STATISTICAL ANALYSIS PLAN

A PHASE 1/2 TRIAL OF SRA737 (A CHK1 INHIBITOR) ADMINISTERED ORALLY IN SUBJECTS WITH ADVANCED CANCER

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Sponsor:	Sierra Oncology, Inc.
	6701 Commerce Center Drive, Plymouth, MI 48170
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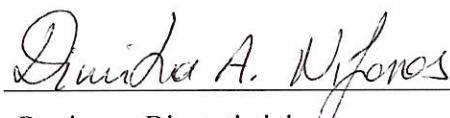
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Sponsor:	Sierra Oncology, Inc
Protocol Number:	SRA737-01
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Sponsor Approval

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 and the clinical development plan.

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LIST OF ABBREVIATIONS

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BP	Blood Pressure
CI	Confidence Interval
CR	Complete Response
CRC	Colorectal Cancer
CTC	Circulating Tumor Cell
ctDNA	Circulating Tumor Deoxyribonucleic Acid
DCR	Disease Control Rate
DLT	Dose Limiting Toxicity
DOR	Duration of response
ECG	Electrocardiogram
ECHO	Echocardiogram
eCRF	Electronic Case Report Form
HGSOC	High Grade Serous Ovarian Cancer
HNSCC	Head and Neck Squamous Cell Carcinoma
mCRPC	Metastatic Castration-Resistant Prostate Cancer
MTD	Maximum Tolerated Dose
NA	Not Available
NE	Not Evaluable
NGS	Next Generation Sequencing
NHL	Non-Hodgkin Lymphoma
NSCLC	Non-Small Cell Lung Cancer
ORR	Overall Response Rate
OS	Overall Survival

Abbreviation	Description
PBMC	Peripheral Blood Mononuclear Cell
PD	Progressive Disease
PDn	Pharmacodynamics
PFS	Progression Free Survival
PK	Pharmacokinetics
PR	Partial Response
PSA	Prostate Specific Antigen
RP2D	Recommended Phase 2 Dose
SAP	Statistical Analysis Plan
SCCA	Squamous Cell Carcinoma of the Anus
SD	Stable Disease
SDTM	Study Data Tabulation Model
TEAE	Treatment Emergent Adverse Events
TLF	Table, Listing, and Figure
TTP	Time to Progression
TTR	Time to Response
WHO	World Health Organization

1. OVERVIEW

The purpose of the Statistical Analysis Plan (SAP) for this study is to provide a framework for statistically rigorous study data analysis in support of the protocol objectives, without bias or analytical deficiencies.

Specifically, this Plan has the following purpose:

To prospectively (a priori) outline the types of analyses and presentations of data that will form the basis for conclusions to be reached that will answer the study objectives outlined in the protocol and to explain in detail how the data will be handled and analyzed, adhering to commonly-accepted standards and practices of biostatistical analysis in the pharmaceutical industry.

2. STUDY OBJECTIVES

2.1. Primary Objective

- To establish the safety profile of SRA737

- To determine the maximum tolerated dose (MTD) with 1 or more schedules of administration of SRA737

- To propose a recommended Phase 2 dose and schedule of SRA737

- To evaluate the preliminary efficacy of SRA737 including efficacy in prospectively-selected genetically-defined subjects enrolled into indication-specific expansion cohorts

2.2. Secondary Objective(s)

- To characterize the pharmacokinetic profile of SRA737

- To assess the relationship between response and the presence of selected genetic alterations detected in tumor tissue and/or circulating tumor deoxyribonucleic acid (ctDNA)

2.3. Exploratory Objective(s)

- To investigate the pharmacodynamics (PDn) of SRA737 in tumor tissue

- To investigate the pharmacodynamics of SRA737 in surrogate tissues such as blood or peripheral blood mononuclear cell (PBMCs)

- To explore possible clinical predictors of outcomes

- To explore the relationship between exposure (Pharmacokinetics) and QT/QTc, other electrocardiogram (ECG) parameters and cardiovascular safety findings

3.   STUDY METHODS

3.1.   Overall Study Design and Plan

This is a multicenter, first-in-human, Phase 1/2, open-label, dose-escalation trial in subjects with advanced solid tumors or non-Hodgkin lymphoma (NHL), with cohort-expansion phase in 6 indication-specific expansion cohorts. The trial consists of 2 stages:

Stage 1: Dose escalation phase

Utilizing an accelerated titration design, cohorts consisting initially of a single subject will receive escalating doses of SRA737, starting in Cohort 1 with 20 mg/day administered orally on a continuous daily dosing schedule in 28-day cycles. The dose will be escalated in each subsequent cohort until the MTD has been identified, unless determined otherwise by the Sponsor in consultation with the Chief Investigator, for example, if an alternative schedule is pursued instead. Once a SRA737-related, Grade 2 toxicity is observed in a dose escalation cohort during Cycle 1, that cohort will be expanded to 3 to 6 subjects, and subsequent dose level cohorts will follow a rolling 6 design.

Stage 2: Cohort expansion phase

Subjects with the following tumor indications will be enrolled into the Cohort Expansion Phase to facilitate a preliminary exploration of the efficacy of SRA737::

- Previously treated metastatic colorectal cancer (CRC)

- High grade serous ovarian cancer (HGSOC); further designated as those without CCNE1 gene amplification and those with CCNE1 gene amplification (or alternative genetic alteration with similar functional effect)

- Metastatic castration-resistant prostate cancer (mCRPC)

- Advanced non-small cell lung cancer (NSCLC)

- Head and neck squamous cell carcinoma (HNSCC) and squamous cell carcinoma of the anus (SCCA)

3.2.   Administration of Study Drug

SRA737 will be administered orally on a continuous daily dosing schedule in 28-day cycles. Alternate dosing schedules may also be explored. Subjects may continue to receive treatment as

long as none of the treatment discontinuation criteria are met as defined in Section 5.6 of the protocol.

3.3.   Study Procedures

Refer to protocol Section 7.6 and 7.7 for schedule of assessments. There are five distinctive phases in the study

- Screening evaluations (After signing informed consent, and prior to first dose)

- First dose for intensive PK (single day, Day -7 to Day -4)

- Treatment phase (28-day cycles)

- Safety follow-up (30 days after last dose of SRA737)

- Long-term follow-up (every 16 weeks)

4.   STUDY ENDPOINTS

Study endpoints corresponding to the study objectives are listed below. Secondary endpoints and exploratory endpoints will be summarized and analyzed in separate reports and analysis plan for those endpoints will not be included in this document. As a result, the analysis datasets and outputs corresponding to these endpoints will not be included within the scope of this SAP.

4.1.   Primary Endpoints

- Safety parameters including adverse events (AEs), laboratory tests, and vital signs

- MTD: the highest dose at which $\leq 33\%$ of subjects have a dose limiting toxicity (DLT) in a cohort of up to 6 subjects

- Recommended Phase 2 Dose (RP2D)

- Objective response rate (ORR)

- Disease control rate (DCR)

- Time to response (TTR)

- Duration of response (DOR)

- Progression-free survival (PFS)

- Time to progression (TTP)

- Overall survival (OS)

If there are no subjects with response (complete or partial response), TTR and DOR related summaries and listings will not be generated.

4.2. Secondary Endpoints

- Plasma concentration-time profile and calculation of pharmacokinetic (PK) parameters including, but not limited to: AUC_{inf}, AUC_{tau}, C_{max}, C_{min}, T_{max}, and $t_{1/2}$

- ORR and gene alterations in tumor tissue or ctDNA at baseline as measured by next generation sequencing (NGS)

4.3. Exploratory Endpoints

- Proof of target engagement and changes in mechanism of action biomarkers between baseline and on treatment with SRA737, including, but not limited to: pSer296 Chk1, pS317 Chk1 and total Chk1

- Proof of target engagement and changes in mechanism of action biomarkers between baseline and on treatment with SRA737, including but not limited to: pS317 Chk1, pS345 Chk1, total Chk1, gammaH2AX and RAD51

- Characteristics such as performance status, prior therapy, indication and other known or potential prognostic or predictive factors

- Association of QT, QTc, blood pressure (BP), heart rate, other ECG intervals with time-matched PK concentrations. Profile of QTc over the dosing interval

5. DATA CAPTURE AND PROCESSING

Clinical study data will be captured on electronic case report forms (eCRF) and maintained in a Medidata Rave clinical database. The study data will be stored on the SAS server to facilitate further downstream activities. The study data will be mapped using study data tabulation model (SDTM). Data points used for summaries and analyses will be mapped from SDTM to analysis data model (ADaM).

6. ANALYSIS AND REPORTING

6.1. Interim Analysis

There will also be 2 planned interim reviews on the accumulating data. These are not formal statistical interims, and the reviews are conducted in part for subject safety. There will be no

adjustment to significance levels for reviews of the accumulating data during the trial. The planned reviews will occur at the following time points:

- At the completion of subject follow-up for the last subject enrolled at the end of the dose escalation

- At the completion of the expansion cohort for each indication.

6.2. Final Analysis

The final analysis will be conducted after one of the following conditions is met:

- The trial is terminated early.

- The end of trial, which is defined as the date when the last subject has completed the Safety Follow-up visit or the long-term follow-up visit (whichever is later).

Additional analysis may be conducted for regulatory, publication, or decision making purposes.

7. SAMPLE SIZE DETERMINATION

The study will enroll up to 170 subjects in total including an estimated 30–50 subjects during dose escalation and 6 indication-specific expansion cohorts each consisting of approximately 20 prospectively-selected genetically-defined subjects. The sample size for dose escalation is based on assumptions of the likely MTD based on allometric scaling and will depend on the number of dose levels required to establish the MTD and RP2D. The final number of subjects enrolled into the trial will depend on the number of dose levels, the number of subjects who participate in both the Dose Escalation and Cohort Expansion phases, and potentially alternative dose schedules explored. A planned sample size of 20 subjects enrolled in each indication-specific expansion cohort will permit confirmation that the 95% confidence intervals around an observed ORR in each cohort is ± 16%.

8. ANALYSIS POPULATIONS

8.1. Safety Evaluable Population

Safety evaluable population includes all enrolled subjects who receive at least 1 dose of SRA737. Subjects who received the single dose for PK evaluation but never received study treatment during the treatment phase are also included in this population.

8.2. Response Evaluable Population

Response evaluable population includes all enrolled subjects who satisfy all of the following conditions. Two sets of criteria are defined for the 2nd condition and hence two response

evaluable populations will be defined: (a) is the original definition per protocol, used in statistical outputs (unless specified otherwise) and (b) is the alternative definition used in exploratory efficacy analysis as described in the CSR. To differentiate the two definitions in the outputs the population line in the TLFs will be "Response Evaluable Population" for definition (a) and "Response Evaluable Population (Alternative Definition)" for definition (b).

1. Have measurable disease and assessment at baseline (for inclusion in expansion cohorts, subjects also need to meet the appropriate protocol criteria for genetically-defined tumor)

2. Two sets of criteria are defined below (a or b) based on the dosing information

   a. Received at least 75% of 1 cycle of study medication, OR
   b. An alternative definition might be used for some exploratory efficacy analysis: Received at least 75% of cycle 1 study medication at ≥ 300 mg or continued on-study after 2 cycles of treatment at any dose level.

3. Have at least one post-baseline disease assessment OR discontinued treatment due to adverse event or disease progression or death

8.3. Pharmacokinetics Evaluable Population

All subjects who receive at least 1 dose of SRA737 and provide at least 1 evaluable PK concentration will be included in the PK analysis. Plasma concentration data will be eligible for inclusion into PK analyses if the subject receives the full dose and does not vomit within 4-hours postdose. Because the endpoints using this population are not reported in the SAP this population will not be included in the ADaM datasets.

8.4. Pharmacokinetics/Corrected QT Interval Evaluable Population

All enrolled subjects who receive at least 1 dose of SRA737 and for whom adequate QTc and ECG data are available will be evaluable for PK/QTc analyses. Because the endpoints using this population are not reported in the SAP this population will not be included in the ADaM datasets.

8.5. Pharmacodynamics Evaluable Population

All enrolled subjects who receive at least 1 dose of SRA737 who have evaluable data for each specific PDn assessment will be evaluable for PDn. Because the endpoints using this population are not reported in the SAP this population will not be included in the ADaM datasets.

9. GENERAL CONSIDERATIONS FOR STATISTICAL ANALYSIS

9.1. General Principles for Data Analysis

9.1.1. Multicenter Study

The summaries and analyses will be conducted by pooling data from all study centers. If it is identified that a site has disproportionate number of protocol deviations additional summaries excluding the site in question might be carried out.

9.1.2. Testing Strategy and Multiplicity Adjustments

No formal multiplicity adjustment will be performed. All statistical results such as p-values and confidence interval (CI) are supportive in nature.

9.1.3. Examination of Subgroups

Efficacy analyses based on the subgroups defined by tumor type and genetic criteria may be carried out. Additional subgroups might be added if identified during the course of the trial.

9.2. General Data Handling Conventions

9.2.1. Data Displays for Reporting

For tables and figures the data will be displayed as shown in the following tables. Any abbreviation used in the column text will be displayed in full description text in the footnote of the output.

Unless specified otherwise all tables will have corresponding listings supporting the table summaries. The default ordering of the listings is by disease categories, site ID, subject ID, test or parameter name (if applicable), sequence number (AE, medical history, or medication), date of event or date of collection (if applicable).

For study population and efficacy, the columns will be grouped by the primary tumor type regardless if a subject was enrolled under escalation or expansion stage.

Table 1: Data Display for Study Population and Efficacy

Column Text Display	Description **Verbatim terms included in the grouping** **(including misspelling and specific terms present in the clinical data)**	Display Order

CRC	Metastatic Colorectal Cancer
	    Metastatic colorectal
	    Metastatic Colorectal Carcinoma With Abdomial* Mass
	    Colorectal Adenocarcinoma
		1

HGSOC	High Grade Serous Ovarian Cancer
	    Platinum resistant ovarian
	    Carcinosarcoma Of Ovary – CCNE1 Amplification: No
	    High grade serous ovarian cancer
	    Platinum-Resistant High Grade Papillary Serous Carcinoma Of The Ovary
	    Serous Adenocarcinoma Peritoneum/Ovary
		2

NSCLC	Advanced Non-small cell Lung Cancer Advanced non small cell lung	3

mCRPC	Metastatic Castration-Resistant Prostate Cancer
	    Metastatic castration resistent* prostate
	    Prostate Adenocarcinoma
	    Adenocarcinoma of Prostate
		4

HNSCC/SCCA	Head and Neck Squamous Cell Carcinoma Head and neck squamous cell	5
	Squamous cell carcinoma of the anus	
Other	Disease types not included in the previous columns	6
Overall	All subjects in the population	7

    * Misspelling are present in the clinical database and will be kept verbatim for programming purposes

For safety summaries, the columns will be group based on Cycle 1 Day 1 total dose level. For subjects without Day 1 treatment they will be included in the "<=800mg" column.

Table 2: Data Display for Safety

Column Text Display	Description	Display Order
<=800mg	SRA737 daily total dose <= 800 mg	1
>800mg	SRA737 daily total dose > 800 mg, including BID dosing frequency	2
Overall	All subjects in the population	3

9.2.2. Reporting Conventions

The general programming considerations for tables, listings, and figures (TLFs) are provided in Section 15. Actual formats and layouts may be altered slightly to accommodate actual data or statistics. Minor format changes will not require updates to the SAP. The TLF numbering and general content follow the ICH E3 guidelines.

In general, continuous variables will be summarized to include the population sample size (N), number of subjects with available data (n), arithmetic mean, standard deviation, median, minimum, Q1, Q3 and maximum values. Categorical variables will be summarized by the population size (N), number of subjects in each category, and the percentage of subjects in each category. A missing category will be added as the last category if appropriate.

The data analyses will be conducted using the SAS® System (SAS Institute Inc., Cary, NC) version 9.4 or above. The eClinical Solutions' standard operating procedures will be followed for the validation of all SAS programs and outputs.

9.2.3. Early Withdrawal and Missing Data

All subjects who withdrew early from the study will be included in the reporting if they meet the definition of the analysis population specified in Section 8, regardless whether they were replaced for the purpose of DLT assessment.

In general, missing data will not be imputed and only observed values will be analyzed except for the data mentioned below.

If the date of diagnosis on the cancer diagnosis CRF page is partially missing, it will be imputed using the following rules for the purpose of calculating "Time Since Initial Diagnosis" summary.

- If only the day part is missing, day 15 will be used for imputation

- If both day and month parts are missing, July 1st will be used for imputation

If the relationship of an AE record is missing the AE will be considered "Related" to the study treatment for reporting purpose. If the Common Terminology Criteria for Adverse Events (CTCAE) grade of an AE is missing every effort should be made to acquire the information from the investigator. Grade 3 will be assigned to a missing grade for reporting purposes.

In general, missing or partial dates will not be imputed except for AE or medication start and end date.

The general imputation rules of partial missing date for both AE and concomitant medication are detailed below:

For AE or medication start date

If the year portion is missing no imputation will be performed.

If the day portion is missing, the following rules will be implemented:

- Impute with first day of the month if the year and month of the start date is not equal to the year and month of the first study treatment (including PK dose)

- Impute with date of first study treatment if the year and month of the start date is the same as the date of the first study treatment (including PK dose)

If the month portion is missing, the following rules will be implemented:

- Impute with first day of the year if the year of the start date is not equal to the year of the first study treatment (including PK dose)

- Impute with date of first study treatment if the year of the start date is the same as the date of the first study treatment (including PK dose)

For AE or medication end date

If the year portion is missing no imputation will be done.

If the day or month portion is missing:

- Impute with the last day of the month (or of the year). If the imputed date is later than the date of death, the death date will be used to impute the end date.

9.2.4.   Analysis Visiting Windows

No analysis visit window will be defined for safety data or efficacy data except for the tumor marker data. All post-baseline radiological disease assessments will be used for analyses purpose. Nominal clinical visits that are defined in the protocol "Schedule of Event" will be used for summary of safety endpoints. Any unscheduled safety data will not be included in the by-visit summary and will be included in the listings.

9.3.   Data Definition and Deviations

9.3.1.   Baseline and Change from Baseline

In general, the last recorded value prior to the first study treatment will serve as the baseline measurement for the safety endpoints such as lab, vital signs, and electrocardiograms (ECGs). The first treatment could be the first dose for PK collection or, if PK dose is not implemented, the first dose during the treatment phase. If there are multiple results collected on the same day, the collection done at later time, with the repeat status, or with a later sequence number will be used.

Change from baseline will be calculated as the post baseline value minus the baseline value. Percentage change from baseline will be calculated as the change from baseline divided by the

baseline value, multiplied by 100. If either the baseline or post-baseline value is missing, then change from baseline and percentage change from baseline will be set to missing.

9.3.2. Study Day and Duration

Study day is relative to the start date of the first treatment of the treatment phase. As stated above subjects may have the first dose for intensive PK purpose prior to the first treatment of the treatment phase. In such cases the study day will not align with the very first dose subjects received. It is set up this way to be consistent with the protocol "Day" definition and to avoid confusion in the listings when the study day is used. There is no study Day 0 defined.

- For an assessment that occurred on or after the study treatment:
  Study day = Date of assessment – date of first study treatment in treatment phase + 1

- For an assessment that occurred prior to the study treatment:
  Study day = Date of assessment – date of first study treatment in treatment phase

A duration between any two dates (such as AE duration) expressed in days will be calculated using the following conventions: Duration = later date – earlier date + 1.

10. SUBJECTS BASELINE CHARACTERISTICS, DEMOGRAPHICS AND MEDICATIONS

10.1. Subject Disposition and Withdrawals

Subject disposition will be summarized for all screened subjects. The summary for the screened population will include number of subjects who received at least one study treatment and who were screen failures.

Disposition summary will be based on the safety evaluable population. The following categories will be presented: treatment discontinuation and reasons, study discontinuation and reasons.

Number of subjects received Cycle 1 day 1 dose, included, and not included in the response evaluable population (both definitions) and reason for exclusion will be summarized.

10.2. Protocol Deviation

Protocol deviations were collected in the protocol deviation log. Major protocol deviations will be summarized by site and by deviation categories. All deviations, both major and minor, will be listed. Major protocol deviations are those in the deviation log that had a level classified as "Level 2". All the other deviations will be classified as minor protocol deviations.

10.3. Demographics and Other Baseline Characteristics

All demographic and baseline characteristic data will be summarized using descriptive statistics for safety evaluable population.

The summary table for demographics and baseline characteristics will include the following information:

- Age (years), age category (<65, ≥65 years)

- Sex (male, female)

- Ethnicity (Hispanic or Latino, not Hispanic or Latino)

- Race (eCRF collected race. If more than one race was checked it will be reported as "Other")

- Weight (kg) and height (cm) collected at baseline

- World Health Organization (WHO) performance status at baseline

Baseline cancer characteristics will include the following:

- Time since initial cancer diagnosis (months)

- Stage at screening

Prior cancer treatment includes prior anti-cancer therapy, prior radiotherapy, and prior surgical procedures. If there are more than one prior anti-cancer therapy collected for a subject, the last one (based on regimen start date) will be summarized including the following:

- Received prior anti-cancer therapy

- Line of Therapy (1, 2, 3, 4, 5, 6+)

- Reason for discontinuation of anti-cancer therapy (CRF terms)

- Prior radiotherapy (yes, no)

- Prior surgical procedures (yes, no)

10.4. Medical History and Concomitant Diseases

Medical history was not coded. Details of each medical history will be listed for the safety evaluable population.

10.5. Prior and Concomitant Medication

Prior and concomitant medications will be summarized for the safety evaluable population. Medications will be coded using the World Health Organization (WHO) Drug B2-Sept 2016 version. These medications will be further classified as follows.

- Prior medication is defined as those medications that started prior to the study treatment (collected within 28 days prior to the first dose). If medications started prior to the study treatment and were ongoing after the study treatment, they will be considered as both prior and concomitant medications.

- Concomitant medication is defined as those taken on or after the study treatment. If medications started prior to the study treatment and were ongoing after the study treatment, those medication will be considered as concomitant medication as well.

If a medication's start date is completely missing, it will be counted in both prior and concomitant summaries. The number and percentage of subjects taking prior and concomitant medications will be summarized by Anatomical Therapeutical Chemical (ATC) Levels 2 and preferred terms (standardized drug name) by descending frequency based on all the subjects in the population.

11. EFFICACY ANALYSIS

Unless specified otherwise all efficacy analyses will be based on the response evaluable population. An alternative definition of response evaluable population is defined in Section 8.2 and additional efficacy summaries may be repeated using the alternative definition if the differences are deemed clinically meaningful.

11.1. Overall Response

11.1.1. Overall Response Rate

Overall response rate will be assessed by the investigator per RECIST criteria version 1.1. Partial or complete response should be confirmed by a repeat tumor imaging assessment not less than 4 weeks from the date the response was first documented. The confirmed responses will be derived based on the overall responses by timepoint using the logics below:

Table 3: Confirmed Response per RECIST 1.1

Initial Response	Subsequent Timepoint	Confirmed Response
Complete Response (CR)	CR at least 4 weeks after initial CR (or consecutive CRs with at most one NE in between with the last CR at least 4 weeks after initial CR)	CR
	CR less than 4 weeks	SD

Initial Response	Subsequent Timepoint	Confirmed Response
	PD or Not Evaluable (NE) or no subsequent assessment	SD if CR is at least 6 weeks from Cycle 1 Day 1, otherwise PD or NE
Partial Response (PR)	PR/CR at least 4 weeks after initial PR (or consecutive PRs/CRs with NEs in between with the last PR/CR at least 4 weeks after initial PR)	PR
	PR/CR less than 4 weeks, or SD	SD
	PD or NE or no subsequent assessment	SD if PR is at least 6 weeks from Cycle 1 Day 1, otherwise PD or NE
Stable Disease (SD)	PD or NE, SD, or no subsequent assessment	SD if SD is at least 6 weeks from Cycle 1 Day 1, otherwise PD or NE
Progressive Disease (PD)	Any assessment or no subsequent assessment	PD

The best overall confirmed response will be the best confirmed response from the above following the order of CR > PR > SD > PD > NE

The best overall response will be summarized for the following endpoints with count and percentage:

- CR

- PR

- SD

- PD

- NE

- ORR (CR + PR) with 95% CI (Wilson method [1])

- DCR (CR + PR + SD) with 95% CI (Wilson method)

11.1.2.   Time to Response (TTR)

Time to response is define as time from Cycle 1 Day 1 to the date of first best overall confirmed response of CR or PR and will be summarized as a continuous outcome. Subjects without CR or PR as the best confirmed response are not included in the TTR summary. Summary of TTR may not be generated if there are not enough subjects with responses to create meaningful summaries.

11.1.3. Duration of Response (DOR)

Duration of response is defined as time from the first best overall confirmed response of CR or PR to the date of disease progression or death. If a subject did not experience the event, DOR will be censored. The event and censoring rules for DOR will be the same as the rules for PFS (Section 11.3). DOR will be analyzed using the Kaplan-Meier method. The output will include count and percentage of subjects with events or censored outcome including the type of event and censoring. Median DOR and 95% CI based on log-log transformation will be provided. Landmark analyses of DOR at various timepoints may be carried out if of clinical interest. Kaplan-Meier plot supporting the table summary may also be generated.

Subjects without CR or PR as the best confirmed response are not included in the DOR analyses. Summary of DOR may not be generated if there are not enough subjects with responses to create meaningful summaries.

11.1.4. Duration of Stable Disease

Duration of stable disease is defined as time from Cycle 1 Day 1 to the date of disease progression or death. If a subject did not experience the event, duration of stable disease will be censored. The event and censoring rules for duration of stable disease will be the same as the rules for PFS (Section 11.3). Duration of stable disease will only be presented in the listing that supports the exploratory efficacy analyses.

Duration of disease is only defined for subjects with any CR, PR, or SD prior to the first PD or subjects who did not experience PD.

11.1.5. Change in Target Tumor Size

At each timepoint of imaging assessment the sum of the longest diameter of all the target lesions are derived. The change and percentage change from baseline to the post-baseline nadir will be summarized. A waterfall plot of best percent change from baseline (from baseline to nadir) by tumor type cohorts will be provided.

11.1.6. Response Criteria for mCRPC Subjects

In addition to the RECIST criteria, response for subjects with mCRPC will also be evaluated by prostate specific antigen (PSA) and Circulating Tumor Cell (CTC). The PSA and CTC data will be presented in listings for mCRPC subjects to facilitate the review of the responses.

11.2. Time to Progression (TTP)

Time to progression is defined as time from the Cycle 1 Day 1 to the earliest date of radiographic disease progression per RECIST 1.1. If a subject did not experience progressive disease, TTP is censored at the last imaging assessment. TTP will be analyzed using the Kaplan-Meier method. The output will include count and percentage of subjects with events or censored outcome including the type of event and censoring. Median TTP and 95% CI based on log-log

transformation will be provided. Landmark analyses at various timepoints may be carried out if of clinical interest. Kaplan-Meier plot supporting the table summary may also be generated.

In addition to TTP by RECIST 1.1 criteria based only on the radiographic assessments, a second definition of TTP which incorporates the clinical progression will be used. The clinical progression is based on the medical review of the reasons of treatment discontinuation or study continuation. If a subject is considered having clinical progression the date of treatment or study discontinuation will be used as date of clinical progression and the TTP is defined as time from Cycle 1 Day 1 to the earliest date of clinical or radiographic disease progression.

11.3. Progression-free Survival (PFS)

Progression-free survival is defined as time from Cycle 1 Day 1 to the earliest date of radiographic disease progression per RECIST 1.1 or death, whichever happens first. The detailed event and censoring rules are shown in the table below following the hierarchical order of the logic:

Table 4:   Event and Censoring Rules for PFS

Situation	Date of Progression or Censoring	Outcome
Death or progression after more than 1 missed imaging visit	Date of last adequate assessment before missed visits	Censored
Death or progression without more than 1 missed visit	Earliest date of death or progression	Event
No Death or progression	Date of last imaging assessment	Censored
No post-baseline assessment	Date of Cycle 1 Day 1	Censored

PFS will be analyzed using the Kaplan-Meier method. The output will include count and percentage of subjects with events or censored outcome including the type of event and censoring. Median PFS and 95% CI based on log-log transformation will be provided. Landmark analyses at various timepoints may be carried out if of clinical interest. Kaplan-Meier plot supporting the table summary may also be generated.

11.4. Overall Survival (OS)

Overall survival is defined as time from the Cycle 1 Day 1 to the date of death. If a subject doesn't have a recorded death in the database, OS will be censored at the date at which the subject is last known to be alive. The last known alive date is based on searching the last date from the following CRF forms:

- Treatment start and end date from the continuous dosing page

- Treatment start date from the first dose page

- Date of off-treatment

- Date of follow-up or date of death from the follow-up page

- Date of visits

OS will be analyzed using the Kaplan-Meier method. The output will include count and percentage of subjects with death or censored outcome. Median OS and 95% CI based on log-log transformation will be provided. Landmark analyses at various timepoints may be carried out if of clinical interest. Kaplan-Meier plot supporting the table summary may also be generated.

12. SAFETY ANALYSIS

All safety analyses will be based on the safety evaluable population.

12.1. Extent of Exposure and Compliance

Duration of treatment is defined as from the date of first dose in the treatment phase to the date of last dose taken from the SEA737 drug administration CRF page. If a subject only received the first dose for PK, the duration of treatment will be set to 1 day. In addition to the numeric summary of duration of treatment, the count and percentage of the following intervals will be presented:

- >= 4 weeks

- >= 8 weeks

- >= 12 weeks

- >= 16 weeks

- >= 20 weeks

Cycle 1 compliance is used as part of the definition of the response evaluable population and will be summarized as numeric result and categorical result ($\geq$ 75% and < 75%). Cycle 1 compliance is from the SRA737 drug administration form for both QD and BID frequencies. For subject without compliance information on the CRF, the compliance will be calculated as follows:

Compliance = (Cycle 1 last dose date - first dose date + 1 - days when dose was not given) / 28 *100%

12.2. Adverse Events

Adverse events will be coded using MedDRA version 19.1.

An AE will be considered a treatment emergent adverse event (TEAE) if it begins or worsens in severity after the first dose of study treatment (including the dose for PK purpose). Partial AE

start dates will be imputed as detailed in Section 9.2.3. If an AE start date is completely missing it will be considered a TEAE.

Summary tables will be based on TEAEs. The incidence of TEAEs will be presented using counts and percentages of subjects with TEAEs and tabulated by SOC and PT. SOC will be sorted in descending frequency and PT within SOC will be sorted by descending frequency based on the incidence of all subjects in the population. If a subject has multiple occurrences (start and stop) of an event associated with a specific SOC or PT within a SOC, a subject will only be counted once in the incidence count for the SOC or PT within SOC respectively.

An overall summary table of AEs will be presented detailing the number and percentage of subjects for the following categories. One additional overall summary of AEs by disease categories instead of Cycle 1 total dose with the same AE categories below will also be presented.

- At least one TEAE;

- At least one Treatment-Related TEAE;

- At least one Grade ≥ 3 TEAE

- At least one Grade ≥ 3 Treatment-Related TEAE;

- At least one Serious TEAE;

- At least one Serious Treatment-Related TEAE;

- At least one Serious AE Occurred Prior to First Dose

- At least one TEAE leading to Treatment Withdrawn;

- At least one Treatment-Related TEAE leading to Treatment Withdrawn;

Except for all TEAEs which will be summarized by SOC and PT, the incidence of all other TEAEs by PT will be presented for the following in descending frequency based on the incidence of all subjects in the population.

- All TEAEs;

- Treatment-related TEAEs;

- TEAEs with Grade ≥ 3;

- Treatment-related TEAEs with Grade ≥ 3;

- Serious TEAEs;

- Treatment-related serious TEAEs;

- Serious AEs Occurred Prior to First Dose

- TEAEs leading to Treatment Withdrawn

- Treatment-related TEAEs leading to Treatment Withdrawn

A Treatment related AE is defined as an AE for which the investigator classifies the relationship to study treatment as being "Highly probable", "Probable", or "Possible" on Adverse Event eCRF. Missing relationship and toxicity grade will be imputed per Section 9.2.3.

12.3.   Laboratory Evaluations

Biochemistry and hematology laboratory tests are scheduled to be collected before the first dose for PK, at Day 1, 8, 15, and 22 for each cycle (frequency could be reduced at later cycles), and at the safety follow-up (30 days after the last dose). Troponin T or I are collected before the first dose for PK, Day 1 and Day 8 of Cycle 1 and Day 1 of Cycle 2 and Cycle 6, and at the safety follow-up. Urinalysis is collected before the first dose for PK, Day 1 of each cycle, and at the safety follow-up.

All continuous laboratory parameters in biochemistry and hematology will be summarized descriptively by actual value at each scheduled visit and the corresponding changes from baseline. The maximum post-baseline and minimum post-baseline (including both scheduled and unscheduled results) will also be provided before the by-visit summary. All parameters will be summarized in SI units.

Shift tables from baseline to visit will be provided for hematology and chemistry parameters to display low, normal, high, and missing values by treatment group in a 3-by-3 contingency table. Denominators for percentages will be the number of subjects with non-missing data at the specific assessment and baseline.

Urinalysis results will only be provided in the listing.

12.4.   Serum Tumor Markers

Serum tumor markers are scheduled to be collected before the first dose for PK and at the end of every 4 weeks (+/- 1 week) from Cycle 1 Day 1. Given there are no designated visit for tumor marker collection, the following windowing rules will be applied for summary purpose.

Table 5:   Analysis Visit Windowing Rules for Tumor Markers

Analysis Visit Name	Target Study Day	Visit Windowing
Baseline	NA	Last assessment prior to first dose
End of Cycle 1	28	21 to 35
End of Cycle 2	56	49 to 63

Analysis Visit Name	Target Study Day	Visit Windowing
End of Cycle n	28 * n	(28 * n - 7) to (28 * n + 7)

Once the analysis visit windowing rules are applied, the result closest to the target study day will be used for summary purpose. If multiple results have the same distance to the target study day the later one will be used. If both results fall on the same day, the one with the larger sequence number will be used.

CEA, PSA, and CA-125 will be summarized descriptively by actual value at each analysis visit and change from baseline at each post-baseline visit. All other tumor markers will be listed only.

12.5.   Vital Signs

Vital sign data including blood pressure, pulse rate, and body temperature are collected before the first dose for PK, Day 1, 8, 15, and 22 of Cycle 1, Day 1 of the subsequent cycles, and at the safety follow-up.

For all parameters, actual values and change from baseline will be presented for scheduled visits using descriptive statistics for continuous variables.

12.6.   ECG

Both central and local ECG data are collected in this study. Local ECGs are collected at screening, Cycle 1 Day 1, Cycle 2 Day 1, every third cycle Day 1, and at the safety follow-up. Central ECGs are collected at pre-dose and 2 hours after the first PK dose and at pre-dose, 1, 2, 4, 6, and 24 hours after the Cycle 1 Day 22 dose.

Both local and central ECGs include ventricular rate, QRS rate, QT interval, QTcF interval, PR interval, RR interval, and interpretation. Local ECG parameters will be presented using the actual values and change from baseline for each of the scheduled visits using descriptive statistics for continuous variables. If triplicates are collected for ECG parameters, the average value of the triplicates and the last interpretation will be used for reporting purpose.

The Central ECGs will be analyzed with the PK data to explore the exposure-QTc relationship in a separate report and will not be covered in this SAP.

12.7.   Physical Examination

A complete physical examination is performed and data is collected at Screening. Subsequent physical examination is only carried out as symptom directed. Since abnormal physical examination results are recorded as medical history or adverse events, no additional summaries or listings will be provided for physical examination.

12.8.   Echocardiogram (ECHO)

ECHO is collected at Screening, Cycle 2 Day 1, and at the safety follow-up. ECHO includes left ventricular ejection fraction and result interpretation. ECHO results will be listed only.

13.   CHANGES FROM ANALYSES PLANNED IN THE PROTOCOL

The following are the changes from the analyses planned in the protocol

- Protocol section 3.6 defined 6 indication-specific cohorts in the expansion phase. The summaries based on the disease types will be adjusted based on the actual enrollment. Refer to Section 9.2.1 for the definition of each disease type.

- Exploratory objectives and endpoints related to biomarkers in protocol Section 3.1.3 and SAP Section 4.3 were not collected in the study.

- In protocol Section 3.1.3 and SAP Section 4.3 one of the exploratory endpoints is "Association of QT, QTc, blood pressure, heart rate, other ECG intervals with time-matched PK concentrations. Profile of QTc over the dosing interval". A summary PK report and QTc report will be provided in the clinical study report, but separate analysis of the endpoints listed here will not be done.

- In protocol Section 11 and SAP Section 6.1 timing of interim analyses are specified. These interim analyses will not be presented and justification will be provided in the clinical study report.

- Alternative definition of response evaluable population was added in Section 8.2.

14.   REFERENCES

[1] E. B. Wilson, "Probable Inference, the Law of Succession, and Statistical Inference," *J. Am. Stat. Assoc.*, vol. 22, no. 158, pp. 209–212, Jun. 1927, doi: 10.1080/01621459.1927.10502953.

15.   PROGRAMMING CONSIDERATIONS

All tables, data listings, figures, and statistical analyses will be generated using SAS® for Windows, Release 9.4 (SAS® Institute Inc., Cary, NC, USA). Computer-generated table, listing and figure output will adhere to the following specifications.

15.1.   General Considerations

- One SAS program can create several outputs.

- Each output will be stored in a separate file.

- Output files will be delivered in rtf and pdf format. Tables, Listings and Figures will be combined in separate files.

- Numbering of TFLs will follow ICH E3 guidance

15.2.   Table, Listing, and Figure Format

15.2.1.   General

- All TLFs will be produced in landscape format, unless otherwise specified.

- All TLFs will be produced using the Courier New font, size 9

- The data displays for all TLFs will have a minimum 1-inch margin on all 4 sides.

- Headers and footers for figures will be in Courier New font, size 9.

- Legends will be used for all figures with more than 1 variable, group, or item displayed.

- TLFs will be in black and white (no color), unless otherwise specified

- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text, will not be used in the TLFs, unless otherwise specified. On some occasions, superscripts 1, 2, or 3 may be used.

- Only standard keyboard characters will be used in the TLFs. Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used. Hexadecimal-derived characters will be used, where possible, if they are appropriate to help display math symbols (e.g., μ). Certain subscripts and superscripts (e.g., cm2, Cmax) will be employed on a case-by-case basis.

- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats, as appropriate.

15.2.2.   Headers

- All output should have the following header at the top left of each page:

  – Sierra Oncology, Inc. SRA737-01

- All output should have Page n of N at the top or bottom right corner of each page. TLFs should be internally paginated in relation to the total length (i.e., the page number should appear sequentially as page n of N, where N is the total number of pages in the table).

- The date the output was generated should appear along with the program name as a footer on each page.

15.2.3. Footnotes

- A solid line spanning the margins will separate the body of the data display from the footnotes.

- All footnotes will be left justified with single-line spacing immediately below the solid line underneath the data display.

- Footnotes should always begin with "Note:" if an informational footnote, or [1], [2], [3], etc. if a reference footnote. Each new footnote should start on a new line where possible.

- Subject specific footnotes should be avoided, where possible.

- Footnotes will be used sparingly and must add value to the table, figure, or data listing. If more than six lines of footnotes are planned, then a cover page may be used to display footnotes, and only those essential to comprehension of the data will be repeated on each page.

- The last line of the footnote section will be a standard source line that indicates the name of the program used to produce the data display, date the program was run, and the listing source (i.e., 'Cross-Reference: Listing 16.X.X.X, SAS Program: T_XXX.sas, Generated: DDMMMYYYYTHH:MM).

15.2.4. Display Titles

- Each TLF should be identified by the designation and a numeral. (i.e., Table 14.1.1). ICH E3 numbering is strongly recommended but sponsor preferences should be obtained prior to final determination. A decimal system (x.y and x.y.z) should be used to identify TLFs with related contents. The title is centered. The analysis population should be identified on the line immediately following the title. The title and table designation are single spaced. A solid line spanning the margins will separate the display titles from the table contents.

- Column headers. There will be 1 blank line between the last title and the solid line.

15.2.5. Column Headers

- For numeric variables, include "unit" in column or row heading when appropriate.

- Analysis set sizes will be presented for each treatment group in the column heading as (N = xx) (or in the row headings if applicable). This is distinct from the 'n' used for the descriptive statistics representing the number of subjects in the analysis set.

15.3.   Body of the Data Display

15.3.1.   General Conventions

Data in columns of a table or listing should be formatted as follows:

- Whole numbers (e.g., counts) are right-justified; and

- Numbers containing fractional portions are decimal aligned.

- If there are no data to report for a particular display (ie no deaths or fatal AEs) then a table will be produced with the planned title and the phrase "no data to report" will be displayed in the body of the table.

15.3.2.   Table Conventions

- Units will be included where available

- If the categories of a parameter are ordered, then all categories between the maximum and minimum category should be presented in the table, even if n=0 for all treatment groups in a given category that is between the minimum and maximum level for that parameter. For example, the frequency distribution for toxicity grade of an adverse event.

- Where percentages are presented in these tables, zero percentages will not be presented and so any counts of 0 will be presented as 0 and not as 0 (0%).

- If the categories are not ordered (e.g., Medical History, Reasons for Discontinuation from the Study, etc.), then only those categories for which there is at least 1 subject represented in 1 or more groups should be included.

- An Unknown or Missing category should be added to any parameter for which information is not available for 1 or more subjects.

- Unless otherwise specified, the estimated mean and median for a set of values should be printed out to 1 more significant digit than the original values, and standard deviations should be printed out to 2 more significant digits than the original values. The minimum and maximum should report the same significant digits as the original values.

- P-values should be output in the format: "0.xxx", where xxx is the value rounded to 3 decimal places. Any p-value less than 0.001 will be presented as <0.001. If the p-

value should be less than 0.0001 then present as <0.0001. If the p-value is returned as >0.999 then present as >0.999

- Percentage values should be printed to one decimal place, in parentheses with no spaces, one space after the count (e.g., 7 (12.8%), 13 (5.4%)). Unless otherwise noted, for all percentages, the number of subjects in the analysis population for the treatment group who have an observation will be the denominator. Percentages after zero counts should not be displayed and percentages equating to 100% should be presented as 100%, without any decimal places.

15.3.3. Listing Conventions

- Missing data should be represented on subject listings as either a hyphen ("-") or as "N/A", whichever is appropriate.

- Dates should be printed in SAS® DATE9.format ("ddMMMyyyy": 01JUL2000). Missing portions of dates should be represented on subject listings as dashes (--JUL2000). Dates that are missing because they are not applicable for the subject are output as "N/A", unless otherwise specified.

- All observed time values must be presented using a 24-hour clock HH:MM or HH:MM:SS format (e.g., 11:26:45, or 11:26). Time will only be reported if it was measured as part of the study.

- Units will be included where available

15.3.4. Figure Conventions

- Unless otherwise specified, for all figures, study visits and/or time will be displayed on the X-axis and endpoint (e.g., change from baseline) values will be displayed on the Y-axis.

- The same symbol and line type will be used for each treatment group across figures.

16. TABLE OF CONTENTS FOR DATA DISPLAY

16.1. Output Tables

Table 6: **List of Output Tables**

Title		Population
Study Population		
14.1.1	Subject Disposition	Screened
14.1.2	Demographics and Baseline Characteristics	Safety
14.1.3.1	Prior Medication	Safety
14.1.3.2	Concomitant Medication	Safety
14.1.3.3	Major Protocol Deviations	Safety
14.1.4	Reasons for Exclusion from Analysis	Safety
Efficacy Endpoints		
14.2.1.1	Best Overall Response per RECIST 1.1	Response
14.2.1.2	Target Lesion Change from Baseline to Nadir	Response
14.2.2.1	Time to Progression per RECIST 1.1	Response
14.2.2.2	Time to Progression Incorporating Clinical Progression	Response
14.2.2.3	Progression-free Survival per RECIST 1.1	Response
14.2.3.1	Overall Survival	Response
Safety Endpoints		
Exposure		
14.3.1	Extent of Exposure and Compliance	Safety
Adverse Events		
14.3.2.1.1	Overall Summary of Subjects with Adverse Events	Safety
14.3.2.1.2	Overall Summary of Subjects with Adverse Events by Disease Categories	Safety
14.3.2.2	Summary of Subjects with Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety
14.3.2.3	Summary of Subjects with Treatment-Emergent Adverse Events by Preferred Term	Safety
14.3.2.4	Summary of Subjects with Treatment-Related Treatment-Emergent Adverse Events by Preferred Term	Safety
14.3.2.5	Summary of Subjects with Treatment-Emergent Adverse Events with Grade ≥ 3 by Preferred Term	Safety
14.3.2.6	Summary of Subjects with Treatment-Related Treatment-Emergent Adverse Events with Grade ≥ 3 by Preferred Term	Safety

Title	Population
14.3.2.7 Summary of Subjects with Serious Treatment-Emergent Adverse Events by Preferred Term	Safety
14.3.2.8 Summary of Subjects with Serious Treatment-Related Treatment-Emergent Adverse Events by Preferred Term	Safety
14.3.2.9 Summary of Subjects with Serious Adverse Events Occurred Prior to First Dose by Preferred Term	Safety
14.3.2.10 Summary of Subjects with Treatment-Emergent Adverse Events Leading to Treatment Withdrawn by Preferred Term	Safety
14.3.2.11 Summary of Subjects with Treatment-Related Treatment-Emergent Adverse Events Leading to Treatment Withdrawn by Preferred Term	Safety
Laboratory data	
14.3.3.1 Hematology Laboratory Parameters	Safety
14.3.3.2 Shift Table of L/N/H Classification for Hematology Laboratory Parameters from Baseline	Safety
14.3.3.3 Biochemistry Laboratory Parameters	Safety
14.3.3.4 Shift Table of L/N/H Classification for Biochemistry Laboratory Parameters from Baseline	Safety
14.3.3.5 Tumor Marker Parameters	Safety
Other Safety	
14.3.4 Vital Sign Parameters	Safety
14.3.5 Local Electrocardiograms Parameters	Safety
Note: PK and QTc reports will be provided in the clinical study report. Separate analysis of these endpoints will not be done.	

16.2. Output Figures

Table 7: **List of Output Figures**

Title	Population
Efficacy Endpoints	Response
14.2.1.1 Waterfall Plot of Target Lesion Best Change from Baseline	Response
14.2.1.2 Kaplan Meier Plot of Time to Progression per RECIST 1.1	Response
14.2.1.3 Kaplan Meier Plot of Time to Progression Incorporating Clinical Progression	Response
14.2.1.4 Kaplan Meier Plot of Progression-free Survival per RECIST 1.1	Response
14.2.1.5 Kaplan Meier Plot of Overall Survival	Response

16.3.   Output Listings

Table 8:   List of Output Listings

Title		Population
Study Population		
16.2.1.1	Listing of Subject Disposition	Safety
16.2.1.2	Listing of Subject Demographics and Baseline Characteristics	Safety
16.2.1.3	Listing of Medical History	Safety
16.2.1.4	Listing of Prior and Concomitant Medications	Safety
16.2.1.5	Listing of Prior Anti-cancer Therapies	Safety
16.2.1.6	Listing of Protocol Deviations	Safety
16.2.1.7	Listing of Analysis Populations	Safety
16.2.1.8	Listing of Subject Disposition in Escalation Stage	Safety
16.2.1.9	Listing of Genetic Alternation	Safety
Efficacy		
16.2.2.1	Listing of Lesions Measurements and Responses by Timepoint	Response
16.2.2.2	Listing of Time to Progression	Response
16.2.2.3	Listing of Time to Progression Incorporating Clinical Progression	Response
16.2.2.4	Listing of Progression-free Survival	Response
16.2.2.5	Listing of Overall Survival	Response
16.2.2.6	Listing of WHO Performance Status	Response
16.2.2.7	Listing of Data for Exploratory Analysis	Response
16.2.2.8	Listing of Prostate Specific Antigen	Response
16.2.2.9	Listing of Circulating Tumor Cell	Response
Safety		
16.2.3.1	Listing of Treatment Exposure and Compliance	Safety
16.2.3.2.1	Listing of Adverse Events	Safety
16.2.3.2.2	Listing of Serious Adverse Events	Safety
16.2.3.2.3	Listing of Serious Adverse Events Occurred Prior to First Dose	Safety
16.2.3.2.4	Listing of Treatment-Related Treatment Emergent Adverse Events Leading to Treatment Withdrawn	Safety
16.2.3.2.5	Listing of Dose Limiting Toxicity Adverse Events	Safety
16.2.3.2.6	Listing of Death	All Subjects

Title		Population
16.2.3.3	Listing of Hematology Laboratory Results	Safety
16.2.3.4	Listing of Biochemistry Laboratory Results	Safety
16.2.3.5	Listing of Urinalysis Laboratory Results	Safety
16.2.3.6	Listing of Tumor Marker Results	Safety
16.2.3.7	Listing of Vital Sign Results	Safety
16.2.3.8	Listing of ECG Results	Safety
16.2.3.9	Listing of ECHO Results	Safety
Note: PK and QTc reports will be provided in the clinical study report. Separate listing of these data will not be done.		

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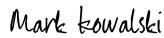
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Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

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You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: itadmin@sierraoncology.com

To advise Sierra Oncology Inc.- GxP Account of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at itadmin@sierraoncology.com and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

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To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to itadmin@sierraoncology.com and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

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i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

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