Statistical Analysis Plan
SDNX-275-0602 (TRIO025)

Title	A Randomized, Placebo-controlled, Double-blind, Multicenter Phase 2 Study of Atezolizumab With or Without Entinostat in Patients with Advanced Triple Negative Breast Cancer, with a Phase 1b Lead in Phase
Study Number	SNDX-275-0602 (TRIO025)
Document Number	DM-025-037
Version Number	1.0
Product Name	Entinostat (SNDX-275)
Indication	Advanced Triple Negative Breast Cancer (aTNBC)
Study Phase	1b / 2
Sponsor	Syndax Pharmaceuticals, Inc. 400 Totten Pond Road, Suite 110 Waltham, MA 02154
Version Date	08-Jun-2017

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STATISTICAL ANALYSIS PLAN APPROVAL SHEET

Protocol Number: SNDX-275-0602 (TRIO025) **Product:** Entinostat (SNDX-275)

Protocol Title:

A Randomized, Placebo-controlled, Double-blind, Multicenter Phase 2 Study of Atezolizumab With or Without Entinostat in Patients with Advanced Triple Negative Breast Cancer, with a Phase 1b Lead in Phase.

Author: [redacted]

Version Number: 1.0 **Version Date:** 08-Jun-2017

The undersigned have reviewed this plan and find it to be consistent with the requirements of the protocol as it applies to their respective areas.

	Date	**Signature**
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TABLE OF CONTENTS

List of Abbreviations

ADaM	Analysis Data Model
ADSL	Subject-level Analysis Dataset
AEs	Adverse Events
aTNBC	Advanced Triple Negative Breast Cancer
CBR	Clinical Benefit Rate
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CR	Complete Response
CTCAE	Common Terminology Criteria for Adverse Events
DLT	Dose-limiting Toxicity
DOR	Duration of Response
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic Case Report Form
FAS	Full Analysis Set
FASFL	Full Analysis Set Population Flag
HER2	Human Epidermal Growth Factor Receptor 2
irRECIST	Immune-related RECIST
IDDI	International Drug Development Institute
IV	Intravenous
IWRS	Interactive Web Response System

KM	Kaplan-Meier
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
NCI	National Cancer Institute
NE	Not evaluable
ORR	Objective Response Rate
OS	Overall Survival
PD	Progressive Disease
PFS	Progression Free Survival
PO	*per os* (Oral Administration)
PPROTFL	Per-protocol Population Flag
PR	Partial Response
PT	Preferred Term
Q1	First Quartile (25th percentile)
Q3	Third Quartile (75th percentile)
RDI	Relative Dose Intensity
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	Recommended Phase 2 Dose
SAEs	Serious Adverse Events
SAFFL	Safety Population Flag
SAP	Statistical Analysis Plan
SD	Stable Disease
SOC	System Organ Class

TEAEs	Treatment Emergent Adverse Events
TLF	Tables, Listings, and Figures
TRIO	Translational Research in Oncology
TTR	Time To Response
WHODD	World Health Organization Drug Dictionary

Revision History

Not applicable; this is the initial version of Statistical Analysis Plan.

1. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the detailed statistical methodology for executing the statistical analyses to assess the antitumor activity and safety profile of atezolizumab in combination with entinostat versus atezolizumab alone in treatment of advanced triple negative breast cancer (aTNBC) according to SNDX-275-0602 (TRIO025) protocol version 1.0.
Statistical analysis will be performed by TRIO using SAS® software Version 9.3 which meets the requirement as stated in the protocol.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary objective for each phase of the study is as follows:

Phase 1b (Dose Determination Cohort): To determine the dose-limiting toxicities (DLT) and maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of entinostat (SNDX-275) given in combination with atezolizumab.
Phase 2 (Expansion Cohort): To perform an evaluation of the efficacy of entinostat at the RP2D in combination with atezolizumab in patients with aTNBC, as determined by the duration of progression-free survival (PFS) based on the local investigator's assessment of progressive disease Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1).

2.2 Secondary Objectives

2.2.1 Efficacy

To evaluate the efficacy of entinostat in combination with atezolizumab in patients with aTNBC, as determined by:

- PFS based on immune-related RECIST (irRECIST)
- Overall response rate (ORR) (complete response [CR] or partial response [PR]) based on RECIST 1.1
- ORR (irCR or irPR) based on irRECIST
- Clinical benefit rate (CBR) (CR or PR or stable disease [SD] for at least 24 weeks) based on RECIST 1.1
- CBR (irCR, irPR or irSD for at least 24 weeks) based on irRECIST
- Overall survival (OS)

In patients with best overall response of CR or PR based on RECIST 1.1 and irCR or irPR based on irRECIST:

- Duration of response (DOR)
- Time to response (TTR)

2.2.2 Safety

To evaluate safety and the tolerability of entinostat in combination with atezolizumab, as measured by clinical adverse events (AEs) and laboratory parameters.

2.3 Exploratory Objectives

The exploratory study objectives are to:

- [redacted].
- [redacted]
- [redacted].
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted].

The exploratory objectives will be performed afterwards and detailed in a separate document(s).

3. STUDY DESIGN

This is a Phase 1b/2 study evaluating the combination of entinostat plus atezolizumab in patients with aTNBC. The study has 2 phases: an open-label Dose Determination Phase (Phase 1b) followed by an Expansion Phase (Phase 2).

The Expansion Phase will evaluate the efficacy and safety of entinostat when administered at the RP2D with atezolizumab in patients with aTNBC in a randomized, double-blind, placebo-controlled setting.

3.1 Phase 1b Dose Determination Phase

This study phase employs a classical 3+3 design, with the determination of DLT and the MTD or RP2D at cycle 1 based on the combination of entinostat (at the dose of 5mg, 3mg or 2mg weekly) with atezolizumab at a fixed dose of 1200 mg iv. Six patients will need to be treated in a dose level for it to be considered MTD or the RP2D. The recommended dose for Phase 2 investigation will be the higher of either 2, 3, or 5mg weekly PO that results in less than a 33% incidence of DLT.

Note: Based on evaluation of the safety and tolerability data gathered during the dose determination phase together with data from other clinical trials, it may also be decided that accrual will take place at an alternate dose level or dosing schedule via a protocol amendment.

Up to 18 patients are expected to be enrolled in the Dose Determination Phase of the study.

3.2 Phase 2 Expansion Phase

The phase 2 expansion phase is a randomized, multicenter, double-blind, placebo-controlled study phase. Randomization for this portion of the study is stratified by geographic location (US vs. rest of world).

70 eligible patients are randomly assigned in a 1:1 ratio to either:

- **Entinostat per os (p.o.) weekly at the RP2D combined with atezolizumab at a fixed dose of 1200 mg iv every 3 weeks**

  OR

- **Placebo combined with atezolizumab at a fixed dose of 1200 mg iv every 3 weeks**

Patients will follow the same schedule of study visits and assessments as specified in the Dose Determination Phase (with the exception of the tumor tissue biopsy at C2D15). Patients may

continue study treatment until documented progressive disease, intolerable toxicity or meets one of the study withdrawal criteria (Protocol Section 11).

Patients will be followed for overall survival (OS) until death (due to any cause) or the Sponsor terminates the trial.

4. STUDY ENDPOINTS

4.1 Phase 1b Dose Determination Phase

The primary endpoint of the Phase 1b Dose Determination portion of the study is the determination of the DLT, MTD or RP2D of entinostat in combination with atezolizumab at the dose of 1200mg . The following safety endpoints will also be assessed:

- AEs
- Clinical laboratory parameters, vital signs, physical examinations, and ECGs

Exploratory endpoints will also be assessed [redacted] and are discussed in a separate SAP.

4.2 Phase 2 Expansion Phase

4.2.1 Primary Efficacy Endpoint

The primary efficacy endpoint is PFS as determined by the local investigator using RECIST 1.1.

4.2.2 Secondary Efficacy Endpoints

- PFS determined by the local investigator using irRECIST
- ORR (CR or PR) by RECIST 1.1
- ORR (irCR or irPR) by irRECIST
- CBR (CR, PR or SD for at least 24 weeks) by RECIST 1.1
- CBR (irCR, irPR, or irSD for at least 24 weeks) by irRECIST
- OS

In patients who experience a response to treatment based on RECIST 1.1 (CR or PR) or on irRECIST (irCR or irPR):

- DOR
- TTR

4.2.3 Safety

Safety endpoints are:

- AEs
- Clinical laboratory parameters, vital signs, physical examinations, and ECGs

4.2.4 Exploratory

The exploratory endpoints will be discussed in separate SAP(s).

5. STATISTICAL CONSIDERATIONS

5.1 Hypothesis for Phase 2

The primary efficacy analysis will be the comparison of the distribution of PFS between the two treatment groups using a stratified logrank test at one-sided 10 % level of significance, i.e.:

H_o: PFS in experimental arm (entinostat + atezolizumab) = PFS in control arm (placebo + atezolizumab)

vs.

H_a: PFS in experimental arm (entinostat + atezolizumab) > PFS in control arm (placebo + atezolizumab)

5.2 Sample Size

5.2.1 Phase 1b Dose Determination Phase

Three to six patients will be enrolled in each dose cohort based on a standard Phase 1 dose-finding scheme.

A starting sample size of 3 evaluable patients per dose cohort, expanding to 6 in the event of a marginal DLT rate (33%) was deemed to be a safe and conventional approach in dose-finding. Assuming a true DLT rate of 5% or less, there would be a 3% chance that dose escalation would be halted in a given cohort (i.e. observing 2 or more patients with DLT). If a true DLT rate of 50% is assumed, then there would be an 83% chance that dose escalation would be halted in a given cohort.

6 patients will need to be treated in a dose level for it to be considered as MTD or RP2D.

Patients who discontinued the study for reasons other than study drug related toxicities before completing Cycle 1 will be replaced.
Therefore, between 6 and 18 patients will be included in the Dose Determination Phase.

5.2.2 Phase 2 Expansion Phase

The following assumptions are made:

- Patients in the control arm have true median PFS of 4 months
- Patients in the experimental arm have true median PFS of 7 months (under exponential distribution, true PFS hazard ratio of 0.57)
- Expected accrual duration will be 9 months and an additional 9 months of follow-upThe α type I error rate is set to 10% (1-sided)
- The β type II error rate is set to 20% (i.e. the power of the trial will be 80%)

Under these assumptions, 70 patients (35 per arm) will be enrolled in the trial, which is projected to result in 60 PFS failures, defined as documented disease progression by RECIST 1.1 or death due to any cause without documented disease progression beforehand, within approximately 18 months of the first patient randomized.
It is anticipated that the number of patients that drop out without PFS failure will be low (2-3%). Depending on the actual number of such dropouts, the number of patients accrued maybe increased by 6-10 patients to accommodate for a higher-than-expected number of dropouts.

5.3 Randomization and Stratification

The randomization technique used for the study is a stochastic minimization, using minimization probability parameter of 0.80. The randomization is performed via ID-net (which is the IWRS from IDDI).

Prior to dosing, eligible patients are randomized in a 1:1 ratio into 2 treatment arms, stratified by geographic location.

5.4 Timing of Analyses

5.4.1 Phase 1b Dose Determination Phase

A safety analysis will be performed at the completion of the dose determination phase.

5.4.2 Phase 2 Expansion Phase

The following analyses are planned:

- An interim safety analysis will be performed following the completion of Cycle 1 for the first 20 patients enrolled in the Phase 2 expansion phase, and will utilize a Data Safety Monitoring Board (DSMB).
- An interim efficacy analysis will be performed when 45 PFS events have observed. Data cut-off for the analysis will be based on the calendar date of the 45th PFS event (per RECSIT 1.1). Safety and secondary endpoints will also be evaluated. The same data cut-off used for the PFS analysis is also used for the corresponding analysis of safety and secondary endpoints.
- Primary efficacy analysis will be performed when 60 PFS events are observed. Similarly, the data cut-off for the primary analysis will be based on the calendar date of the 60th PFS event. Safety and secondary endpoints will coincide with the primary PFS analysis.
- End of study analysis for safety and OS analysis will be performed when the last patient terminates study treatment.

6. DEFINITIONS

6.1 Progression-Free Survival (PFS)

The duration of PFS, defined as the number of months from randomization to the earlier of progressive disease or death due to any cause. One month is considered 30.4375 days.

PFS (months) = (Date of Progression or Censoring – Date of Randomization + 1) ÷ 30.4375

Patients who meet one or more of the following conditions at the time of primary analysis will be censored:

- No screening or post-screening disease assessments unless death occurred prior to the first planned assessment.
- Initiation of a new anticancer therapy in the absence of documented progression.
- Death or progressive disease after missing 2 or more consecutively scheduled disease assessment visits
- Last known to be alive and progression-free on or before the data cut-off date

The following table, adopted from FDA guidance "*Guidance for Industry Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics*" (May 2007) illustrates how the cases will be handled for primary analysis. If a patient is censored satisfying more than one criteria, the situation with the earliest date will be considered.

Table 1 – Primary Rules for Determining Date of Progression or Censor for Primary Progression-Free Survival

	Situation	Date of Progression or Censoring	Outcome
1	Death before first PD assessment	Date of death	Progressed
2	Death or disease progression between planned disease assessments	Date of death or first disease assessment showing disease progression, whichever occurs first	Progressed
3	No baseline tumor assessments	Date of randomization	Censored
4	New anticancer treatment started (in absence of documented progression)	Date of last radiological assessment of measured lesions prior to the start of the new anticancer treatment	Censored
5	Death or progression after more than 2 or more consecutive visits	Date of last radiological assessment of measured lesions without documented disease progression that is before the first missed visit	Censored
6	Last known to be alive and progression-free on or before the data cut-off date	Date of last radiological assessment of measured lesions	Censored

The following sensitivity analyses will also be provided:

Table 2 – Progression-Free Survival Sensitivity Analysis

Analysis #	Definition and/or changes from primary analysis; unless otherwise stated, the same PFS censoring rules will be applied
1	Per-protocol analysis set, instead of full analysis set
2	PFS events occurring immediately after two or more missing visits will not be censored
3	Patients who discontinue treatment due to any reason other than disease progression or death are censored at the date of last tumor assessment prior to (or at) treatment discontinuation
4	Patients who received new anticancer treatment without documented progression will not be censored
5	Worst case analysis: A patient who is lost to follow-up (or withdrew consent from study participation) before documented progression will be considered progressed at first scheduled radiological assessment date after lost to follow-up (or withdrew consent) (i.e. last radiological assessment + 42 days)

All analyses described above will use the same methodologies as the primary analysis, except changes as noted in the second column. Each analysis will modify only the rule as stated in the specific row; i.e. rows will not be combined unless otherwise specified.

6.2 Objective Response Rate (ORR)

ORR is defined as the crude proportion of patients achieving a best overall response of CR or PR assessed using RECIST 1.1. The best overall response assessed using irRECIST will also be analyzed separately and the corresponding ORR will be calculated. The overall response will be determined locally by the investigator at each scheduled assessment.

Per protocol (Section 10.3.1.3), 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 following table will be followed to assign a best overall response based on the achievement and confirmation of two consecutive assessments according to RECIST 1.1:

Overall response First time point	Overall response Subsequent time point (at Least 4 Weeks Later)	Best Overall Response
CR	CR	CR

Overall response First time point	Overall response Subsequent time point (at Least 4 Weeks Later)	Best Overall Response
CR	PR	PR
CR	SD	SD
CR	PD	PD
CR	NE	SD
PR	CR	PR
PR	PR	PR
PR	SD	SD
PR	PD	PD
PR	NE	SD

$$ORR_{RECIST1.1} = \frac{\#\ of\ patients\ with\ best\ overall\ response\ as\ CR\ or\ PR}{Total\ number\ of\ patients}$$

Similarly, irCR or irPR based on irRECIST will also be confirmed.

The following table is therefore used for best overall response based on irRECIST:

Overall response First time point	Overall response Subsequent time point (at Least 4 Weeks Later)	Best Overall Response
irCR	irCR	irCR
irCR	irPR	irPR
irCR	irSD	irSD
irCR	irPD	irPD
irCR	irNE	irSD
irPR	irCR	irPR
irPR	irPR	irPR
irPR	irSD	irSD
irPR	irPD	irPD
irPR	irNE	irSD

And ORR based on irRECIST is calculated as follows:

$$ORR_{irRECIST} = \frac{\#\ of\ patients\ with\ best\ overall\ response\ as\ irCR\ or\ irPR}{Total\ number\ of\ patients}$$

6.3 Clinical Benefit Rate (CBR)

CBR is estimated based on the crude proportion of patients in each treatment arm whose best overall response during the course of study treatment is CR, PR or SD lasting for at least 24 weeks (measured from the date of randomization to the last date where SD is reported).

$$CBR_{RECIST\ 1.1} = \frac{\#\ of\ patients\ with\ best\ confirmed\ overall\ response\ as\ CR/PR/\ SD_{lasting\_for\geq 24\_weeks}}{Total\ number\ of\ patients}$$

Similarly, CBR is calculated based on irRECIST as below:

$$CBR_{irRECIST} = \frac{\#\ of\ patients\ with\ best\ confirmed\ overall\ response\ as\ irCR/irPR/irSD_{lasting\_for\geq 24\_weeks}}{Total\ number\ of\ patients}$$

6.4 Overall Survival (OS)

OS is defined as the number of months from randomization to date of death from any cause. Patients who are alive or lost to follow-up as of a data analysis cutoff date will be right-censored.
OS (months) = (Date of Death/Censoring – Date of Randomization + 1) ÷ 30.4375

6.5 Duration of Response (DOR)

DOR is defined as the number of months from the date where a CR / PR (based on RECIST 1.1) or irCR / irPR (based on irRECIST) was firstly observed, to the first date that recurrent or progressive disease is documented. DOR will be calculated for patients who achieved a confirmed CR / PR or irCR / irPR. The same censoring rules for primary analysis will also apply here for patients who achieved a confirmed CR / PR or irCR / irPR. Patients with no baseline or post-baseline assessments will not be analyzed.
$DOR_{RECIST\ 1.1}$ (months) = (Date of Progressive Disease – Date of CR/PR + 1) ÷ 30.4375
$DOR_{irRECIST}$ (months) = (Date of Progressive Disease – Date of irCR/irPR + 1) ÷ 30.4375

6.6 Time to Response (TTR)

TTR is defined for the subset of patients that achieve best overall response of confirmed CR/PR or confirmed irCR/irPR as the number of months from date of randomization to date of the initial documented response of CR/PR (based on RECIST 1.1) or irCR/irPR (based on irRECIST).

$TTR_{RECIST\ 1.1}$ (months) = (Date of CR/PR – Date of Randomization + 1) ÷ 30.4375

$TTR_{irRECIST}$ (months) = (Date of irCR/irPR – Date of Randomization + 1) ÷ 30.4375

6.7 Dose-limiting Toxicity (DLT)

DLT is defined as the occurrence of specific events defined in Section 9.6 of the protocol within the first cycle of treatment (i.e. between Day 1 to Day 21 of Cycle 1) of entinostat in combination with atezolizumab that are considered by the investigator to be at least possibly related to study drug using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

6.8 Maximum Tolerated Dose (MTD)

MTD is defined as the highest dose level at which < 33% of 6 patients experience DLT.

6.9 Recommended Phase 2 Dose (RP2D)

RP2D will be equal to or less than the preliminary MTD. This will be determined in discussion with the sponsor, the study medical monitor and dose determination phase investigators.

6.10 Treatment Emergent Adverse Events (TEAEs)

TEAEs is defined as AEs that start on or after the first administration of study treatment or AEs that start before the first administration of study treatment but worsened after study treatment is initiated.

6.11 Other Definitions

6.11.1 Baseline

The last available assessment done on or before the date of first dose of study treatment.
If patients have no value as defined above, the baseline value will be missing.

6.11.2 Date of First Dose

The date of first dose (of study drug) is derived as the first date when a nonzero and nonmissing dose of study drug is administered. This can also be referred to as the start of the study treatment.

6.11.3 Date of Last Dose

The date of last dose (of study drug) is derived as the last date when a nonzero and nonmissing dose of study drug is administered.

6.11.4 Last Contact Date

The last contact date will be derived for patients not known to have died at the analysis cut-off using the latest complete date among the following dates which precede the cut-off date:

- All assessment dates (e.g. vital signs assessment, performance status assessment, tumor assessments, etc.)
- Date patient was last known alive
- Start and stop dates of concomitant medications
- Start and stop dates of adverse events
- Date of last dose
- Date of registration (Phase 1b)/randomization (Phase 2)

7. STUDY POPULATION

7.1 Full Analysis Set (FAS)

The **Full Analysis Set (FAS)** includes all patients who were enrolled (for Phase 1b) or randomized (for Phase 2) to study treatment, regardless of whether they actually received study medication. All efficacy analyses will be evaluated based on data from this population set according to the treatment group they were assigned to at registration/randomization and based on the strata they were originally assigned to at the time of randomization. This population set will be identified using the FASFL (Full Analysis Set Population Flag) as defined in Subject-Level Analysis Dataset (ADSL) according to Analysis Data Model (ADaM).

7.2 Per-protocol Analysis Set

The **Per-protocol Analysis Set** consists of all patients who were enrolled/randomized and did not have any important deviations (i.e. excludes patients with important deviations from FAS). The list of patients who are identified with important deviations will be provided to biostatistician(s) by TRIO Project Management. This population set will be identified using the PPROTFL (Per-Protocol Population Flag) as defined in ADSL according to ADaM.

7.3 Safety Analysis Set

The **Safety Analysis Set** consists of all patients who receive any study treatment, and will be used for the analysis of safety data in both Phase 1b and Phase 2 portions of the study. This population will be based on the first dose received at cycle 1, if this differs from that to which the subject was randomized and will be used for the analysis of safety data. This population set will be identified using the SAFFL (Safety Population Flag) as defined in ADSL according to ADaM.

8. INTERIM ANALYSIS AND EARLY STOPPING RULE

One interim safety analysis is planned during the Phase 2 of the study after the first 20 patients are treated for one cycle. As mentioned in section 5.3.2, the result of this analysis will be reviewed by DSMB who will act in an advisory capacity to the Sponsor with respect to safeguarding the interests of trial patients and assessing the safety of the interventions administered during the trial. As per Section 13.2 of the protocol, an interim efficacy analysis is performed when 45 PFS events are observed to support the Sponsor's product development plans and ongoing resourcing activities. Although there are no plans to terminate the study early, the DSMB will review the results and decision will be made in collaboration with the Sponsor as well as the Steering Committee should the study needs to be terminated.

9. DATA SCREENING AND ACCEPTANCE

9.1 General Principles

For the planned analyses, data acceptance will be based on the creation and review of the tables, listings, and figures (TLF) in collaboration with Data Management and Project Management according to TRIO Standard Guideline SG8.1 "Validation of Statistical Analysis". In general, TLF programs will be created prior to a database snapshot or database lock. Dry run(s) of TLF programs will be done in order to review for extreme, unusual, and missing values. Such cases will be identified to Data Management and Project Management for further investigation and potential resolution prior to a snapshot or lock of the database. As data issues are detected, additional procedures might be needed in order to ensure resolution in subsequent data transfer(s).

For the final analysis, all procedures will be run to ensure previously identified data issues have been resolved. The TLF programs will also be run and the outputs will be reviewed to ensure no further data issues are found.

9.2 Unblinding Plan

For the Phase 2 Expansion Phase of this study, all TRIO personnel will be blinded. At the time of statistical analysis, only the Independent Statistician, who does not work on the study directly, will be unblinded. He/she will obtain the unblinded randomization file as well as unblinded medication list in order to unblind the data and perform the analysis accordingly. All relevant unblinded files will be stored separately on the network and access to the unblinded data will be restricted to the Independent Statistician only. Refer to TRIO Standard Operating Procedure SOP 5.7 "Blinding and Unblinding".

9.3 Data Handling and Electronic Data Transfer

All clinical data will be entered directly by the designated users at the site into the database using Oracle Clinical Remote Data Capture (OCRDC) according to electronic Case Report Form (eCRF) and will be extracted in the form of raw SAS® datasets by Data Management. Data extracts will be provided to biostatistician(s) on a regular basis. Once the final data queries have been generated and resolved, the database will be deemed "locked" and final database extract will be performed after official data snapshots are completed. The data used for all the analyses will be archived.

9.4 Handling of Incomplete and Missing Data

Missing and incomplete data will be identified for investigation, and possible resolution, by Data Management and Project Management prior to an official database snapshot or database lock through review of TLF.

Missing Data: All analyses and descriptive summaries will be based on the reported data. Unless otherwise specified, missing data will not be imputed or "carried forward."

Partial or Missing Date for Adverse Events and Concomitant Medications:

Imputation Rules for Partial or Missing Stop Dates:

If the month and year are present, impute the last day of that month.

If only the year is present, impute December 31 of that year.

If the stop date is entirely missing, assume the event or medication is ongoing.

If a partial or complete stop date is present and the 'ongoing' box is checked, then it will be assumed that the adverse event or concomitant medication stopped and the stop date will be imputed if partial.

Imputation Rules for Partial or Missing Start Dates

Start Date		Stop Date						
		Complete: *yyyymmdd*		**Partial: *yyyymm***		**Partial: *yyyy***		**Missing**
		< 1st dose	≥ 1st dose	< 1st dose *yyyymm*	≥ 1st dose *yyyymm*	< 1st dose *yyyy*	≥ 1st dose *yyyy*	
Partial: *yyyymm*	= 1st dose *yyyymm*	2	1	2	1	n/a	1	1
	≠ 1st dose *yyyymm*		2		2	2	2	2
Partial: *yyyy*	= 1st dose *yyyy*	3	1	3	1	n/a	1	1
	≠ 1st dose *yyyy*		3		3	3	3	3
Missing		4	1	4	1	4	1	1

1 = Impute the date of first dose

2 = Impute the first of the month

3 = Impute January 1 of the year

4 = Impute January 1 of the stop year

9.5 Outliers

Outliers will be identified through a review of TLF for investigation by Data Management and Project Management. All outlier data will be included in the analyses presented in this SAP. Any unconfirmed outlier data will be followed up by Project Management.

9.6 Validation Plan

SAS® version 9.3 on the Windows system will be used for all TLF creation. The verification of the outputs, the analysis datasets as well as the review of all programs and macros created specifically for this study, will be conducted as outlined in TRIO Standard Operating Procedures SOP 8.3 "Conduct of Statistical Analysis", SOP 8.4 "Preparation of Statistical Analysis" and Standard Guidelines SG 8.1 "Validation of Statistical Analysis".

10. STATISTICAL METHODS OF ANALYSIS

Categorical variables will be summarized in frequency tables, with the counts and percentage of patients in each category. Percentages given in the summary tables will be rounded and thus may not always add up to exactly 100 percent. For continuous variables, summary statistics will include number of patients, mean, standard deviation, first quartile (Q1), median, third quartile (Q3), minimum and maximum values (range).

10.1 Patient Disposition

The patient disposition will be tabulated using the FAS. Frequency count and respective percentages of patients who were in each analysis set (i.e. FAS, Per-protocol, and Safety), and discontinued from treatment and/or study will be summarized by treatment group. The reason for discontinuation (from treatment and/or from study participation where applicable) will be summarized considering the categories specified in the case report forms. Listings of disposition information and analysis population will be provided as well.

Protocol Deviation including eligibility deviations of the inclusion/exclusion criteria will be summarized and listed for FAS, by treatment group.

The stratifications factor (for Phase 2 portion) will also be tabulated by treatment group.

10.2 Demographics and Disease Characteristics

The following demographics and baseline characteristics will be summarized and listed for the FAS by treatment group:

Demographics:

- Age, *INT (Date of enrollment/randomization – Date of birth) / 365.25)*
  - *INT = integer part*
  - *Since only the year of birth is collected (YYYY), we assume the full date to be 31-Dec-YYYY*
- Race
- Ethnicity
- Menopausal Status
- Weight at Baseline
- Height at Baseline
- ECOG Status at Baseline

Disease Characteristics:

- Time from Initial Diagnosis to Randomization
- Primary Tumor Location
- Staging at Initial Diagnosis
- Histopathological Type at Initial Diagnosis
- Histopathological Grade at Initial Diagnosis
- Disease Status at Registration
- Time from Metastatic / Locally Recurrent Disease to Randomization
- Local Estrogen Receptor Status
- Local Progesterone Receptor Status
- Local HER2 Status

10.3 Prior Surgery for Breast Cancer

Number of patients who underwent prior surgeries will be summarized by type and location of surgery. A listing will also be provided.

10.4 Prior Systemic Anti-Cancer Therapy

Number of regimens of prior systemic anti-cancer therapies will be summarized by type and indication. A listing will be provided to show the specifics of the therapies.

10.5 Prior Radiation Therapy

Number of radiation therapies will be summarized by site and indication. A listing will be provided to show the specifics of all reported radiation therapies.

10.6 Medical History

The medical history is coded by the most current version of Medical Dictionary for Regulatory Activities (MedDRA), and will be summarized for FAS by System Organ Class (SOC) and Preferred Term (PT) by treatment group.

10.7 Extent of Exposure

Number of Cycles, Duration of Treatment, Cumulative Dose and Relative Dose Intensity (RDI) will be summarized by treatment for the safety analysis set.

Atezolizumab:

- Number of Cycles: number of cycles having total dose > 0 mg reported
- Duration of Treatment (weeks) = [(Date of last dose - date of first dose) + 21] ÷ 7
- Cumulative Dose (mg) = sum of total dose administered as reported
- Weekly Dose Intensity (mg/week) = (Cumulative Dose) ÷ (Duration of Treatment)
- Planned Weekly Dose Intensity (mg/week) = 1200mg ÷ 3 weeks = 400
- RDI (%) = (Weekly Dose Intensity ÷ Planned Weekly Dose Intensity) × 100

Entinostat:

- Number of Cycles: number of cycles having total dose > 0 mg reported
- Duration of Treatment (weeks) = [(Date of last dose - date of first dose) + 21] ÷ 7
- Cumulative Dose (mg) = sum of total dose administered as reported
- Weekly Dose Intensity (mg/week) = (Cumulative Dose) ÷ (Duration of Treatment)
- Planned Weekly Dose Intensity (mg/week) = (Dose Cohort as assigned in Phase 1b or RP2D in Phase 2) ÷ 3 weeks
- RDI (%) = (Weekly Dose Intensity ÷ Planned Weekly Dose Intensity) × 100

The RDI will be additionally presented categorized (i.e., number and percentage of patients with RDI of < 60%, 60 - < 80%, 80 - < 90%, 90 - < 110%, ≥ 110%).

The number and percentage of patients with dose interruptions/discontinuations or reduced (entinostat/placebo at Phase 2 only), along with their respective reasons will be summarized.

For entinostat/placebo, the compliance will be summarized by visit using the following calculation:

$$Compliance\ (\%) = \frac{Number\ of\ Tabs\ taken + Number\ of\ Tabs\ Returned}{Number\ of\ Tabs\ Dispensed} \times 100$$

10.8 Efficacy Analyses

Efficacy data for the primary endpoint and the secondary endpoints will be analyzed for the FAS and, where appropriate, the Per-protocol Set. Sensitivity analyses and subgroup analyses will be conducted as appropriate; refer to Table 2 and Table 3. Summaries and figures of the efficacy endpoints will be generated by treatment group as per randomization.

10.8.1 PFS

The duration of PFS will be summarized descriptively using Kaplan-Meier (KM) curves. Inferential comparisons between treatment arms will be made using stratified log-rank test, stratifying on

geographic location (US vs. Rest of World). The KM estimate of the PFS survival distribution function will be computed for each treatment group using PROC LIFETEST with method=KM option in SAS. For each treatment group, the KM estimates for the median PFS time, the first and third quartiles will be presented, along with approximate 95% confidence intervals (CI) calculated using Greenwood's formula. Example of PROC LIFETEST code with and without stratification is presented below:

```
* Unstratified;
proc lifetest data=<PFS> method=km;
 time <pfsmonth>*<pfscens>(1);
 strata <trt>;
run;

* Stratified;
proc lifetest data=<PFS> method=km;
 time <pfsmonth>*<pfscens>(1);
 strata  <geographical region> / group= <trt>;
run;
```

The effect of treatment on PFS will also be compared using a stratified Cox proportional hazards model. The hazard ratio with two-sided 95% CI will be derived from the stratified Cox proportional hazards model using PROC PHREG with ties=EXACT option in the model. Homogeneity in the hazard ratios between randomization strata will be examined by Wald's test. The corresponding results without stratification will be reported as supplemental analyses.

Example of PROC PHREG code with and without stratification is presented below:

```
* Unstratified;
proc phreg data=PFS;
class trt(ref='1');
model dfsmonth*dfscens(1)=trt / risklimits ties=exact;
run;


* Stratified;
proc phreg data=PFS;
class trt(ref='1');
model dfsmonth*dfscens(1)=trt / risklimits ties=exact;
strata <geographical region>;
run;
```

Testing of Proportional Hazard assumption will also be done using the following stratified model:

```
proc phreg data=pfs;
    model <pfsmonths>*<pfscens>(1)= <trt> / risklimits Ties=exact;
       assess var=(<trt>) ph / crpanel resample seed=199;
       strata <geographical region>;
  run;
```

In addition, Hazard Ratio for treatment effect will be estimated using a multivariate Cox proportional hazards model to be constructed by selecting variables among all the potential variables listed in the subgroup analysis (see Section 10.10) using stepwise selection method with entry p-value 0.05 and exit p-value 0.1. The treatment factor will be kept out of the model throughout the covariate selection process and only added into the final model. HR for treatment effect and corresponding 95% confidence interval (CI) will be estimated from the final model.
Note that a covariate may be removed from the analysis if the number of patients/events representing one level of that variable is insufficient or data collected on that variable are insufficient.

A sensitivity analysis will be performed to assess the impact of the different censoring mechanisms and deviations from the planned schedule of disease assessments; refer to Table 2.

10.8.2 ORR

The ORR observed in the treatment groups will be compared adjusting for the stratification variables using the Cochran-Mantel-Haenszel (CMH) test using PROC FREQ in SAS. A 95% CI will be calculated by treatment arm for the true ORR.
Example of PROC FREQ for testing ORR is provided below:

```
proc freq data=<ORR>;
   tables <trt> * <Response> / relrisk cmh;
   weight Count;
run;
```

The best overall response outcome (CR/PR/SD/PD/NE) will be summarized and tabulated for the FAS by treatment group.

10.8.3 CBR

The analysis of CBR will be based on the methods described above for ORR.

10.8.4 OS

The analysis of OS will be based on methods described above for PFS.

10.8.5 DOR and TTR

DOR and TTR will be summarized descriptively for each treatment arm using the KM method. Inferential comparisons between treatment arms for DOR and TTR are not planned.

10.8.6 Anticancer therapy after end of study treatment

A summary of number of patients received anticancer therapy after end of study treatment will be tabulated by the type of therapy according to treatment group.

10.9 Safety Analyses

Safety analyses will be performed on the safety analysis set.

10.9.1 Physical Examinations

The number of patients who had done complete and/or symptom-directed physical examinations at each visit will be tabulated by treatment group.

10.9.2 Adverse Events

The reported AE term will be coded using the current version of the MedDRA. The severity of AE will be presented as reported by the investigator based on NCI CTCAE version 4.03.
Incidence of TEAE will be tabulated by SOC, PT for:

- All TEAEs
- TEAEs by relationship to study treatment and maximum severity grade
- TEAEs with action of study treatment delayed/interrupted or dose reduced
- TEAEs with action of study treatment discontinued
- Serious Adverse Events (SAE) (not Serious TEAEs)

In the event a patient experiences repeat episodes of the same AE, the event with the highest severity grade and strongest causal relationship to study treatment will be used for purposes of incidence tabulations.
All AEs leading to deaths will be summarized (not TEAEs). An AE will be considered as leading to death if it has a grade 5.
Detailed listings for all AEs will be provided. A flag will be used to identify which AE is considered as treatment emergent.
For the Phase 1b dose determination phase, the observed DLT rate in each dose cohort will be calculated by the crude proportion of patients who experienced DLT with a 2-sided 95% exact binomial CI.

10.9.3 Death

All deaths will be reported in a patient listing, which will include the primary cause of death, and the number of days between the date of last dose to study drug and death.

10.9.4 Laboratory Values

Hematology and serum blood chemistry will be summarized in descriptive statistics by calculating the mean, standard deviation, median, and range for the following:

- Baseline value
- Minimum post baseline value
- Maximum post baseline value
- Average post baseline value
- Last post baseline value

Laboratory values will be assigned toxicity grade when available using NCI CTCAE version 4.03. Shift tables in laboratory toxicity grades (comparing baseline grade with worst post-baseline grade) will be analyzed using standard shift tables, presenting number and proportion of patients and their maximum grade shift.
For laboratory tests without a toxicity grading scale, the shift table will present directional shifts from baseline to above or below the laboratory standard normal range using the maximum increase and/or decrease observed throughout the course of treatment/observation.

10.9.5 ECOG Performance Status

Tabulation of ECOG Performance Status results will be done for the following:

- Baseline value
- Minimum post baseline value
- Maximum post baseline value
- Last post baseline value

A shift table will be provided as well from baseline status to the worst status of post-baseline time points.

10.9.6 Vital Signs

Vital sign measurements will be summarized by descriptive statistics in the same manner described for laboratory values.

10.9.7 Electrocardiogram (ECG)

ECG results will be tabulated in terms of frequency and percentage of patients according to findings reported by investigators at the assessed time points.

10.9.8 Concomitant Medication

Prior and concomitant medications are coded to the current version of World Health Organization Drug Dictionary (WHODD). The generic term will be tabulated and listed by patient.

10.10 Subgroup Analysis

Subgroup analyses will be done for PFS and OS to assess internal consistency of study results and whether there is significant treatment heterogeneity across any of the subgroups. Tests within each subgroup and tests for subgroup-by-treatment-interaction terms will use an unstratified test from an unstratified Cox proportional hazards model. Additionally, these subgroup analyses will also be performed using a stratified test/model.
The following subgroup analyses are planned:

Table 3 – Planned Subgroup Analyses

Subgroup	**Reason**
Geographical region (US vs. Rest of World)	IWRS stratification factor
Prior endocrine therapy	Baseline demographic or prognostic factor
Prior chemotherapy	Baseline demographic or prognostic factor
Prior adjuvant/neoadjuvant systemic anticancer therapy	Baseline demographic or prognostic factor
ECOG 0 vs. ECOG 1	Baseline demographic or prognostic factor
Disease stage at study entry: unresectable locally recurrent vs. metastatic	Baseline demographic or prognostic factor
Number of metastatic sites: ≥ 3 vs. < 3 (based on the location/organ; i.e. 3 liver lesions count	Baseline demographic or prognostic factor

as 1 metastatic site)	
Disease-free interval: none, < 24 months, vs. > 24months (based on the first surgery expected to be curative, to the first relapse/progression date)	Baseline demographic or prognostic factor

10.11 Pharmacokinetic and Antidrug Antibody Analyses –

It will be done in a separate document.

10.12 Correlative Analyses

It will be done in a separate document.

11. LIST OF PLANNED TABLES, FIGURES, LISTINGS

11.1 Planned Tables

Title	Population	Description
Patient Disposition	FAS	Tabulates the disposition of all patients by treatment group, including the number of patients in each population set as well as the number of patients discontinued from study treatment, and the number of patients discontinued from study. The reason for drug discontinuation and study discontinuation will also be summarized.
Stratification Factors	FAS	Tabulates the stratification factor (Geographic Location – US vs. Rest of World) by treatment group. (Phase 2 only.)
Protocol Deviations	FAS	Tabulate the number of patients who reported protocol deviations by deviation category for each treatment group.
Eligibility Deviations	FAS	Tabulates the number of patients who violates inclusion/exclusion criteria by criterion for each

Title	Population	Description
		treatment group
Baseline Demographics	FAS	Tabulates summary statistics of the demographics (age, race, ethnicity, menopausal status, weight, height and ECOG status at baseline).
Disease Characteristics	FAS and Safety	Tabulates summary statistics for time from initial diagnosis to randomization, primary tumor location, staging at initial diagnosis, histopathological type at initial diagnosis, histopathological grade at initial diagnosis, disease status at registration, time from metastatic/locally recurrent disease to randomization, hormonal receptor status, and HER2 status.
Prior Surgery for Breast Cancer	FAS	Tabulates the number of patients with type and location of surgery for each treatment group.
Prior Systemic Anti-Cancer Therapy	FAS	Tabulates the number of patients by type and indication of the systemic cancer therapy for each treatment group.
Prior Radiation Therapy	FAS	Tabulates the number of patients by site and indication of prior radiation therapy for each treatment group.
Medical History	FAS	Summarizes medical history by SOC and PT for each treatment group.
Study Drug Exposure	Safety	Summarizes the number of cycles, the duration of treatment, cumulative dose, and RDI by treatment group. The number of dose interruptions/discontinuation or reduction will also be summarized.
Compliance	Safety	Compliance assessment will be summarized by each visit.
Dose Limiting Toxicity	Safety	Tabulates the number of patients experienced DLT

Title	Population	Description
		and the corresponding DLT at cycle 1 and 2 for each treatment group. For Phase 1b only.
Progression-Free Survival	FAS[1]	Summary of PFS results including treatment comparison results. Separate tables will be done for PFS based on RECIST 1.1 and irRECIST.
Progression-Free Survival	FAS[1]	Summary of PFS results including treatment comparison results (sensitivity analysis). Separate tables will be done for PFS based on RECIST 1.1 and irRECIST.
Objective Response Rate	FAS[1]	Summary of ORR results including treatment comparison results. Separate tables will be done for ORR based on RECIST 1.1 and irRECIST.
Clinical Benefit Rate	FAS[1]	Summary of CBR results including treatment comparison results. Separate tables will be done for CBR done based on RECIST 1.1 and irRECIST.
Overall Survival	FAS[1]	Summary of OS results by treatment group.
Duration of Response (those with CR/PR or irCR/irPR	FAS[1]	Summary of DOR results by treatment group.
Time to Response (same comment as above)	FAS[1]	Summary of TTR results by treatment group.
TEAEs Overview	Safety	Tabulates the number of patients with TEAEs, Related TEAEs, Grade 3 / 4 TEAEs, TEAEs with action taken as dose reduced or drug interrupted, TEAEs leading to drug withdrawn, SAE, Fatal AE. For Phase1b, the DLT rate will be presented.

Title	Population	Description
TEAEs	Safety	Summary by SOC and PT for each treatment group.
TEAEs	Safety	Summary by PT for each treatment group ordered by frequency.
TEAEs per Maximum Grade	Safety	Summary by SOC and PT for each treatment group.
TEAEs Related to Entinostat	Safety	Summary by SOC and PT for each treatment group.
TEAEs Related to Entinostat per Maximum Grade	Safety	Summary by SOC and PT for each treatment group.
Grade 3 / 4 TEAEs	Safety	Summary by SOC and PT for each treatment group.
Grade 3 / 4 TEAEs	Safety	Summary by PT for each treatment group ordered by frequency.
TEAEs Related to Atezolizumab	Safety	Summary by SOC and PT for each treatment group.
TEAEs Related to Atezolizumab per Maximum Grade	Safety	Summary by SOC and PT for each treatment group.
TEAEs Related to Entinostat and/or Atezolizumab	Safety	Summary by SOC and PT for each treatment group.
TEAEs Related to Entinostat and/or Atezolizumab per Maximum Grade	Safety	Summary by SOC and PT for each treatment group.
TEAEs with Action Taken as Treatment delayed/interrupted for Entinostat	Safety	Summary by SOC and PT for each treatment group.
TEAEs with Action Taken as Treatment delayed/interrupted for Atezolizumab	Safety	Summary by SOC and PT for each treatment group.
TEAEs with Action Taken as Dose Reduced	Safety	Summary by SOC and PT for each treatment group. (For Phase 2 only)

Title	Population	Description
for Entinostat		
TEAEs Leading to Treatment Discontinuation	Safety	Summary by SOC and PT for each treatment group.
TEAEs Leading to Treatment Discontinuation	Safety	Summary by PT for each treatment group ordered by frequency.
SAE	Safety	Summary by SOC and PT for each treatment group.
AEs Leading to Death	Safety	Summary by SOC and PT for each treatment group.
Laboratory Values	Safety	Summary of each laboratory parameter at baseline, minimum post baseline value, maximum post baseline value, average post baseline value and last post baseline value for each treatment group. In addition, shift tables will be presented.
ECOG Performance Status	Safety	Summary of ECOG performance status at each baseline, minimum post baseline value, maximum post baseline value, last post baseline value for each treatment group. In addition, a shift table will be presented.
Vital Signs	Safety	Summary of descriptive statistics for each vital sign measurements will be done for baseline value, minimum post baseline value, maximum post baseline value, average post baseline value, and last post baseline value for each treatment group.
ECG	Safety	Tabulate the frequency and percentage of patients according to findings reported at each time point for each treatment group.
Prior and Concomitant Medications	Safety	Tabulate the frequency and percentage of patients according to generic name. Summary will be presented separately for prior medications and

Title	Population	Description
		concomitant medications.
Anticancer Therapy Received after end of study treatment	FAS	Tabulate the frequency and percentage of patients according to type of anticancer therapy received after end of study treatment.

[1] Separate tables to be produced based on per-protocol analysis set if needed.

11.2 Planned Listings

Title	Population	Description
Screen Failures	N/A	Listing of screen failures and the corresponding reason(s) of failures.
Patient Accountability	FAS	Listing of all patients and with population indicators, treatment groups. For patients who discontinued from treatment and/or study, include the reason of respective discontinuations.
Demographics	FAS	Listing of demographics.
Disease Characteristics	FAS	Listing of disease characteristics.
Prior Surgery	FAS	Listing of prior surgery.
Prior Systemic Anti-Cancer Therapy	FAS	Listing of prior systemic anti-cancer therapy.
Prior Radiation Therapy	FAS	Listing of prior radiation therapy.
Study Drug Exposure	Safety	Listing of patients for extent of exposure by visit.
Study Drug Exposure Summary	Safety	Listing of patients for summary of exposure (e.g. number of cycles, duration of treatment, cumulative dose, weekly dose intensity, RDI).
Efficacy Parameters	FAS	Listing of all efficacy parameters for each patient, including PFS, OS, best overall response, duration of response, and time to response.
Tumor Assessment	FAS	Listing of tumor assessment including lesion number, date of assessment, lesion measurement/response, and time-point overall response assessed by RECIST 1.1 and irRECIST.
Anticancer Treatment Received after End of Study Treatment	FAS	Listing of anticancer therapies received after end of study treatment; the listing includes the type of therapy, start date, end date (or ongoing)
AEs	Safety	Listing of all AE for each patient; the listing includes the verbatim term, PT, SOC, seriousness, worst grade, start date, outcome, stop date, relationship to study drug, action taken for study drug, and treatment

Title	Population	Description
		emergent flag.
TEAEs Related to Entinostat	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs Related to Atezolizumab	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs Related to Entinostat and/or Atezolizumab	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs with Action Taken for Drug Interrupted for Entinostat	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs with Action Taken for Dose Reduced for Entinostat	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs with Action Taken of Drug Interrupted for Atezolizumab	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
TEAEs Leading to Study Treatment Discontinuation	Safety	Listing of TEAEs in this category using the same structure as the AEs listing with the omission of treatment emergent flag.
SAEs	Safety	Listing of TEAEs in this category using the same structure as the AEs listing .
AEs Leading to Death	Safety	Listing of TEAEs in this category using the same structure as the AEs listing.
Deaths	Safety	Listing of patients who died, including primary cause of death, date of death, date of last dose, and the number of days from date of last dose to death.
Laboratory Values	Safety	Listing of all laboratory values and their assigned toxicity grade (where applicable).
ECOG Performance Status	Safety	Listing of ECOG at each assessment.
Vital Signs	Safety	Listing of all vital signs results at each assessment.
Prior and Concomitant Medications	Safety	Listing of all prior and concomitant medications; the listing includes verbatim product name, generic name, start date, end date (or ongoing) and indication.
Post Study Follow-up	Safety	Listing of patients who are being followed in post

Title	Population	Description
		study follow-up visits.

11.3 Planned Figures

Title	Population	Description
PFS	FAS	KM plot of PFS by treatment group. Forest plots are done for subgroup analyses.
OS	FAS	KM plot and Forest plots of OS by treatment group.
DOR	FAS	KM plot of DOR by treatment group.
TTR	FAS	Swimmer plot of TTR by treatment group.
BOR	FAS	Waterfall plot and Spider plot of BOR for RECIST and irRECIST by treatment group.