Baseline

PK Phase:

For all evaluations unless otherwise noted, baseline for PK Phase is defined as the most recent measurement prior to the first administration of study drug in PK phase. Baseline can be the same date as first dose, given the measurement is expected prior to first dose when only date information is available.

Extension Phase:

For all evaluations unless otherwise noted, baseline is defined as the most recent measurement prior to the first administration of study drug in Extension phase. Baseline can be the same date as first dose, given the measurement is expected prior to first dose when only date information is available.

8.2 Definition of Relative Study Days

Unless otherwise noted, relative study days (Rel Days) of an evaluation are defined as number of days relative to the first dose date of study drug which is designated as Day 1, and the preceding day is Day -1, the day before that is Day -2, etc. Relative study days are calculated as an evaluation date minus first dose date of study drug, and plus 1 day if evaluation date is on or after first dose date.

Relative study days take negative values if evaluation date occurs prior to first dose date, and take positive values if evaluation date occurs on or after first dose date of study drug.

8.3 Analysis Visit Window

For safety parameters excluding clinical laboratory data, measurements collected from unscheduled visits will not be included in the by-visit summary tables but will be included in the listings. Early termination visits for safety measurements will not be mapped to any scheduled post-baseline visit, but will be used as the last assessment during treatment period.

8.4 Safety Data Handling

For all safety data, only observed data will be used for analyses, and missing data will not be imputed.

8.5 Handling of Partial Dates for AEs

When determining the treatment emergent AE, partial dates will be handled as follows.

- If the day of the month is missing, the onset day will be set to the first day of the month unless it is the same month and year as study treatment. In this case, the onset date will be assumed to be the date of treatment.
- If the onset day and month are both missing, the day and month will be assumed to be January 1, unless the event occurred in the same year as the study treatment. In this case,

the event onset will be coded to the day of treatment to conservatively report the event as treatment-emergent.

- A missing onset date will be coded as the day of treatment. If the resulting onset date is after a reported date of resolution, the onset date will be set equal to the date of resolution.
- Imputation of partial dates is used only to determine whether an event is treatment-emergent; data listings will present the partial date as recorded in the eCRF.

8.6 Handling of Partial Dates for Medications

When determining prior or concomitant medications, partial start dates of prior and concomitant medications will be assumed to be the earliest possible date consistent with the partial date. Partial stop dates of prior and concomitant medications will be assumed to be the latest possible date consistent with the partial date. In the case of completely missing stop date, medication will be assumed to be ongoing. In the case of complete missing start date, medication will be assumed to be prior medication.

PHARMACOKINETIC DATA ANALYSIS PLAN

PROTOCOL NUMBER:	3000-01-003
PROTOCOL TITLE:	An Open-Label, Non-Randomized, Multicenter Study to Determine the Pharmacokinetics and Safety of Niraparib Following A Single Oral Dose in Patients with Advanced Solid Tumors and Either Normal Hepatic Function or Moderate Hepatic Impairment
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1 INTRODUCTION

This study is an open-label non-randomized, multicenter study to determine the pharmacokinetics and safety of niraparib following a single oral dose in patients with advanced solid tumors and either normal hepatic function or moderate hepatic impairment.

Niraparib is extensively metabolized and eliminated primarily by hepatic and renal pathways. The purpose of this study is to evaluate pharmacokinetics and safety of niraparib in patients with moderate hepatic impairment, for the purpose of providing recommendations to guide the initial dose and dose titration in this patient population.

This data analysis plan is consistent with Section 11, Pharmacokinetic Assessments of the study protocol (An Open-Label, Non-Randomized, Multicenter Study to Determine the Pharmacokinetics and Safety of Niraparib Following A Single Oral Dose in Patients with Advanced Solid Tumors and Either Normal Hepatic Function or Moderate Hepatic Impairment Version3, Amendment 2, dated 15 January 2018) and includes additional details of the estimates of pharmacokinetic (PK) parameters, statistical analysis of the PK parameters, and summaries to be included in the pharmacokinetic analysis report.

2 STUDY DESIGN AND OBJECTIVES

2.1 Study Design

This is a Phase 1, open-label, parallel-group, single-dose study in patients with advanced solid tumors and with either normal hepatic function or moderate hepatic impairment.

Patients with solid tumors were recruited and enrolled within the following groups:

- Group 1: normal hepatic function (total bilirubin [BILI] and aspartate aminotransferase [AST] ≤ upper limit of normal [ULN])
- Group 2: moderate hepatic impairment (BILI >1.5 × to 3 × ULN) and any degree of AST elevation

All patients will receive a single dose of 300 mg niraparib administered as 3 × 100 mg capsules on Day 1. Patients will undergo PK sampling up to 168 hours (7 days) following niraparib administration. Pharmacokinetic parameters to be calculated include area under the concentration × time curve calculated to last measured concentration (AUC_{0-t}), area under the concentration × time curve calculated to infinity ($AUC_{0-\infty}$), maximum concentration (C_{max}), time to maximum concentration (t_{max}), terminal half-life ($t_{½}$), and apparent total clearance (CL/F). Protein binding parameters to be calculated include fraction of unbound drug (Fu) and clearance of free drug (CLfu/F). The study will be considered complete when the final PK evaluable patient completes all assessments in the PK phase of the study.

During the PK Phase of the study, patients should come to the clinic on the morning of Day 1 of the PK period following a 12-hour overnight fast. During the overnight fast, patients are

permitted to consume water (but no other beverages) until up to 2 hours prior to dosing of the study drug. Patients may take their routine medications with sips of water.

Patients will receive a single dose (300 mg) of the formulation with approximately 250 ml of water on Day 1 of the PK period. Patients may resume their regular diet 4 hours after taking the study drug.

2.2 Study Objectives

The PK objectives of this study are:

The primary objectives of this study are as follows:

- To characterize the pharmacokinetics (PK) of niraparib and its major metabolite (M1) if appropriate when administered as a single dose in cancer patients with normal hepatic function compared to patients with moderate hepatic impairment.

The secondary objectives of this study are as follows:

- To evaluate the safety of niraparib when administered as a single dose in patients with moderate hepatic impairment.
- To obtain additional safety data through the extension phase, in which patients have the option to continue receiving niraparib.

This PK analysis plan and the resulting PK report will address the PK objectives of the study. The PK report will be included as an appendix to the clinical CSR.

3 PHARMACOKINETIC ASSESSMENTS

3.1 Pharmacokinetic Analysis

Blood will be collected during the study for PK assessments and protein binding at the timepoints relative to niraparib dosing as described below. In total, approximately 80 mL of blood will be collected from each patient.

Pharmacokinetic Assessments	
Timepoint	**Collection window**
Predose	within 30 minutes prior to dosing
1 hr postdose	± 5 min
2 hrs postdose	± 5 min
3 hrs postdose	± 5 min
4 hrs postdose	± 5 min
6 hrs postdose	± 15 min

8 hrs postdose	± 15 min
12 hrs postdose	± 15 min
24 hrs postdose	± 30 min
48 hrs postdose	± 60 min
72 hrs postdose	± 60 min
120 hrs postdose	± 120 min
168 hrs postdose	± 120 min
Plasma protein binding	
Predose	within 30 minutes prior to dosing
3 hrs postdose	± 5 min
168 hrs postdose	± 120 min

The volume of blood collected for PK assessments from each patient (approximately 5 mL per sample) during the study will be approximately 65 mL. Blood sample collection, processing, and shipping details will be outlined in a separate laboratory manual. In brief, blood will be collected into potassium ethylene diamine tetraacetic acid (K_3EDTA) tubes, processed and plasma analyzed by a validated method of liquid chromatography coupled to tandem mass spectrometry detection (LC/MS/MS) for determination of the concentrations of niraparib and M1 if appropriate. The pharmacokinetic parameters (Section 11.1) will be calculated from the plasma concentration-time profiles.

The total volume of blood collected during the study for plasma protein binding from each patient (approximately 5 mL per sample) will be approximately 15 mL. Blood sample collection, processing, and shipping details will be outlined in a separate laboratory manual. In brief, plasma protein binding will be performed by equilibrium dialysis (MWCO 10kD). At the end of dialysis, aliquots from both compartments will be analyzed to determine the concentration of the unchanged drug using a modified LC/MS/MS method.

The following PK parameters will be calculated, within Phoenix WinNonlin Version 8.0, if appropriate:

- C_{max}: Observed maximum plasma concentration
- t_{max}: Time to C_{max}
- Kel:, the terminal elimination rate constant, will be estimated at terminal phase by linear regression after log-transformation of the concentrations
    - Only those data points that are judged to describe the terminal log-linear decline will be used in the regression.

  - A minimum number of three descending data points in the terminal phase will be used in calculating Kel with the line of regression starting at any post-C_{max} data point (C_{max} should not be part of the regression slope).
  - The adjusted correlation coefficient (R^2 adj) in general should be greater than 0.80.
  - An appropriate number of decimal places should be used for Kel to enable the reported value of $t_{1/2}$ to be calculated.

- AUC_{0-t}: Area under the concentration-time curve up to the last observable concentration calculated using linear trapezoidal summation from time 0 to time t, where t is the time of the last measurable concentration (C_t);
- AUC_{0-inf}: Area under the concentration-time curve up to infinity calculated using linear trapezoidal summation from time 0 to time infinity using the linear up log down method, $AUC_{(0-inf)} = AUC_{(0-t)} + C_t/Kel$, where Kel is the terminal elimination rate constant (the slope of elimination phase of the log-concentration versus time plot) and C_t is the last measurable plasma concentration. AUC_{0-inf} will not be reported if the % extrapolated exceeds 20% ;
- CL/F: Apparent total clearance of drug after oral administration, calculated as CL/F = Dose/AUC. Units will be volume / time (e.g. L/hr);
- $t_{1/2}$: Terminal half-life time estimated by 0.693/Kel (Kel is determined by the slope of terminal phase of log concentration versus time plot).

Additional plasma samples will be drawn for the assessment of unbound concentrations of niraparib. The following will be calculated for protein binding:

- Fu: Fraction of unbound niraparib
- CLfu/F: Clearance of free niraparib

The mean plasma concentration over time by hepatic function group and the individual subject plasma concentration versus time data will be plotted. Nominal times will be used for plotting the mean plasma concentrations over time by hepatic function group and actual sampling times will be used for the individual figures and for the non-compartmental analysis.

The PK parameters will be summarized descriptively including the number of observations, arithmetic mean, SD, CV, minimum, median, maximum, geometric mean and geometric CV%.

All PK parameters will be rounded to 3 significant figures except for Tmax which will be rounded to two decimal places.

Mean SD, Median, Min, Max, and geometric mean will be presented to 3 significant figures for all PK parameters except Tmax, Tmax will be presented to 2 decimal places; CV% and geometric CV% will be presented to 1 decimal place.

3.2 Non-Quantifiable Concentrations

All plasma concentration values reported as No Results/Not Reportable (NR) values will be treated as missing and will appear in the data set as ".". Values below the quantifiable limit (BQL) that occur prior to the first measurable concentration will be treated as zero. All other BQL values will be treated as missing and set to ".".

3.3 Statistical Analysis of PK parameters of Niraparib

To assess the effects of hepatic impairment on niraparib PK, linear models will be applied to the log-transformed C_{max}, and AUC_{0-t}, AUC_{0-inf}. The independent variable in the analyses will be liver function (normal hepatic function [control] or moderate hepatic impairment). Point estimates and 90% CIs for differences between means on the log scale will be exponentiated to express the results as ratios of geometric means on the original scale. Patients with normal hepatic function (Group 2) will be used as reference group to which Group 1 will be compared. No adjustments will be made for multiplicity.

Box plots of PK parameters (C_{max}, AUC_{0-t}, AUC_{0-inf}, CL/F, and CLfu/F) by hepatic function group will be provided.

The effect of hepatic dysfunction on unbound concentrations of niraparib may be assessed applying a general linear model with a factor for hepatic impairment status.

Descriptive statistics (number, arithmetic mean, arithmetic standard deviation [SD], median, minimum, maximum, geometric mean, and geometric coefficient of variation [CV%]) will be calculated for plasma concentrations and PK parameters of niraparib and M1 if appropriate.

4 TABLES, FIGURES AND LISTINGS (MOCKS)

List of Figures

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4.1 Figures

Figure 4.1-1 Mean niraparib concentrations (units) by hepatic function group (linear scale)

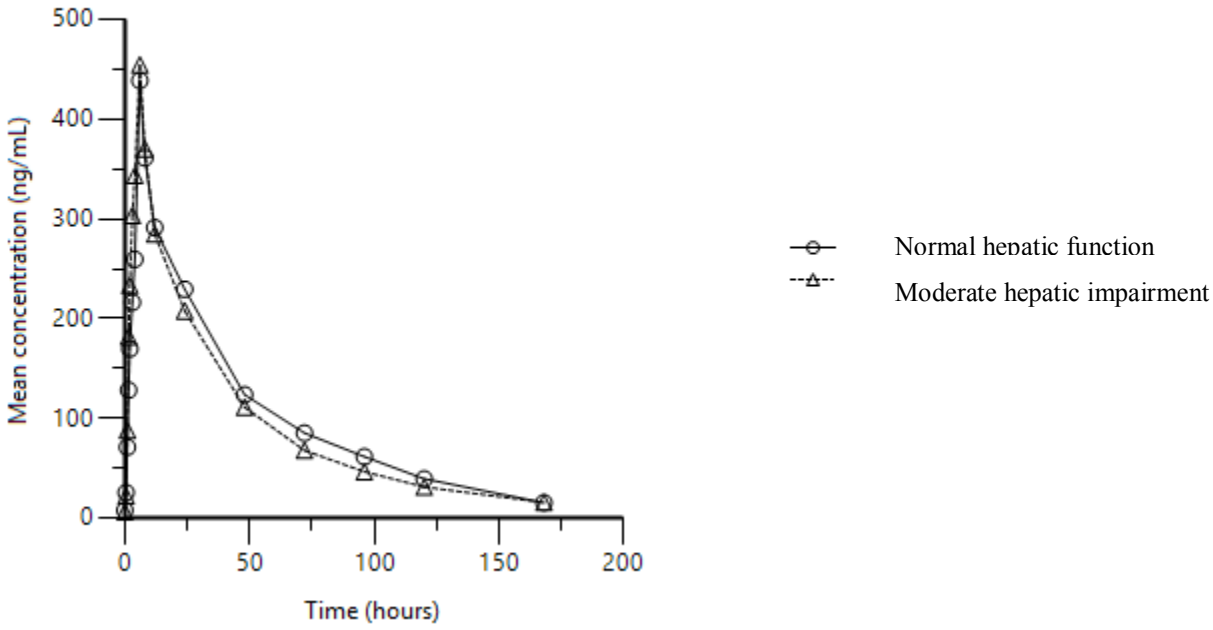


Figure 4.1-2 Mean niraparib concentrations (units) by hepatic function group (log-linear scale)

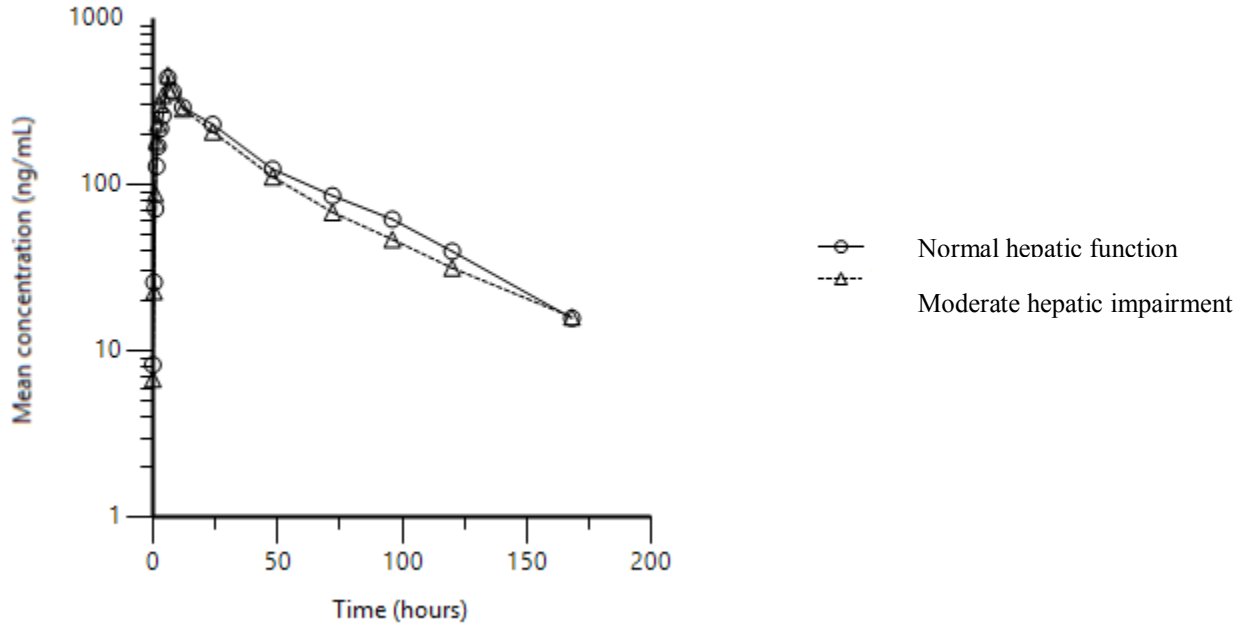
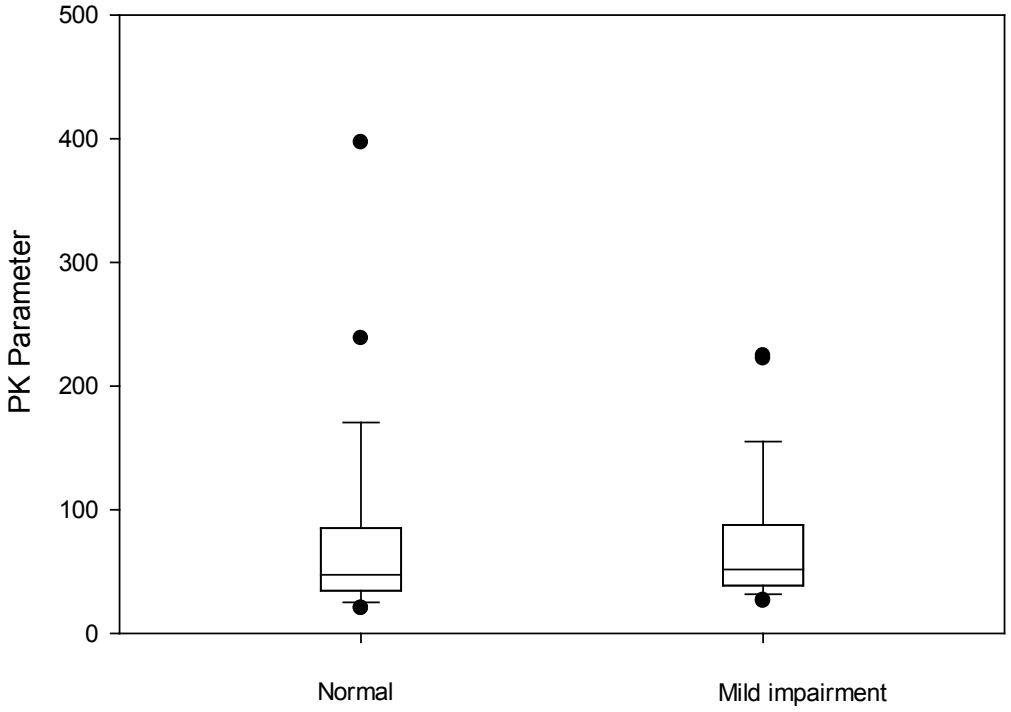


Figure 4.1-3 Mean (+SD) concentration time profiles for niraparib following administration to patients with moderate hepatic impairment or normal hepatic function

Figure 4.1-4 Boxplot of Niraparib PK parameters by hepatic function



4.2 Tables

Table 4.2-1 Summary of Plasma Concentrations (units) of Niraparib by Hepatic Function

		Time (hours)					
		0	**xxx**	**xxx**	**xxx**	**xxx**	**xxx**
Group		**XXX concentration (units)**					
Normal	N	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Moderate Hepatic Impairment	N	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Table 4.2-2 Summary of Pharmacokinetic Parameters of Niraparib by Hepatic Function

Group		Tmax (units)	Cmax (units)	AUC_{0-t} (units)	AUC_{0-inf} (units)	Vz/F (units)	CL/F (units)	Kel (units)	t1/2 (units)
Normal	N	X	X	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
Moderate Hepatic Impairment	N	X	X	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X

4.3 Subject Data Listings

Listing 4.3-1 Niraparib Plasma Concentrations (unit) Following Dose Administration of 300 mg Niraparib to Patients with Normal Hepatic Function

		Time (hours)					
		0	**XXX**	**XXX**	**XXX**	**XXX**	**XXX**
Group	**Subject**	**XXX Concentration (unit)**					
Normal	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	…	X.X	X.X	X.X	X.X	X.X	X.X
	N	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Listing 4.3-2 Niraparib Plasma Concentrations (unit) Following Dose Administration of 300 mg Niraparib to Patients with Moderate Hepatic Impairment

		Time (hours)					
		0	**XXX**	**XXX**	**XXX**	**XXX**	**XXX**
Group	**Subject**	**XXX Concentration (unit)**					
Moderate Hepatic Impairment	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	XXX	X.X	X.X	X.X	X.X	X.X	X.X
	…	X.X	X.X	X.X	X.X	X.X	X.X
	N	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Listing 4.3-3 Niraparib Plasma Pharmacokinetic Parameters Following Administration of 300 mg Niraparib to Patients with Normal Hepatic Function

Group	Subject	Tmax (units)	C_{max} (units)	AUC_{0-t} (units)	AUC_{0-inf} (units)	Vz/F (units)	CL/F (units)	Kel (units)	t1/2 (units)
Normal	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	…	…	…	…	…	…	…	…	…
	N	X	X	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X

Listing 4.3-4 Niraparib Plasma Pharmacokinetic Parameters Following Administration of 300 mg Niraparib to Patients with Moderate Hepatic Impairment

Group	**Subject**	**Tmax (units)**	**C_{max} (units)**	**AUC_{0-t} (units)**	**AUC_{0-inf} (units)**	**Vz/F (units)**	**CL/F (units)**	**Kel (units)**	**t1/2 (units)**
Moderate Hepatic Impairment	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	XXX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	…	…	…	…	…	…	…	…	…
	N	X	X	X	X	X	X	X	X
	Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Min	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Max	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	CV%	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X

4.4 Individual Subject Plots

Figure 4.4-1 Individual Niraparib Concentrations Following Administration of Niraparib to Patients with Moderate Hepatic Impairment or Normal Hepatic Function

1 Subject per plot

Figure 4.4-2 Combined Individual Niraparib Concentrations Following Administration of Niraparib to Patients with Moderate Hepatic Impairment or Normal Hepatic Function

By group

Additional Tables or Figures may be generated if deemed appropriate.