Strategia Therapeutics, Inc.

BSC-101-01

A Phase 1/2a study of E6201 for the treatment of advanced hematologic malignancies with FLT3 and/or Ras mutations, including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) or chronic myelomonocytic leukemia (CMML)

Statistical Analysis Plan

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Version 1.0

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1. Project Overview

1.1. Project Design

(Protocol Amendment #6). This is a Phase 1/2a, dose-escalation study of E6201, a dual MEK1 and FLT3 inhibitor, in subjects with advanced hematologic malignancies with documented FLT3 and/or Ras mutations. The Phase 1 portion of the study will be conducted as a safety run-in in up to 30 subjects to establish a recommended Phase 2 dose (RP2D). The Phase 2a portion of the study will evaluate three specific patient groups: Cohort 1 will enroll up to 26 patients with relapsed or refractory AML and confirmed FLT3 mutation (with or without a Ras mutation) without prior exposure to a FLT3 inhibitor, Cohort 2 will enroll up to 26 patients with relapsed or refractory AML and confirmed FLT3 mutation (with or without a Ras mutation) with prior exposure to a FLT3 inhibitor, and Cohort 3 will enroll up to 10 patients with relapsed or refractory AML with a confirmed Ras mutation and no FLT3 mutation. Cohorts 1 and 2 of the expansion phase will incorporate a Simon 2-stage optimal design. A total of up to N= 92 subjects will be enrolled in the study.

The accrual phase for the Phase 1 Safety Run-in portion is expected to be 24 – 27 months. The expected accrual for the Phase 2a Expansion portion is expected to be 12 months, for a total accrual period of 36 – 39 months. With the last subject followed for up to 6 months, a total study duration of 42 – 45 months is anticipated. The anticipated accrual rate for the Phase 2a portion is 4 – 6 subjects per month across all sites.

During the study, a Safety Review Committee (SRC), consisting of the actively recruiting investigators, the Medical Monitor and Boston Strategics will review data from each cohort on an ongoing basis.

Subjects who demonstrate clinical benefit (objective response or stable disease) will be allowed to continue therapy with E6201 until progression of disease, observation of unacceptable adverse events, intercurrent illness or changes in the patient's condition that prevents further study participation. Subjects will be instructed to contact their study doctor for ophthalmic evaluation should they experience disturbances in their vision.

Safety will be assessed through the monitoring of adverse events (AEs), clinical laboratory parameters (hematology and serum chemistry), vital sign measurements, ECGs and physical examinations. Adverse events will be classified according to the Medical Dictionary for Regulatory Affairs (MedDRA) and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03.

Efficacy assessment for AML will be performed using a modification of the recommendations of the International Working Group (IWG) for Diagnosis, Standardization of Response Criteria, Treatment Outcomes, and Reporting Standards for Therapeutic Trials in Acute Myeloid Leukemia. Efficacy assessments for subjects with MDS or CMML will be performed using a modification of the IWG Response Criteria in Myelodysplasia.

Pharmacokinetic determinations of E6201 in plasma will be made. Levels of pERK, pFLT3, pAKT, FLT3 ITD allelic burden, FLT3 ligand and plasma inhibitory assay (PIA) for FLT3, will be measured in blood and/or bone marrow samples collected from each subject. Additional markers or mutation analysis will be undertaken, if needed. Details of the PK analysis will be outlined in a separate Pharmacokinetic Report Analysis Plan.

1.2. Objectives

1.2.1. Primary Objective

- Phase 1: To determine the safety and tolerability of E6201 in subjects with FLT3+ and/or Ras+ AML, MDS or CMML and to establish a recommended Phase 2 dose (RP2D)
- Phase 2a: To evaluate the overall response rates (ORR) in subjects who receive E6201 for the treatment of FLT3+ and/or Ras+ relapsed/refractory AML

1.2.2. Secondary Objectives

- To evaluate duration of response
- To evaluate progression-free survival (PFS)
- To evaluate overall survival (OS)
- To evaluate the pharmacokinetics (PK) of E6201
- To explore pharmacodynamic (PD) changes from baseline in signal transduction markers in blood or/and bone marrow: pERK, pFLT3 and pAKT
- To explore quantitative changes from baseline in FLT3 internal tandem duplication (FLT3 ITD), FLT3 tyrosine kinase domain (TKD) and Ras+ allelic burden, FLT3 ligand and plasma inhibitory assay (PIA) for FLT3, and evaluate the correlation between FLT3 and Ras+ allelic burden and objective response
- To determine the safety and tolerability of E6201 at the RP2D (Phase 2a)

1.3. Treatment(s)

1.3.1. Treatment Assignments

Phase 1 (Safety Run-In): Phase 1 (Safety Run-In): Following Screening, a total of up to 30 subjects in up to 5 dose cohorts will be enrolled to establish the RP2D. The safety run-in phase will be a standard 3+3 cohort design.

Dose Level 1: 240 mg/m^2 weekly Days 1, 8, 15 and 22, repeated every 28 days (=1 cycle)
Dose Level 2: 320 mg/m^2 weekly Days 1, 8, 15 and 22, repeated every 28 days
Dose Level 3: 160 mg/m^2 twice weekly Days 1, 4, 8, 11, 15,18, 22 and 25, repeated every 28 days (=1 cycle)
Dose Level 4: 240 mg/m^2 twice weekly Days 1, 4, 8, 11, 15, 18, 22 and 25, repeated every 28 days (=1 cycle)
Dose Level 5: 320 mg/m^2 twice weekly Days 1, 4, 8, 11, 15, 18, 22 and 25, repeated every 28 days

Phase 2a (Expansion): Once the Phase 1 Safety Run-In portion of the study is complete and an RP2D is established, additional subjects will be enrolled into the Phase 2 Expansion portion in three cohorts. Cohort 1 will enroll up to 26 patients with relapsed or refractory AML and confirmed FLT3 mutation (with or without a Ras mutation) without prior exposure to a FLT3 inhibitor. Cohort 2 will enroll up to 26 patients with relapsed or refractory AML and confirmed FLT3 mutation (with or without a Ras mutation) with prior exposure to a FLT3 inhibitor. Cohort 3 will enroll up to 10 patients with relapsed or refractory AML with a confirmed Ras mutation and no FLT3 mutation. Cohorts 1 and 2 of the Expansion Phase will incorporate a Simon 2-stage optimal design. Subjects with AML enrolled in the Phase 1

portion of the study at the RP2D will count towards the Phase 2a accrual for the appropriate cohort.

1.3.2. Selection and Timing of Doses

Phase 1 (Safety Run-In):
In the first cohort, the dose of E6201 will be 240 mg/m^2, administered as an intravenous (IV) infusion over 2 hours once weekly (Dose Level 1), on Days 1, 8, 15 and 22 of a 28- day schedule (=1 cycle). A minimum of 3 subjects will be treated. If 1 of 3 subjects experiences DLT during Cycle 1, the cohort will be expanded to 6. If ≥ 2 of 6 subjects experiences DLT by Day 28, no dose escalation to Dose Level 2 will occur. However, if 0 of 3 or ≤ 1 of 6 subjects treated at Dose Level 1 experience DLT by Day 28, dose escalation will proceed to the next cohort, 320 mg/m^2 weekly (Dose Level 2), administered by IV infusion over 2 hours on Days 1, 8, 15 and 22 of a 28-day schedule. A minimum of 3 subjects will be treated at this dose level. If 1 of 3 subjects treated at Dose Level 2 experiences DLT during Cycle 1, the cohort will be expanded to 6 subjects. If ≥ 2 of 6 subjects experience DLT by Day 28, no further dose escalation will occur.

However, if 0 of 3 or ≤ 1 of 6 subjects treated at Dose Level 2 experience DLT by Day 28, dose escalation will proceed to the next dose cohort, 160 mg/m^2 administered as an IV infusion over 2 hours twice weekly (Dose Level 3), on Days 1, 4, 8, 11, 15, 18, 22 and 25 of a 28-day schedule (=1 cycle). A minimum of 3 subjects will be treated at this dose level. If 1 of 3 subjects treated at Dose Level 3 experiences DLT during Cycle 1, the cohort will be expanded to 6 subjects. If ≥ 2 of 6 subjects experience DLT by Day 28, no further dose escalation will occur.

However, if 0 of 3 or ≤ 1 of 6 subjects treated at Dose Level 3 experiences DLT by Day 28, dose escalation will proceed to the next dose cohort, 240 mg/m^2 administered as an IV infusion over 2 hours twice weekly (Dose Level 4), on Days 1, 4, 8, 11, 15, 18, 22 and 25 of a 28-day schedule. A minimum of 3 subjects will be treated at this dose level. If 1 of 3 subjects treated at Dose Level 4 experiences DLT during Cycle 1, the cohort will be expanded to 6 subjects. If ≥ 2 of 6 subjects experience DLT by Day 28, no further dose escalation will occur.

However, if 0 of 3 or ≤ 1 of 6 subjects treated at Dose Level 4 experiences DLT by Day 28, dose escalation will proceed to the next dose cohort, 320 mg/m^2 administered as an IV infusion over 2 hours twice weekly (Dose Level 5), on Days 1, 4, 8, 11, 15, 18, 22 and 25 of a 28-day schedule. A minimum of 3 subjects will be treated at this dose level. If 1 of 3 subjects treated at Dose Level 5 experiences DLT during Cycle 1, the cohort will be expanded to 6 subjects. If there are ≤ 1 of 6 subjects with DLT at Dose Level 5, this dose (320 mg/m2 twice weekly) will be declared the MTD and RP2D. If, however, ≥ 2 of 6 subjects experiences DLT, then either 320 mg/m2 weekly (Dose Level 2) or 240 mg/m2 twice weekly (Dose Level 4) will be declared the MTD and RP2D based on additional factors (e.g., PK and PD parameters).

Dose-limiting toxicity will be defined as any one of the following events: prolonged myelosuppression (as defined by the National Cancer Institute [NCI] criteria specific for leukemia, i.e., marrow cellularity < 5% at ≥ 6 weeks from start of therapy without evidence of leukemia); ≥ Grade 3 non-hematologic toxicity (excluding Grade 3 nausea, vomiting or diarrhea that is adequately controlled with supportive care and resolves to ≤ Grade 2 within 48 hours, or Grade 3 electrolyte disturbances responsive to correction within 24 hours); ≥

Grade 3 liver function tests (LFTs) lasting > 7 days; treatment interruption > 14 days due to toxicity; or other important medical event.

Phase 2a (Expansion):
Subjects will be enrolled into the Phase 2 Expansion portion in three cohorts. Subjects will receive E6201 weekly or bi-weekly on a 28-day schedule, with the schedule and dose level established in the safety run-in portion of the study.

As of July 17, 2017, this study was terminated due to lack of sufficient efficacy in the Phase 1 dose escalation portion of the study. Therefore, the SAP will include patient listing data and dose cohort summary tables for the 28 patients enrolled in the study.

1.4. Procedures

1.4.1. Subject Identification

Once study eligibility has been determined, a subject will be enrolled into the study and will be assigned a sequential Subject Identification number within each participating site. The identification number will consist of a 2-digit site number, 1-digit cohort number, and a 2 digit subject number. The subject identification number will be assigned sequentially within the cohort. The cohort number will remain the same if a subject's dose is increased or decreased. If a subject is replaced, the identification number will not be reassigned.

1.4.2. Randomization

Not Applicable

1.4.3. Blinding/Unblinding

This is an unblinded study.

1.4.4. Replacement

Subjects who are screened but do not receive E6201, and subjects treated in Cycle 1 who complete < 75% of their prescribed study drug treatment or do not complete C1D28 evaluation due to progression of disease, withdrawal of consent or non-DLT adverse events, will be replaced.

1.4.5. Data Monitoring

Strategia Therapeutics is responsible for ensuring the proper conduct of the study with regard to ethics, protocol adherence, site procedures, integrity of the data, and applicable laws and/or regulations. At regular intervals during the study and following completion of the study, the sponsor's study monitors will contact the study site via visits to the site, telephone calls, and letters in order to review study progress, CRF completion and address any concerns or questions regarding the study conduct. During monitoring visits, the following aspects of study conduct will be carefully reviewed: informed consent of subjects, subject recruitment, subject compliance with the study procedures, source data verification, drug accountability,

use of concomitant therapy by subjects, AE and SAE documentation and reporting, and quality of data. Records pertaining to these aspects are expected to be kept current.

2. Statistical Analysis Considerations

2.1. Sample Size and Power

A total of up to 92 subjects will be enrolled in this study.

Phase 1 (Safety Run-In): The sample size reflects requirements associated with a 3+3 design. A total of 3 to 30 subjects are planned (3 to 6 subjects in each of 5 dose cohorts) with FLT3+ and/or Ras+ AML, MDS or CMML.

Phase 2a (Expansion):

Cohort 1: The statistical objective for Cohort 1 in the dose expansion portion of the study is evaluation of the objective response (OR) rate within 3 cycles of treatment with E6201 in patients with AML and FLT3 mutation, or FLT3 plus Ras mutations, without prior exposure to a FLT3 inhibitor. If there is at least 1 OR in the first 8 patients, 18 additional patients will be enrolled in Stage II, for a total of 26 evaluable patients. If there are at least 4 ORs in a total of N=26, the alternative hypothesis will be accepted. This design provides a type I error of 5% and power of 85% when the true OR rate is 25%.

Cohort 2: The statistical objective for Cohort 2 in the dose expansion portion of the study is evaluation of the objective response (OR) rate within 3 cycles of treatment with E6201 in patients with AML and FLT3 mutation, or FLT3 plus Ras mutations, with prior exposure to a FLT3 inhibitor. Based on Simon's 2-stage optimal design, eleven (11) patients will be enrolled in Stage I. If there are zero (0) ORs in these 11 patients, the cohort will be terminated. If there is at least 1 OR in the first 11 patients, 15 additional patients will be enrolled in Stage II, for a total of 26 patients. If there are at least 2 ORs in a total of N=26, the alternative hypothesis will be accepted. This design provides a type I error of 5% and power of 80% when the true OR rate is 15% or greater.

Cohort 3: We will evaluate the objective response (OR) rate within 3 cycles of treatment with E6201 in up to 10 patients with AML and Ras mutation but no mutation in FLT3. A response rate of 20% in this patient population is considered clinically meaningful.

2.2. Analysis Populations

The full analysis set (FAS) includes all subjects who are administered any fraction of a dose of study medication. For a particular measure, the per-protocol set (PPS) includes those subjects in the FAS who have had a valid baseline and one or more post-treatment assessments for that measure of interest.

The E6201 PK population consists of all subjects in the FAS who complete all PK assessments. The E6201 PD population consists of all subjects in the FAS who complete all PD assessments. Details of the analysis will be outlined in the Pharmacokinetic Report Analysis Plan.

2.2.1. Intent-to-Treat (ITT) Population

This population will not be used in the analysis.

2.2.2. Randomized Population

Since this is not a randomized study, there is no randomized population.

2.2.3. Per Protocol Population

All efficacy endpoints will be initially based on the subjects receiving any fraction of a dose of study medication and having at least one post-baseline value (PPS) for a particular efficacy endpoint. For each efficacy endpoint, an assessment for any subject may be performed at a time point deemed appropriate by the investigator.

2.2.4. Safety Population

All safety endpoints will be based on the FAS dataset.

2.2.5. Screen Failure Population

This population will not be used in the analysis.

2.3. Data Handling

2.3.1. Measurement Times

2.3.1.1. Visit Windows

Visit windows will not be used. The visit time point entered on the case report forms will be used. Unscheduled assessments, if any, will be listed, but will not be included in tabulations by visit.

2.3.1.2. Baseline Values

The screening assessments are performed within 28 days of Cycle 1, Day 1, before the first dose of study medication. Unless otherwise mentioned, baseline will be the last observation before patients receive initially assigned dose. Generally, this will be Cycle 1 Day 1 pre-dose measurements. If a pre-dose assessment is not performed on Cycle 1 Day 1, the immediate previous non-missing value, including screening, will be treated as baseline. If there are multiple baseline assessments, the most recent one will be flagged as the baseline value and will be used for statistical analysis (evaluations may occur on the same day as Study Day 1, prior to dosing).

2.3.2. Missing Data Conventions

Unless otherwise specified, missing data will be considered missing and will not be imputed.

2.3.3. Imputation of Incomplete Dates

Imputation of partial dates may be performed during the data analysis and will be documented. For start date of Adverse Event (AE) or Concomitant Medication (CM) with a missing day, the imputed date is the first day of the month. For stop date of AE or CM with a missing day, the imputed date is the last day of the month. For start date with both missing day and missing month, the imputed date is the subject start study date if AE or CM start year is the same as study start year. Otherwise, the imputed start date is the first day of the year. For stop date with both missing day and missing month, the imputed date is the subject end of study date if AE or CM stop year is the same as the study end year. Otherwise, the imputed stop date is the last day of the year.

2.4. Statistical Methods

2.4.1. General Overview and Plan of Analysis

All data will be analyzed using Statistical Analysis System (SAS Version 9.4 or higher for Windows, SAS Institute, Cary, NC). Continuous variables will be summarized using number, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using frequencies and percentages.

2.4.2. Hypothesis Testing

No formal hypothesis tests are planned.

2.4.3. Modeling

Not Applicable in this study.

2.4.4. Multiplicity Issues/Multiple Comparisons

There is no planned Multiplicity Issues/Multiple Comparisons analysis for this study.

2.4.5. Project Center Effects

The study will be conducted at The University of Texas M.D. Anderson Cancer Center with Gautam Borthakur, M.D. serving as Study Chair. Additional clinical sites include Moffitt Cancer Center (Kendra Sweet, MD), Health ONE Cares (Michael Maris, MD) and Methodist Hospital, San Antonio (Jose Cruz, MD).

2.4.6. Interim Analysis

No formal interim analysis is planned. Appropriate safety listings and summary tables will be generated for Scientific Review Committee meetings and Development Safety Update Reports (DSURs).

2.4.7. Pharmacokinetic and Pharmacodynamic Analyses

Pharmacokinetic and Pharmacodynamic data will be summarized in a separate report.

3. Statistical Analysis

Data will be presented for clinical review and interpretation. Categorical variables will be summarized using frequency counts and percentages. Continuous variables will be summarized using descriptive statistics (n, mean, SD, median, minimum, and maximum). All listings will be presented for the FAS population except for PK and PD data.

3.1. Enrollment and Disposition of Subjects

Enrolled individuals are referred to as "subjects". Subjects with advanced hematologic malignancies with FLT3 and/or Ras mutations, including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) or chronic myelomonocytic leukemia (CMML) will be included.

Major selection criteria are: age ≥ 18 years with confirmed diagnosis of FLT3+ and/or Ras+ higher-risk MDS/CMML (Phase 1 only), or relapsed or refractory AML with a FLT3 and/or Ras mutation. In the absence of rapidly-progressing disease, ≥ 3 weeks after prior cancer treatment for the disease under study, with the exception of hydroxyurea to control peripheral blast counts allowed during the first 2 cycles. Subjects must have recovered from all acute toxicities (≤ Grade 1), have adequate renal and hepatic function, and no known history of significant cardiac disease.

The analyses of subject disposition will be performed on the FAS population for all subjects and by dose cohort. The number of subjects treated, completed study and those who terminated early from the study, along with their reasons for early termination, will be presented.

3.2. Baseline Characteristics

3.2.1. Demographic

Summary statistics for demographic characteristics will be presented for subjects by dose cohort using the full analysis set (FAS) population. Tabulations will be performed for age, sex (male or female), ethnicity (Hispanic/Latino or other), and race (American Indian or Alaska Native, Black or African American, White, Asian, Native Hawaiian or Other Pacific Islander, Unknown, or other). Age will be calculated as the number of complete years between a subject's date of birth and the date of screening visit. Demographic characteristics will be presented in listing for each subject.

3.2.2. Physical Characteristics

Physical characteristics will be presented in listing for each subject.

3.2.3. Disease Characteristics

The baseline disease assessment (AML and MDS/CMML), prior FLT3 inhibitor exposure, prior cancer therapy, medical history findings, and major protocol deviations will be presented in listings for each subject.

3.2.4. Concomitant Medications

Prior and concomitant medications will be listed.

3.3. Analysis of Efficacy

3.3.1. Primary Endpoints

No primary endpoints analysis will be provided.

3.3.2. Secondary Endpoints

No secondary endpoints analysis will be provided.

3.3.3. Exploratory/Other Analyses

Pharmacokinetic and pharmacodynamic analyses will be provided by an outside laboratory.

3.4. Analysis of Safety and Tolerability

3.4.1. Study Drug Administration

The study drug exposure will be summarized by dose cohort. The study drug administration will be presented in listing for each subject.

3.4.2. Adverse Events

All AEs will be coded based on the Medical Dictionary for Regulatory Affairs (MedDRA; Version 17.0 or higher). An AE will be considered a treatment emergent adverse event (TEAE) if the onset is after the first dose of study drug or if the condition was present at baseline but worsened after the first dose. All other AEs will be considered preexisting events.

All AEs for each subject will be listed, including Treatment Emergent status, intensity grading, relationship to study drug, action taken and outcome. Subject listings of deaths, serious TEAEs, and TEAEs leading to treatment discontinuation will be presented.

TEAE summaries will be produced for each dose cohort for subjects in FAS population. All TEAE summaries will show the number and percentage of subjects experiencing at least 1 TEAE for each preferred term, arranged by system organ class, and the number of unique occurrences of the event. Separate summaries will be produced by relationship to study medication and by severity. Subjects with multiple events will be counted only once per SOC

and preferred term. For each level of summarization, the event with the highest level of severity, grade, or strongest drug relationship will be presented. TEAEs with Grade 3 or Grade 4 and drug-related TEAES with Grade 3 or Grade 4 will be summarized. TEAEs leading to study drug interruption or discontinuation, and Serious TEAEs will be provided in separate listings.

3.4.3. Clinical Laboratory Results

Laboratory data will be listed for each subject using FAS population. Laboratory values will be graded according to the NCI-CTCAE version 4.03 criteria. Laboratory results will be summarized by dose cohort using number of non-missing observations, mean, standard deviation, median, minimum, and maximum.

3.4.4. Vital Signs

Vital sign measurements include temperature, blood pressure and pulse rate. Vital signs will be listed for each subject. Actual vital sign results will be summarized by dose cohort using number of non-missing observations, mean, standard deviation, median, minimum and maximum by dose cohort.

3.4.5. Physical/Other Examinations

Data collected for physical examinations, ECGs and related measures will be listed for each subject.

3.4.6. Treatment Discontinuation, Project Termination, and Death

The participants who discontinued (with reasons) and deaths will be listed.

4. Proposed Summary Tables, Figures and Listings

4.1. Mock Tables

The following tables will be presented by dose cohort.

4.1.1. Subject Disposition

- Subject Disposition

4.1.2. Demographics and Baseline Characteristics

- Demographics and Baseline Characteristics

4.1.3. Safety Summaries

4.1.3.1. Study Drug Administration

- Summary of Study Drug Exposure

4.1.3.2. Adverse Events Summaries

- Summary of Treatment Emergent Adverse Events
- Treatment Emergent Adverse Events by System Organ Class and Preferred Term
- Treatment Emergent Adverse Events by Severity
- Treatment Emergent Adverse Events by Relationship to Study Drug
- Grade 3 and Grade 4 Treatment Emergent Adverse Events by Relationship to Study Drug
- Serious Treatment Emergent Adverse Events
- Serious Treatment Emergent Adverse Events Related to Study Drug

4.1.3.3. Laboratory Assessments

- Hematology Laboratory Results by Visit
- Chemistry Laboratory Results by Visit

4.1.3.4. Other Safety Summaries

- Summary of Vital Sign Results

4.2. Mock Figures

No figures will be presented in the analysis.

4.3. Mock Listings

- Inclusion Criteria Not Met
- Exclusion Criteria Not Met
- Protocol Violations/Deviations/Exemptions
- Demographics
- End of Treatment
- End of Study
- Baseline Disease Assessment (AML)
- Baseline Disease Assessment (MDS/CMML)
- Medical History
- All Prior FLT3 Inhibitor Exposure and Prior Cancer Therapy
- Physical Examination
- Prior and Concomitant Medications
- Study Drug Administration
- Disease Response Assessment (AML)
- Disease Response Assessment (MDS/CMML)
- Bone Marrow Assessment (BMA)
- Treatment Emergent Adverse Events (TEAE)
- Serious Treatment Emergent Adverse Events
- Treatment Emergent Adverse Events Leading to Dose Adjustment, Temporary Interruption, and Permanent Discontinuation of Study Drug
- Treatment Emergent Adverse Events Leading to Permanent Discontinuation from Study

- Deaths
- Hematology
- Chemistry
- Vital Signs
- 12-lead Electrocardiogram
- Blood Transfusion
- Other Procedures
- Long Term Follow-up