STATISTICAL ANALYSIS PLAN

Protocol Title:	**A Phase 2, Single-Arm, Open-Label Study of Trilaciclib Administered Prior to Sacituzumab Govitecan-hziy in Patients with Unresectable Locally Advanced or Metastatic Triple-Negative Breast Cancer Who Received at Least Two Prior Treatments, at Least One in the Metastatic Setting**
Protocol Version	2.0
Protocol Number:	G1T28-213
Compound:	Trilaciclib for Injection, 300 mg/vial
Study Phase:	Phase 2
Sponsor:	G1 Therapeutics, Inc.
Legal Registered Address:	700 Park Offices Dr. Suite 200 PO Box 110341 Research Triangle Park, NC 27709
Regulatory Agency Identifier Numbers:	IND: 145091 EudraCT: 2019-003826-25
Statistical Analysis Plan Version:	V 2.0
Approval Date:	04 Jun 2024

SAP SIGNATURE PAGE

I have read and understand the contents of this Statistical Analysis Plan, Version 2.0 for Study G1T28-213, and I agree with all the statistical approaches, variable derivations, and data presentation detailed as described in this document.

PPD

04-Jun-2024

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LIST OF ABBREVIATIONS

Abbreviation	Term
aCSR	Abbreviated clinical study report
AE	Adverse event
AESI	Adverse events of special interest
ALC	Absolute lymphocyte count
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Classification
BMI	Body mass index
BOR	Best overall response
BRCA	Breast cancer gene
BSA	Body surface area
BUN	Blood urea nitrogen
C1D1	Cycle 1 Day 1
CBR	Clinical benefit rate
CDK	Cyclin dependent kinase
CI	Confidence interval
CR	Complete response
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DBP	Diastolic blood pressure
DOR	Duration of response
EDC	Electronic data capture
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EDC	Electronic data capture
EOT	End of treament

Abbreviation	Term
ESA	Erythropoiesis-stimulating agent
ETV	End of Treatment Visit
FAS	Full analysis set
G-CSF	Granulocyte colony stimulating factor
Hgb	Hemoglobin
HR	Hazard ratio
ID	Identification
IV	Intravenous
LDH	Lactate dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
NE	Not evaluable
ORR	Objective response rate
OS	Overall survival
PCS	Potentially clinically significant
PD	Progressive disease
PFS	Progression free survival
pMMR/MSS	Proficient mismatch repair/microsatellite stable
PR	Partial response
PT	Preferred term
RBC	Red blood cell
RE	Response evaluable
RECIST	Response Evaluable Criteria in Solid Tumors
SACT	Subsequent anticancer treatment
SAP	Statistical Analysis Plan
SBP	Systolic blood pressure
SD	Stable disease
SE	Standard error
SG	Sacituzumab govitecan-hziy
SI	Standard international
SN	Severe neutropenia

Abbreviation	Term
SOC	System organ class
SPSD	Statistical Programming Supportive Documents
TLF	Tables, listings, and figures
TNBC	Triple-negative breast cancer
TOC	Table of contents
WHO-DD	World Health Organization Drug Dictionary

1. INTRODUCTION

This Statistical Analysis Plan (SAP) provides detailed statistical methods, variable definitions and derivations, and data handling that will be applied to analyze the clinical trial data collected during study G1T28-213, "A Phase 2, Single-Arm, Open-Label Study of Trilaciclib Administered Prior to Sacituzumab Govitecan-hziy in Patients with Unresectable Locally Advanced or Metastatic Triple-Negative Breast Cancer Who Received at Least Two Prior Treatments, at Least One in the Metastatic Setting" based on the protocol Version 2.0 (dated 15 November, 2021).

Statistical Programming Supportive Documents (SPSD) will be developed based on the SAP to serve as companion documents of the SAP to guide programming realization of the SAP. SPSD contain three separate documents:

1. The table of contents (TOC) for planned analyses (in Excel Spreadsheet).
2. The reporting conventions (in Word).
3. The shells or specificities for tables, listings, and figures (TLFs) generation (in Word).

Statistical software SAS® (SAS Institute Inc., Cary, NC) Version 9.4 or later will be used to perform data analyses following the plan as laid out in this SAP.

If there are differences between statistical analysis approaches described in the SAP and those in the protocol, the methods and approaches in the SAP will supersede those in the protocol. Changes and additions to the last signed off version of the SAP will be documented with corresponding rationale in the clinical study report (CSR).

1.1. Study Design

This is a Phase 2, multicenter, open-label, single arm study evaluating the safety and efficacy of trilaciclib administered prior to sacituzumab govitecan-hziy in patients with unresectable, locally advanced or metastatic triple-negative breast cancer (TNBC) who received at least 2 prior treatments, at least 1 in the metastatic setting.

Approximately 45 patients were planned to be enrolled per Protocol Version 2.0. The sponsor decided to close enrollment to this study on February 14, 2023 in order to reallocate resources to other ongoing trilaciclib clinical trials. The final total number of patients enrolled in this study is 30.

Trilaciclib and sacituzumab govitecan-hziy will be administered intravenously (IV) in 21-day cycles as indicated below:

Trilaciclib:

Trilaciclib 240 mg/m2 administered as a 30-minute IV infusion completed within 4 hours prior to the start of sacituzumab govitecan-hziy on Day 1 and Day 8 of each 21-day treatment cycle.

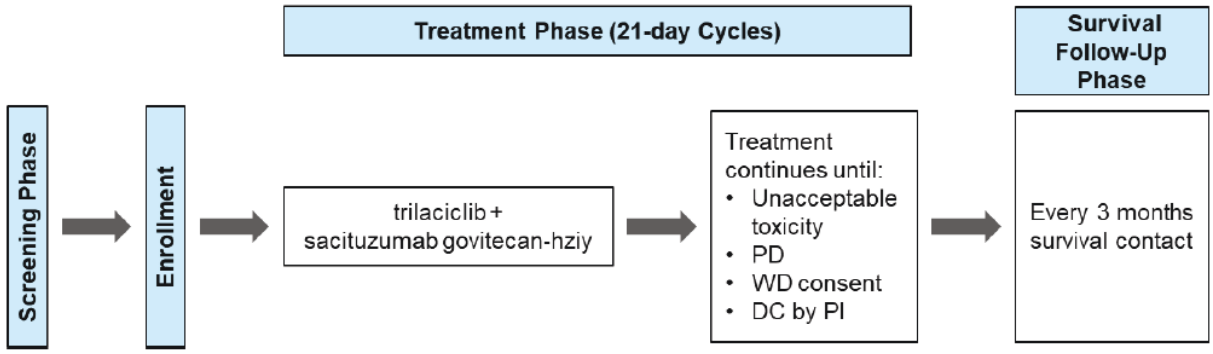
Sacituzumab govitecan-hziy:

Sacituzumab govitecan-hziy 10 mg/kg administered IV on Day 1 and Day 8 of each 21-day treatment cycle. The first infusion is administered over 3 hours and patients are observed during the infusion and for at least 30 minutes following the initial dose for signs or symptoms of infusion-related reactions. Subsequent infusions may be administered over 1 to 2 hours if prior

infusions were tolerated, and patients should be observed during the infusion and for at least 30 minutes after infusion.

The study will include 3 study phases: Screening Phase, Treatment Phase, and Survival Follow-up Phase (Figure 1). The Treatment Phase begins on the day of enrollment and completes at the End of Treatment Visit. Survival Follow-up assessments should occur every 3 months after the End of Treatment Visit.

Figure 1 G1T28-213 Study Design Diagram



DC=discontinued; PD=progressive disease; PI=Principal Investigator; WD=withdraw

Patients enrolled in the study will be eligible to receive treatment until disease progression, unacceptable toxicity, withdrawal of consent, Investigator decision, or the end of the trial, whichever comes first. Treatment cycles will occur consecutively without interruption, except when necessary, to manage toxicities or for administrative reasons. There should be no more than a 3-week delay from the next scheduled dose of sacituzumab govitecan-hziy. A dosing delay >3 weeks from the next scheduled dose may be permitted on a case-by-case basis with the approval of the Investigator and Medical Monitor.

Criteria which patients must meet in order to receive study drug on Day 1 and on Day 8 during treatment are provided in Section 9.2 of the study protocol.

An End of Treatment Visit will occur approximately 14 days following a patient's last dose of study treatment. The first Safety Follow-up visit (which may be a phone call) will occur 30 days after the last dose of study treatment. Patients will be followed for survival approximately every 3 months after the End of Treatment Visit. Survival Follow-up Visits may be done via telephone, email, or clinic visit. Unless otherwise decided by the Sponsor, the study will continue until approximately 70% of patients enrolled in the study have died.

1.2. Study Objectives

Primary:

To evaluate the anti-tumor efficacy of trilaciclib when administered prior to sacituzumab govitecan-hziy as measured by progression free survival (PFS).

Secondary:

To evaluate the anti-tumor efficacy of trilaciclib administered prior to sacituzumab govitecan-hziy as measured by the objective response rate (ORR), duration of objective response (DOR), clinical benefit rate (CBR), and overall survival (OS); evaluate the myeloprotective effects of trilaciclib; and assess the safety and tolerability of trilaciclib administered prior to sacituzumab govitecan-hziy.

Specifically, the primary and secondary objectives and their associated endpoints are described in Table 1.

Table 1 Primary and Secondary Objectives and Endpoints

Objectives	Endpoints
Primary Objective	
To evaluate the anti-tumor activity of trilaciclib when administered prior to sacituzumab govitecan-hziy	• PFS defined as time from the date of first dose of study drug to radiographic disease progression using RECIST v1.1 or death due to any cause, whichever occurs first; for patients without disease progression or death, PFS will be calculated per censoring rules.
Secondary Objective: Efficacy	
To evaluate the anti-tumor activity of trilaciclib when administered prior to sacituzumab govitecan-hziy	• ORR defined as the percentage of patients with BOR of confirmed CR or confirmed PR per RECIST v1.1 • CBR defined as the percentage of patients with a BOR of confirmed CR, confirmed PR, or SD lasting 24 weeks or longer since the first date of study drug administration per RECIST v1.1 • DOR defined as duration of objective response • OS defined as time from the date of first dose of study drug to death due to any cause for those who died; or time to last contact known as alive for those who survived in the study (censored cases)
Secondary Objective: Myeloprotective effects of trilaciclib	
• To evaluate the myeloprotective effects of trilaciclib when administered prior to sacituzumab govitecan-hziy	• Occurrence of SN (during Cycles 1/2 and overall study) • Occurrence of febrile neutropenia • Occurrence of G-CSF administration

Objectives	Endpoints
	• Occurrence of Grade 3/4 decrease of hemoglobin • Occurrence and number of RBC transfusions on/after Week 5 • Occurrence of ESA administration • Occurrence of Grade 3/4 decrease of platelets • Occurrence and number of platelet transfusions • Occurrence of serious infections • Use of IV antibiotics
Secondary objectives: Safety	
To evaluate the safety and tolerability of trilaciclib when administered prior to sacituzumab govitecan-hziy	• Occurrence and severity of AEs by NCI CTCAE v5.0 • Trilaciclib AESIs • Changes in laboratory parameters (hematology and chemistry), vital signs and ECG parameters • Grade 3 or 4 abnormalities in chemistry laboratory parameters • Trilaciclib infusion interruptions • Sacituzumab govitecan-hziy infusion interruptions • Sacituzumab govitecan-hziy dose reduction and cycle delay

AESI=adverse event of special interest; CBR=clinical benefit rate; CR=complete response; CTCAE=Common Terminology Criteria for Adverse Events; ECG=electrocardiogram; ESA= erythropoiesis-stimulating agent;G-CSF= granulocyte colony stimulating factor; IV=intravenous; NCI=National Cancer Institute; ORR=objective response rate; OS=overall survival; PFS=progression free survival; RBC=red blood cell; RECIST=Response Evaluable Criteria in Solid Tumors; SD=stable disease; SN=severe neutropenia;

Other objectives and endpoints of the study can be found in Section 5 of the protocol.

1.3. Sample Size Consideration

The initial sample size was calculated to support the primary objective of the study, that is, to evaluate trilaciclib's effect on PFS when administered prior to sacituzumab govitecan-hziy in patients with locally advanced or metastatic TNBC who received at least 2 prior treatments with at least 1 in the metastatic setting.

This single-arm study was initially planned to enroll 45 patients during the 10-month accrual period with an approximate 30-month total study duration. With 45 patients and 14 months of follow-up after the last patient is dosed, Table 2 presents the required number of PFS events and statistical powers to detect hazard ratios (HRs) of 0.7 and 0. 8 at a 2-sided significance of 0.2 for a median PFS of the historical control group of 5.6 months, which was defined for patients without brain metastases treated with sacituzumab govitecan-hziy in the Phase 3 ASCENT trial (Bardia, 2021). The calculation is based on a one-sample log-rank test (Wu, 2015) with the

assumption that the survival time distributions for both study treatment and historic control group follow the Weibull distribution with a shape parameter of 1.00 (i.e., exponential distribution). PASS 2019, v19.0.8 was used for the power and sample size calculation.

Table 2 Statistical Power

Hazard Ratio	Median PFS for trilaciclib + sacituzumab govitecan-hziy (Months)	Expected number of events in the study	Statistical Power
0.70	8.0	36	80%
0.80	7.0	38	54%

On February 14, 2023, the sponsor decided to close enrollment to this study in order to reallocate resources to other ongoing trilaciclib clinical trials. The final sample size is 30.

2. THE NUMBER OF PLANNED ANALYSES

2.1. Final Planned Analysis - Analyses for Progression Free Survival, Tumor Response Endpoints, Myelosuppression Endpoints, and Overall Survival

The final planned analysis will be conducted when approximately 70% of patients have died (i.e., 21 deaths). Study database will be locked to support the final OS analysis. The following specified analyses will be performed:

- Analysis of progression free survival.
- Analysis of tumor response endpoints (ORR, CBR, and DOR).
- Analysis of myelosuppression endpoints.
- Analysis of overall survival.
- Analysis of safety data.

The final planned analysis will be used to support the abbreviated clinical study report (aCSR).

3. ANALYSIS POPULATIONS

3.1. The Full Analysis Set

The full analysis set (FAS) includes all enrolled patients who received at least one dose of study drug. Unless otherwise specified, the FAS is the primary analysis set for all efficacy analyses.

3.2. The Response Evaluable Population

The Response Evaluable (RE) population includes all patients who are in the FAS, have measurable (target) tumor lesion(s) at baseline tumor assessment per RECIST v1.1, and have either of the following:

1. At least one post-baseline tumor assessment.
2. Discontinued treatment because of clinical progression prior to the first post-baseline tumor scan.
3. Died due to disease progression prior to the first post-baseline tumor scan.

The RE population will be the primary population for efficacy endpoints evaluating tumor responses.

3.3. The safety population

The safety population includes all enrolled patients who received at least one dose of study drug. All safety analyses will be evaluated using the safety population.

4. GENERAL CONSIDERATIONS FOR DATA SUMMARY AND DISPLAY

4.1. Treatment Group Descriptions and Display in Table, Listings and Figures

This is a single-arm study in which all patients are treated with Trilaciclib + Sacituzumab govitecan-hziy. For TLFs that will be generated following SAP execution, the term *overall* will be used to describe all patients in the populations defined in Section 3.

4.2. Data Summary and Precision

General Principles of Data Summary

Data will be summarized for the respective analysis populations described in Section 3 in table format. All summary tables will only include an overall column for patients. In general, continuous variables will be summarized descriptively, i.e., the following summary statistics will be presented:

- Number of patients with non-missing data (indicated by n)
- Mean and standard deviation
- Median
- Q1 (first quartile) and Q3 (third quartile)
- Minimum and maximum values.

Categorical variables will be summarized categorically, i.e., number (n) and percentage of patients in each category will be presented.

General Principle of Data Listings

All collected data and derived variables will be included in patient data listings. An indicator will be provided for any imputed data element (e.g., imputed adverse event [AE] onset date). Columns in listings will be ordered by study site, patient ID, visit, and assessment or event date, if applicable, and then data elements.

General Principles of Precision for Summary Statistics and Calculated Statistical Quantities

The precision of summary statistics for continuous variables, including mean, median, Q1, Q3 minimum, and maximum, will be consistent with the precision of the variable as collected unless the collected data are integers. When the collected data are integers (whole numbers), the summary statistics of mean, median, Q1 and Q3 will be presented in the format with an additional digit after the decimal point. Calculated quantities of variability (e.g., standard deviation, standard error [SE]) will be presented with one more decimal place than the precision of the variable that is collected. The boundaries of a confidence interval (CI) will keep the same precision as the point estimate. The estimated adjusted relative risk will be reported with two decimal places.
For percentages, the total digits will be 3. That is, when the percentage has 2 digits prior to the

decimal point, there will only be 1 decimal place (e.g., 30.5%); while for a percentage that has only 1 digit prior to the decimal point, 2 digits places will be presented after the decimal point (e.g., 0.16%).

Rounding will take place after all calculation steps are completed prior to result display.

4.3. Definitions for Analysis Related Timepoint and Time Interval

Timepoint and time intervals related to efficacy and safety data collected during the treatment period will be summarized. For each specific category of data, the time interval by which the data will be analyzed or summarized will be specified in the respective section in which the data analysis plan is described.

To clarify data inclusion for each time interval of interest and baseline or end values for each given time interval, Table 3 presents definitions for timepoints, timepoint related assessments, and time intervals involved in statistical data analysis or summary.

Table 3 Definitions for Timepoints, Timepoint Related Assessments and Time Intervals

Term	Definition
Start of study (date)	Date of first dose of any study drug
Study baseline (assessment)	The last non-missing value prior to or on the date of the first dose of any study drug at the time that is before the time of the first study drug administration. If the event occurs on the same day as date of first dose of study drug but does not have the exact time captured, the event is assumed to have occurred prior to the first dose of study drug.
Day 1 of Cycle X (date)	The date when the first dose of any study drug for cycle X is administered. Day 1 of Cycle 1 (C1D1) is the same as the start of study.
End of a cycle (date)	It is defined as Day 1 of the subsequent cycle if the cycle is not the last cycle. For the last cycle, it is defined as the date of the End of Treatment Visit (ETV). If the ETV does not occur for a patient, End of the last cycle will be defined as 14 days post the last dose of any study drug.
Duration of a cycle (days)	Total number of days from Day 1 of the cycle to End of the cycle. That is, End of the cycle – Day 1 of the cycle + 1.
Duration of study drug exposure (weeks)	The total number of weeks from Day 1 of Cycle 1 to the End of the last cycle in the study. That is, (End of the last cycle –Day 1 of Cycle 1 + 1) / 7.
Duration of total follow-up (months)	The total number of months from Day 1 of Cycle 1 to either the date of death or last contact date in the study known alive, inclusive. That is, duration of total follow-up=(date of death or date of last contact date known alive – Day 1 of Cycle 1 + 1) /30.4375.

4.4. Study Day

Study Day will be calculated for an event date or an assessment date relative to date of first dose of any study drug to provide additional information for interpretation of the event occurrence. Study Day is calculated as:

- The start date of the event (visit date, onset date of an event, assessment date etc.) – date of first dose of any study drug + 1, if the event occurred on or after the date of first dose of any study drug. The day of first dose of any study drug will be Study Day 1.
- The start date of the event (visit date, onset date of an event, assessment date etc.) − date of first dose of any study drug, if the event occurred prior to the date of first dose of any study drug. The day before the date of first dose of any study drug will be Study Day -1.

4.5. General Principles of Missing Data Handling

In general, the observed data are used for analyses or data summaries. That is, no missing imputation will be performed. However, imputation of missing onset or stop dates for AE and concomitant medication will be adapted to determine the status of each AE and the prior/concomitant/subsequent status of each non-study treatment medication. Please refer to Section 9.2.2 for the rules of imputation of missing AE onset or stop date and Section 5.4 for the rules of imputation of missing concomitant onset or stop dates.

For demographic and baseline characteristics, continuous variables will be summarized based on non-missing observations with the number of patients with non-missing data indicated. For a categorical variable with missing data, a category of “Missing” will be included as a separate category for the summary. That is, the number and percentage of patients in each category of the variable (including “Missing”) will be summarized and reported with the number of patients in the FAS population as the denominator for the percentage calculation.

For primary and secondary efficacy endpoints, handling of missing data is described in Section 8.3.

5. DISPOSITION AND BASELINE CHARACTERISTICS

5.1. Patient Disposition

A summary of patient disposition will be generated using all accumulated data as of the database lock date.

Patient disposition summary will include the following 4 major sections:

1. Disposition of all screened patients who signed informed consent
2. Study drug disposition for patients in the safety population
3. Study disposition for patients in the FAS
4. Deaths among patients in the FAS

The specific details for each section are described below.

1. Disposition of all screened patients

The total number of screened patients who signed informed consent will be presented as two mutually exclusive groups: those who were screen failures and those who were enrolled. For those in the FAS, patients who received at least one dose of any study drug and those who did not are further presented. Unless otherwise stated, the number of patients in the FAS will be the denominator for calculating percentages of patients in each of these categories.

2. Study drug disposition

The disposition for each study drug (trilaciclib and sacituzumab govitecan-hziy) will be summarized for those who have discontinued the study drug. For patients who have discontinued the study drug, the primary reasons for study drug discontinuation will be presented with the percentage of patients in each reason being calculated based on the number of patients who discontinued the study drug.

3. Entered Survival Follow-up

The number and percentage of patients who entered survival follow-up during the study will be summarized. The number of patients in the FAS will be the denominator for the percentage calculation.

4. Study disposition

The number and percentage of patients who discontinued from the study will be summarized. The number of patients in the FAS will be the denominator for the percentage calculation. The primary reason for study discontinuation will also be summarized, and the number of patients who discontinued the study will be the denominator for the percentage calculation for each reason of discontinuation.

5. Death

The number and percentage of patients who died during the study will be summarized overall for the FAS along with the primary reason of death (Progressive Disease, Adverse Event, Other). The number of patients in the FAS will be the denominator for calculating percentages of death,

and the number of patients who died will be the denominator for calculating the percentage of patients within each reason for death.

A summary of enrollment status of all screened patients will also be presented by site.

Study drug and study disposition information will be provided in data listings for all enrolled patients.

5.2. Demographics and Baseline Disease Characteristics

Demographics and baseline disease characteristics will be summarized for the final analysis.

Demographics including age at screening visit, age group (18-65, > 65), sex at birth, child-bearing potential, ethnicity, and race will be summarized for all enrolled patients. In addition, BMI, BSA and Eastern Cooperative Oncology Group (ECOG) score will be summarized. Further, baseline disease characteristics such as stage at screening and at diagnosis, histopathological grade and type at diagnosis, BRCA mutation, TNBC status, and PD-L1 status will be summarized for the FAS.

Data listing for demographics and baseline disease characteristics will be provided for the FAS.

5.3. Medical/Surgical History and Ongoing Conditions

Medical history, surgical history, and ongoing conditions at the Screening Visit will be summarized for the final analysis.

Non-breast cancer related medical history and ongoing medical conditions as collected at baseline will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 26.1 or later, and then summarized. Medical history and ongoing conditions will be presented by system organ class (SOC) and preferred term (PT) with SOC and PT all sorted in descending frequency based on the overall column. A patient will only be counted once within a particular SOC (PT) even if the patient has multiple conditions/diseases in the same SOC (PT).

In addition, a data listing for medical history and ongoing medical conditions collected at the Screening Visit will be provided for the FAS. Furthermore, a data listing for prior surgerical procedures and radiotherapies will be generated for the FAS.

5.4. Prior and Concomitant Medications

Concomitant, non-cancer medications will be summarized for the FAS population. Prior medications will be presented in a data listing.

Concomitant medications are those protocol-permitted medications that were given during the time interval from the first dose of any study drug to the end of the last cycle. Medications collected through electronic case report forms (eCRFs) will be coded to Anatomical Therapeutic Classification (ATC) and PT, where applicable, using the most recent World Health Organization Drug Dictionary (WHO-DD) version WHODrug-Global-B3 202309.

Concomitant medications will be summarized by ATC and PT and presented in a descending order of frequency for ATC and PT within an ATC based on the overall group. If a patient took multiple medications within the same ATC, the patient will only be counted once for that ATC.

Similar logic applies to PT summaries. The number and percentage of patients receiving any concomitant medications will be summarized overall.

Handling of Missing Start and/or End Date for Medications Entered into EDC

Medications with incomplete start and/or end dates will be imputed according to the specifications described below. Those with incomplete start and/or end dates will be assumed to be concomitant if it cannot be shown that the medication was not taken outside of the treatment period.

For completely missing or partially missing start dates:

- If the start date has month and year but day is missing, the first dose date of any study drug will be used if the month and year is the same as the first dose date of any study drug, otherwise, the first day of the month will be used.
- If the start date has year, but day and month are missing, then the first dose date of any study drug will be used if the year is the same as the first dose date of any study drug, otherwise January 1st will be used.
- If the start date is completely missing, then it will be imputed as the first dose date of any study drug.

After the imputation, the imputed start date will be compared with corresponding stop date, if available. If the imputed start date is later than the stop date, the start date will be imputed with the stop date instead.

For completely missing or partially missing stop dates for concomitant medications that are not ongoing at the time of data cutoff:

- If the stop date has month and year but day is missing, the last day of the month will be used.
- If the stop date has year, but day and month are missing, December 31st will be used.
- If the stop date is completely missing, the last dose date of any study drug will be used.

After the imputation, the imputed stop date will be compared against the death date for patients who died. If the date is later than the death date, the date of death will be used to impute the stop date instead.

Prior and concomitant medications will be listed with an indicator for prior or concomitant.

5.5. Summary of Protocol Deviations

5.5.1. Definitions and Process for Identifying Protocol Deviations

Protocol deviation refers to situations where a patient's eligibility for study entry or a specific data collection deviate from the entry criteria or study procedure as specified in the protocol. Protocol deviation cases at the patient level with specific data elements of concern need to be summarized and reported in the CSR. Protocol deviations will be categorized as major or minor. Major protocol deviations are those that could affect the integrity of the data or adversely affect

patients' safety. Criteria that define major or minor protocol deviations will be specified, documented, and signed off on prior to study database lock. Specifically, a protocol deviation specifications document that describes the criteria defining major and minor protocol deviations, the categories of major protocol deviations, and the list of patients who had at least one protocol deviation case with the classification of major or minor will be created and signed off prior to study database lock.

5.5.2. Summary of Protocol Deviations

A protocol deviation summary will be generated for the final analysis.

The number and percentage of patients in the FAS population with protocol deviations will be tabulated for each of the following categories.

- Patients with at least one protocol deviation (major or minor)
- Patients with at least one major protocol deviation
- Patients with at least one protocol deviation in each of the major deviation categories

Protocol deviations will be listed with details and flags indicating major or minor for the FAS population.

6. CLASSIFICATION OF PRIOR, CONCOMITANT, AND SUBSEQUENT ANTICANCER THERAPIES

Prior therapies refer to those anticancer treatments that patients received prior to the first dose date of any study drug, including radiotherapies, surgical procedures, and systemic anticancer therapies.

Concomitant therapies refer to those treatments, other than study drugs, that could be utilized concurrently with study drug(s) as specified in the protocol. That is, the therapies that were given in the time interval from the first dose of any study drug to the end of the last cycle

Subsequent therapies refer to anticancer treatments received following investigational study drug discontinuation while the patient was still in the study (i.e., in the Survival Follow-up period).

The rules of imputation of missing onset or stop dates for medications described in Section 5.4 are, in general, applicable for missing onset or stop dates imputation for anticancer therapies in any format (radiotherapies, surgical procedures, or systemic anticancer therapies).

6.1. Prior Anticancer Therapies

Summaries of prior anticancer therapieswill be generated for the final analysis based on the FAS population. Prior therapies in the adjuvant context will be excluded from the analysis in this section.

The number and percentage of patients with any prior anticancer therapies will be summarized for the FAS population. The number and percentage of patients with any prior radiotherapies, any prior surgical procedures that were related to breast cancer, and any prior systemic anticancer therapies will also be summarized. Prior systemic anticancer therapies will then be further summarized based on ATC and PT and presented in a descending order of frequency for ATC and PT withing an ATC based on the overall group.

Data listings will be produced for all prior anticancer therapies, including detailed information related to prior systemic anticancer therapies such as setting, regimen, start/stop dates, and detailed information related to prior surgical procedures and radiotherapies for the FAS population.

6.2. Concomitant Anticancer Therapies

Summaries for concomitant anticancer therapies will be generated for the FAS population at the final analysis.

The number and percentage of patients receiving any concomitant anticancer surgical procedures or radiotherapies that were related to disease under study will be summarized..

Detailed information for concomitant surgical procedures and radiotherapies will be included in the data listing for the FAS population.

6.3. Subsequent Systemic Anticancer Therapies

Subsequent anticancer treatments (SACT) will be summarized for the FAS population at the final analysis.

The number and percentage of patients receiving at least one SACT in any modality (systemic anticancer therapies, surgical procedure, or radiotherapy) as well as for each of the modalities will be summarized.

In addition, for the subsequent systemic anticancer therapies, the total number of lines of therapy will be summarized both descriptively and categorically. The number of patients who had at least one dose of any systemic anticancer therapies will be the denominatorfor percentage calculation..

Furthermore, the number and percentage of patients with any subsequent systemic anticancer therapies will be summarized based on ATC and PT and presented in a descending order of frequency for ATC and PT within an ATC.The best overall response to each subsequent line of therapy and disease progression status as collected will be presented in data listings.

Handling of Missing Start Date for SACT

SACTs with incomplete start dates will be imputed for the purpose of censoring ORR, CBR, DOR, and PFS, due to start of SACTs. The rules of imputations are described below.

For completely missing or partially missing start dates:

- If the start date has month and year but day is missing, the date of discontinuation of last study drug will be used if the month and year is the same as the date of discontinuation of last study drug, otherwise, the first day of the month will be used.

- If the start date has year, but day and month are missing, then the date of discontinuation of last study drug will be used if the year is the same as the date of discontinuation of last study drug, otherwise January 1st will be used.

- If the start date is completely missing, then it will be imputed as the date of discontinuation of last study drug.

Corresponding data listings will be provided for the FAS population.

7. STUDY DRUG EXPOSURE, DOSE INTENSITY AND MODIFICATION

Analyses described in this section will be based on the safety population unless otherwise specified.

7.1. Duration of Study Drug Exposure

Duration of study drug exposure (weeks) is defined as the duration from Day 1 of Cycle 1 to the End of cycle for the last cycle. That is, duration of drug exposure (weeks) = (End of cycle for the last cycle in the study – Day 1 of Cycle 1 + 1)/7, where the definitions for End of cycle for the last cycle and Day 1 of Cycle 1 are provided in Table 3.

The duration of study drug exposure will be summarized at the final analysis. The total number of cycles that a patient received will be summarized as a continuous variable, as well as a categorical variable. That is, descriptive summary statistics will be provided for the total number of cycles that patients received, and the number and percentage of patients that received exactly 0, 1, 2…, to the maximum number of cycles will also be summarized.

Corresponding data listings will be provided.

7.2. Cumulative Dose and Dose Intensity

Dose administration parameters will be summarized at the final analysis.

The definitions for cumulative delivered dose, delivered dose intensity, relative cumulative dose, and relative dose intensity at the patient level, along with other parameters involved in the calculation of these variables are presented in Table 4. All collected dose information will be used in the calculation.

The calculated cumulative delivered dose, delivered dose intensity, relative cumulative dose, and relative dose intensity will be summarized as continuous variables.

All variables described in Table 4 will be included in the data listing except for the study drug administration schedule.

Table 4 Dose Administration Parameters for Study G1T28-213

Parameter	Meaning	Trilaciclib	Sacituzumab govitecan-hziy
Study drug administration schedule	Drug dose and schedule per protocol	240 mg/m^2 IV on Day 1 and Day 8 of a 21-day cycle	10 mg/kg IV administered on Day 1 and Day 8 of each 21-day cycle.
Cumulative delivered dose [Unit]	Sum of doses over the duration of the study drug administration	Sum of doses over the duration of trilaciclib administration [mg/m^2]*	Sum of doses over the duration of sacituzumab govitecan-hziy administration [mg/kg]
Delivered Dose Intensity [Unit]	Cumulative dose administered per week	Cumulative dose (mg/m^2) / duration of study drug exposure in weeks [(mg/m^2/week)]	Cumulative dose (mg/kg) / duration of study drug exposure in weeks [(mg/kg/week)]
Relative cumulative dose (%)	Cumulative delivered dose over cumulative prescribed dose	[Cumulative delivered dose (mg/m^2) / (240 × 2 × number of cycles) (mg/m^2)]*100	[Cumulative delivered dose (mg/kg) / (10 × 2 × number of cycles) (mg/kg)]*100
Relative dose intensity (%)	Delivered dose intensity over prescribed dose intensity	[Delivered dose intensity/(480/3)]*100	[Delivered dose intensity/20/3]*100

* Actual doses administered were collected in unit of mg on the eCRF. For calculation of cumulative delivered dose and delivered dose intensity, the actual dose administered at any visit will be derived as actual dose (mg) divided by BSA (m2) from the same visit. If BSA value from a visit is missing, it will be imputed as BSA from the previous visit. If BSA value from C1D1 is missing, it will be imputed as BSA from Screening Visit. If BSA from Screening Visit and C1D1 are both missing, BSA value at C1D1 will be imputed as 1.7 m2.

IV = intravenous. BSA = body surface area. C1D1 = Cycle 1 Day 1.

7.3. Study Drug Modifications

Study drug modifications will be summarized at the final analysis.

There are three types of study drug modification: dose reduction, cycle delay, and infusion interruption. The number of protocol-permitted dose reductions for each study drug are summarized in Table 5.

Table 5 Protocol Permitted Dose Reduction by Study Drug

Study Drug	Number of Dose Reductions Allowed
Trilaciclib/placebo	0
Sacituzumab govitecan-hziy	2

Study drug modifications will be summarized in each of the following categories: chemotherapy dose reduction, treatment cycle delay, and infusion interruption. The number and percentage of patients who had any chemotherapy dose reduction, any cycle delay, cycle delay due to hematological toxicity, or any infusion interruption will be summarized.

In addition, more detailed summaries outlined below will be provided.

Dose reduction for Sacituzumab govitecan-hziy. For Sacituzumab govitecan-hziy, the number and percentage of patients who had at least one dose reduction will be summarized. In addition, the number and percentage of patients will be summarized in the following mutually exclusive categories: "Not Applicable (cycle 1 treatment only)", 0, 1, or 2 reductions for the drug. The primary reason for dose reduction will be summarized.

Cycle delay. Information regarding whether a cycle was delayed was collected in the eCRF for each cycle. The number of cycles that have been delayed will be summarized as a continuous variable. In addition, the number and percentage of patients in each of the following mutually exclusive categories will be summarized: "Not Applicable (cycle 1 treatment only)", 0, 1, 2, …, maximum number of delays.

The reasons for cycle delay collected in eCRF are as follows:

- Low neutrophil count
- Low platelet count
- Both low neutrophil count and low platelet count
- Other hematologic toxicity
- Non-hematologic toxicity
- Other

Patients with reasons entered in the "Other" category will be further classified based on medical review of comments collected on the eCRFs into finer categories as appropriate.

Infusion interruption. Infusion interruption was captured in the eCRF for each study drug with the reasons. Any infusion interruption is defined as infusion interruption of any study drug.

The number of any and trilaciclib infusion interruptions will be summarized descriptively and categorically.

Corresponding data listings will be provided for dose modifications.

7.4. Duration of Total Follow-up

Duration of total follow-up will be summarized for the final analysis.

Duration of total follow-up (months) refers to the time interval that a patient participated in this clinical study starting from date of C1D1. It will be calculated based on the definition provided below.

Duration of total follow-up (months) = (date of death or date of last contact date known as alive – date of C1D1 + 1) /30.4375.

The summary statistics for this variable will be included in the summary table for the OS analysis, and the patient level data will be included in the data listing described in Section 8.2.2.

8. EFFICACY ANALYSIS

All efficacy analyses will be performed for the FAS population, unless specified otherwise.

The primary efficacy endpoint for this study is the treatment effects on PFS. PFS and other efficacy endpoints related to tumor response (ORR, CBR, and DOR) and myeloprotection efficacy will also be evaluated based on data collected during the treatment period (see Section 2.1).

The treatment effect on OS will be evaluated when the number of events specified in Section 2.1 are observed for OS. The clinical database will be locked for this analysis. At the time of the final planned analysis, all other efficacy analyses outlined for the study will also be conducted.

8.1. Definitions of Efficacy Endpoints

8.1.1. Primary Efficacy Endpoints – Progression Free Survival

Progressive disease (PD) and tumor response status are programmatically determined according to RECIST v1.1 based on the radiographic tumor assessment data recorded on the eCRF by the Investigator for target lesions, the investigator assessment of non-target lesions, and the status of new lesions. For a patient, the status of PD will be determined using all radiographic tumor scan data assessed prior to or on the date of the data cutoff to conduct the analysis for PFS. In the situation where PD and withdrawal of consent or PD and initiation of subsequent anticancer therapy occurred on the same day for a patient, the PD status will be assumed for that patient.

Radiographic PD and death due to any cause during the study are referred to as PFS events.

PFS is defined as the time (months) from date of C1D1 to the date of the first documented disease progression, or death in the absence of PD for those who had a PFS event, and the time from date of C1D1 to the censoring date for those who did not have a PFS event. Specifically, PFS is calculated as (date of PFS event or censoring – date of C1D1+ 1)/ 30.4375. The analysis for PFS will be based on the FAS.

Details for PFS calculation and censoring rules can be found in Table 6.

Table 6 PFS Calculation and Censoring Rules

Situation	Date of Event or Censoring	Outcome
Disease progression per RECIST Version 1.1	Date of the first documented progression	PFS event
Death without a PD	Date of death	PFS event
Incomplete or no baseline tumor assessments	Date of C1D1	Censored
No progression	Date of the last adequate radiological tumor assessment with no documented disease progression	Censored
Treatment discontinuation for reasons other than disease progression	Date of the last adequate radiological tumor assessment with no documented progression	Censored
Subsequent anticancer treatment started prior to documented disease progression	Date of last adequate radiologic assessment prior to or the date of initiation of subsequent anticancer treatment	Censored

8.1.2. Secondary Efficacy Endpoint – Anti-tumor Efficacy Endpoints

The secondary anti-tumor endpoints include the following, which will be calculated and reported at the final analysis:

- Best overall response (BOR)
- Objective response rate (ORR)
- Clinical benefit rate (CBR)
- Duration of confirmed objective response (DOR)

The analysis of these endpoints will be based on the RE population. Tumor scan data collected during the study will be the basis to classify tumor response status for patients in the RE population.

At each tumor assessment visit, an overall timepoint response by RECIST v1.1 will be determined programmatically using the measurements recorded on the eCRF by the Investigator for target lesions, the Investigator assessment of non-target lesions, and records of new lesions.

If a patient has all or some of the following records prior to the final database lock, the earliest date of those will be used to determine the inclusion of tumor scan data for response status derivation: (i) radiographic disease progression; (ii) withdrawal of consent to obtain scans; (iii) death; (iv) lost to follow-up; or (v) initiation of subsequent anticancer therapy.

Best Overall Response

BOR categorizes a patient's tumor response status into one of following mutually exclusive categories per RECIST v1.1: Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), and Not Evaluable (NE). The minimum duration of stable disease must be 5 weeks starting from the date of Cycle 1 Day 1 (the protocol scheduled tumor assessments is every 6 weeks for the first 36 weeks following Cycle 1 Day 1 (±7 days) and every 9 weeks thereafter (±7 days)).

Objective Response Rate

Achieving an objective response for a patient is defined as having a CR or PR as the BOR. Objective response rate is defined as the proportion of the patients who achieved objective response on the RE population.

Confirmed Objective Response Rate

Confirmed CR or PR will be derived based on the principle described in RECIST v1.1. In the derivation, the minimum interval for confirmation of CR or PR is 4 weeks, and the minimum duration of treatment is 5 weeks (the protocol scheduled tumor assessments is every 6 weeks for the first 36 weeks following Cycle 1 Day 1 (±7 days) and every 9 weeks thereafter (±7 days)). Confirmed ORR (confirmed CR or PR) is defined as the proportion of the patients who achieved confirmed objective response.

Clinical Benefit Rate

Clinical benefit rate is defined as the proportion of patients with BOR of confirmed CR, confirmed PR, or SD lasting 24 weeks or longer, based on the RE population.

Duration of Confirmed Objective Response

DOR is calculated for patients who achieved confirmed CR or PR as the BOR status. It is defined as the time (months) from the date when the objective response of CR or PR was first documented to the date that radiographic progressive disease is documented, or death, whichever comes first. That is, DOR = (Date of documented disease progression or death – date of first documented CR or PR + 1)/30.4375.

Censored DOR follows the same rules as the censoring rules for PFS (see Table 6).

8.1.3. Secondary Efficacy Endpoint – Analysis for Overall Survival

Overall survival is defined as the time (months) from the date of C1D1 to the date of death for patients who died in the study due to any cause or the time to the last contact date known to be alive for those patients who survived as of the final database lock for the final analysis (censored cases). OS will not be censored even if a patient receives subsequent anticancer treatments.

The analysis for OS will be based on the FAS.

8.1.4. Secondary Efficacy Endpoint – Myeloprotection Efficacy Endpoints

Secondary myeloprotection endpoints that are defined to assess trilaciclib's effect on multiple lineage protection during the treatment period are described in Table 7 by lineage (i.e., neutrophils, and red blood cells [RBCs]). Endpoints that evaluate trilaciclib's impact on study drug delivery during the treatment period are also described in Table 7.

Unless otherwise specified, all endpoints described in Table 7 are derived based on data collected through scheduled and unscheduled visits during the treatment period.

Table 7 Myeloprotection Endpoints

Lineage	Endpoint	Type of Variable
Neutrophils	Occurrence of severe neutropenia (during cycles 1/2 and overall study)	Binary
	Occurrence of febrile neutropenia	Binary
	Occurrence of G-CSF administration	Binary
RBCs	Occurrence of Grade 3 or 4 decreased hemoglobin	Binary
Dose Modifications	Occurrence of SG dose reduction	Binary
	Number of SG dose reductions (event rate per 100 cycles)	Counting
	Occurrence of cycle delay due to hematologic toxicity	Binary
	Number of cycle delays due to hematologic toxicity (event rate per 100 cycles)	Counting

G-CSF=granulocyte colony stimulating factor; RBC=red blood cell, SG= sacituzumab govitecan-hziy..

8.1.4.1. Neutrophil-Related Endpoints

Occurrence of Severe Neutropenia (during Cycles 1/2 and overall study)

Occurrence of Severe Neutropenia (Grade 4 neutropenia) for a patient is defined as having as least one ANC value $< 0.5 \times 10^9$/L among all ANC measurements regardless of scheduled or unscheduled visits. Occurrence of Severe Neutropenia is a binary random variable (Yes or No).

Occurrence of Febrile Neutropenia

FN is an AE as reported by the Investigator and captured in the eCRF. A PT term of FEBRILE NEUTROPENIA is used to identify a FN event. The occurrence of FN for a patient is defined as having at least one FN event and is a binary random variable (Yes or No).

Occurrence and Number of Granulocyte Colony Stimulating Factor (G-CSF) Administrations

Administration of G-CSF is collected throughout treatment period. Cycles where G-CSF was administered will be identified by comparing the start and stop dates of each administration of G-CSF to cycle interval. If any of the time intervals in which G-CSF was administered overlapped with any dates between the start of a cycle and the end of the cycle, that cycle will be considered as having a G-CSF administration. Data handling conventions for missing start and stop dates are described in Section 5.4.

The occurrence of G-CSF administration for a patient is defined as having at least one cycle in which G-CSF was administrated for the patient. It is a binary random variable (Yes or No).

The number of cycles with G-CSF administrations for a patient is the total number cycles where the patient received at least one dose of G-CSF. For patients who did not have any G-CSF use and those who were enrolled but did not receive any study treatment, the value of 0 will be assigned.

8.1.4.2. RBC-Related Endpoints

Occurrence of Grade 3 or 4 Decreased Hemoglobin

Occurrence of Grade 3 or 4 decreased hemoglobin (Hgb) for a patient is defined as having at least one Hgb value that was < 8.0 g/dL among all scheduled or unscheduled assessments. It is a binary random variable (Yes or No).

8.1.4.3. Dose Modifications

Occurrence and Number of SG Dose Reduction

The occurrence of a dose reduction for a patient is defined as having at least one dose reduction of SG in a cycle. Occurrence of SG dose reduction is a binary random variable (Yes or No).

Number of SG dose reductions for a patient is defined as the total counts of SG dose reductions. In addition, SG that was permanently discontinued due to toxicity will be also counted as a dose reduction event. The value of 0 will be assigned to those patients who did not have any SG dose reductions. Number of SG dose reductions is a counting random variable and the summary statistics for this variable is event rate per 100 cycles.

Occurrence and Number of Cycle Delays Due to Hematologic Toxicity

Occurrence of cycle delays and the associated reason is collected in detail in the eCRF with the following mutually exclusive categories: Low neutrophil count, Low platelet count, Both low neutrophil count and low platelet count, Other hematologic toxicity, Non-hematologic toxicity, or Other. A cycle that was marked as delayed with the reason of Low neutrophil count, Low platelet count, Both low neutrophil count and low platelet count, or Other hematologic toxicity is considered a delay due to hematologic toxicity.

Occurrence of cycle delays due to hematologic toxicity for a patient is defined as having at least one cycle delay due to hematologic toxicity and is a binary random variable (Yes or No). The number of cycle delays due to hematologic toxicity for a patient is defined as the total number of cycles that were delayed due to such reason for the patient during the treatment period. For patients who did not have any cycle delays due to hematologic toxicity, the value of 0 will be assigned. Number of cycle delays due to toxicity is a counting random variable and the summary statistics for this variable is event rate per 100 cycles.

The analysis of myeloprotection endpoints will be based on the FAS population.

8.2. Statistical Analysis Methods

8.2.1. General Considerations for Efficacy Analysis

Unless otherwise specified, the analyses of the treatment effect on PFS, OS and myeloprotection endpoints will be based on the FAS population. Tumor response analyses including ORR, CBR and DOR will be based on the RE population.

8.2.2. Analysis for Progression Free Survival (PFS) and Overall Survival

For PFS, the number and percentage of patients with a PFS event (radiographic disease progression or died due to any cause) or censored will be summarized along with the reasons for censoring. Furthermore, the number and percentage of patients with disease progression or who died due to any cause will be summarized with the number of PFS events as the denominator for percentage calculation. For OS, the number and percentage of patients who died or are censored will be summarized. In addition, duration of total follow-up will also be summarized.

Kaplan-Meier plots will be generated and the median, 25% and 75% percentile of PFS and OS will be estimated using the Kaplan-Meier method with their corresponding 95% confidence interval calculated based on the method by Brookmeyer and Crowley (1982). Additionally, Kaplan-Meier estimates will be provided for the survival probability along with their 95% confidence intervals (Kalbfleisch, 1980) at selected landmarks of 12, 18, and 24 months for PFS and OS.

Data listings will be generated for PFS and OS, respectively. Tumor scan data will be included in the PFS data listing, while the duration of total follow-up will be included in the OS data listing. For each listing, detailed information supporting the calculation of PFS (or OS) along with the censoring indicator, and reasons for censoring will also be included.

8.2.3. Analysis for Secondary Endpoints - Anti-tumor Efficacy Endpoints

The analysis for BOR, CBR, and ORR (see variable definitions in Section 8.1.2) will be based on the RE population.

Tumor response status classified by BOR will be tabulated with the number and percentage of patients in each category of CR, PR, SD, PD or NE, where the percentages are calculated based on the number of patients in the RE population.

ORR along with its exact 95% two-sided CI using the Clopper-Pearson method will be computed.

Confirmed ORR and CBR will be summarized and analyzed using the same methods as are used for the ORR.

For patients who achieved CR or PR as BOR status, DOR will be analyzed. The Kaplan-Meier method will be used to estimate the median, 25% and 75% percentile of DOR, along with its 95% CI calculated using the method by Brookmeyer and Crowley (1982).

Data listings will include tumor scan data, Investigator determined timepoint responses and BOR, and programmatically derived tumor response status, and confirmed tumor response status.

8.2.4. Analysis for Secondary Endpoints - Myeloprotection Endpoints

Statistical analysis methods for myelosuppression endpoints derived based on data collected during the treatment are described in this section. No corresponding data listings will be provided.

8.2.4.1. Analysis for Binary Myelosuppression Endpoints

For each binary myelosuppression endpoint as specified in Table 7 (Section 8.1.4), the number and percentage of patients with at least one occurrence during the treatment period will be summarized.

8.2.4.2. Analysis for Counting Myelosuppression Endpoints

For the counting myelosuppression endpoints as specified in Table 7 (Section 8.1.4), the total number of the events, and raw event rate per 100 units (weeks or cycles) will be summarized.

8.3. Handling of Missing Data

In general, the observed data will be used for analyses or data summary. That is, no missing data imputation will be performed.

Missing data impact on time-to-event endpoints, including primary endpoint PFS, is in general managed by derivation rules (Section 8.1).

9. SAFETY ANALYSIS

9.1. General Consideration of Safety Analysis

Safety data summaries will be based on the safety population as defined in Section 3.3 of this SAP.

Safety data collected during treatment will be summarized at the final analysis.

Safety and tolerability will be assessed by AEs, laboratory tests, vital signs and ECG. Safety data will be summarized using descriptive statistics for all patients when appropriate. All safety data collected through scheduled and non-scheduled visits during the treatment period will be included in the safety data analyses. The treatment period for a patient is defined as the time interval from date of C1D1 to the date of End of Treatment (EOT) visit. If the EOT visit does not occur for the patient, then 14 days post the last dose in the last cycle will be used as the end date of treatment. Missing safety data will generally not be imputed, unless otherwise specified.

Baseline assessment is, in general, defined as the last non-missing observation prior to receiving the first dose of any study drug.

9.2. Adverse Events

9.2.1. Definition and Classification of Adverse Events

AEs are defined as those AEs occurring on or worsening in severity after the first dose of any study drug (i.e., the conventional treatment-emergent AEs). Only AEs as described above are collected in the study database. All AEs are reported since the first dose of any study drug until end of safety follow-up (30 days after the last dose of study drug). SAEs thought to be related to a study specific procedure are also collected between the time the patient signs the informed consent and the first dose of any study drug.

AEs will be coded from verbatim text to PT and grouped by primary SOC according to MedDRA version 26.1 or later. The severity (toxicity grades 1-5) of AEs will be graded according to the NCI CTCAE version 5.0 by the Investigator.

Hematologic Adverse Events

AEs related to hematologic toxicity will be collapsed based on the PTs from MedDRA version 26.1 or later and will be summarized separately (see Section 9.2.3). Table 8 outlines those PTs that will be collapsed.

Table 8 Hematologic Preferred Terms to be Collapsed

Term presented in the Output	Preferred Term
Neutropenia	Neutropenia
	Neutrophil count decreased
Anemia	Anemia
	Anaemia
	Red blood cell count decreased

Term presented in the Output	Preferred Term
	Hemoglobin decreased
Thrombocytopenia	Thrombocytopenia
	Platelet count decreased
Lymphocytopenia	Lymphocytopenia
	Lymphopenia
	Lymphocyte count decreased
Leukopenia	Leukopenia
	White blood cell count decreased

Trilaciclib Adverse Events of Special Interest

AEs of special interest (AESI) for trilaciclib have been identified, reflecting either the findings in the AEs from the previous studies of trilaciclib or class effects for CDK 4/6 inhibitors. AESI for trilaciclib will be identified by searching MedDRA PTs based on the Customized MedDRA Queries as detailed in Appendix 2.

Specifically, trilaciclib AESI include the following 5 categories:

- Injection site reaction/Phlebitis/Thrombophlebitis
- Acute drug hypersensitivity reaction
- Hepatotoxicity
- Interstitial lung disease /Pneumonitis
- Embolic and thrombotic events, venous

9.2.2. Imputation Rules for Missing Start or Stop Date for Adverse Events

AEs with start/stop dates that are partially or completely missing that are not ongoing at the time of data cutoff will be imputed according to the specifications below in order to classify AEs.

For completely missing or partially missing AE start date:

- If the start date has month and year but day is missing, the first dose date of any study drug will be used if the month and year is the same as the first dose date, otherwise, the first day of the month will be used.
- If the start date has year, but day and month are missing, then the first dose date of any study drug will be used if the year is the same as the first dose date, otherwise January 1st will be used.
- If the start date is completely missing, then it will be imputed as the first dose date of any study drug.

After the imputation, the imputed start date will be compared with AE stop date, if available. If the imputed start date is later than the stop date, the start date will be imputed with the stop date instead.

For completely missing or partially missing AE stop dates:

- If the stop date has month and year but day is missing, the last day of the month will be used.
- If the stop date has year, but day and month are missing, December 31st will be used.
- If the stop date is completely missing, the date of EOT visit will be used; if EOT visit does not exist, then the last dose date + 14 days will be used.

After the imputation, the imputed AE stop date will be compared against the death date for patients who died. If the date is later than the death date, the date of death will be used to impute the stop date instead.

Every attempt will be made to obtain complete information for AEs regarding severity (i.e., CTCAE Grade) and relationship to drug. However, in the rare case of missing data, the following conservative approach will be taken for summary purpose. The non-imputed raw data will be presented in AE listings.

- Missing AE grade will be classified as "Grade 3"
- Missing AE relationship will be classified as "Related"

9.2.3. Analysis for Adverse Events

AEs will be summarized by number and percentage of patients having at least one occurrence at the PT and SOC level overall. Patients with more than one occurrence of the same SOC (PT) will be counted only once within the SOC (PT) categorization. In general, the percentage of patients with an event will be calculated using the number of patients in the safety population as the denominator.

AEs will also be summarized by CTCAE grade and relationship to study drug (to any study drugs and to each individual study drug). Should a patient experience more than one occurrence of the same SOC (PT), the patient's worst occurrence (highest grade or highest related causality) will be used for the analysis and reporting.

In AE summaries, the SOC and PT within a SOC will be presented in descending order based on the incidence from all patients. If the incidence for two or more PTs is equal, these PTs will be presented in an alphabetical order.

An overall AE summary table will be generated to present general information related to AEs including the following categories: number and percentage of patients with any AE, Serious AEs, AEs with CTCAE Grade ≥ 3 or 4, AEs leading to discontinuation of any study drug, AEs leading to death, AEs related to study drug (to any study drug, to trilaciclib/placebo, and to each other study drug), and AESI for trilaciclib/placebo.

In addition, the following summary tables will be generated, and they will be, in general, presented by SOC and PT unless otherwise specified.

1. AEs by decreasing frequency of PT
2. AEs by SOC, PT, and CTCAE Grade
3. AEs with CTCAE Grade 3 or 4 by SOC and PT
4. AEs leading to discontinuation of any study drug
5. AEs leading to death
6. AEs related to any and each study drug
7. Hematological AEs by collapsed PT and CTCAE grade
8. Serious AEs
9. Serious AEs related to any and each study drug
10. AESI for trilaciclib

In the above, hematological AEs will be reported as they are with the exception of item 7 (Hematological AEs by collapsed PT and CTCAE grade), for which the collapsed terms as specified in Table 8 (Section 9.2.1) will be reported.

Corresponding AE listings will be provided to clearly indicate, at the patient level, the AE and SAE occurrence, start/stop date, relative study days to onset or stop, grade and causality for each AE. AESI for trilaciclib/placebo will also be listed with a similar level of detail.

9.3. Clinical Laboratory Data

9.3.1. Laboratory Parameters

Blood and urine samples for the determination of clinical chemistry, hematology, and urinalysis laboratory variables described in Table 9 will be measured according to Schedule of Assessments in Appendix 1.

Table 9 Laboratory Categories and Parameters

Lab Category	Lab Parameters
Chemistry	albumin, alkaline phosphatase (ALP), total bilirubin, calcium, chloride, creatinine, glucose, inorganic phosphorus, potassium, total protein, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), sodium, blood urea nitrogen (BUN)
Hematology	hemoglobin, white blood cell (WBC), platelet counts, absolute neutrophil count (ANC), absolute lymphocyte count (ALC)
Urinalysis	semiquantitative dipstick: specific gravity, pH, evaluation of glucose, protein, bilirubin, ketones, leukocytes, and hemoglobin microscopic examination, including red blood cell (RBC), white blood cell (WBC), and casts will be performed, if necessary

Lab = laboratory.

For hematology parameters, if absolute counts are not provided, those values will be derived from the differential counts by multiplying differential value with leukocyte value from the same sample. The normal ranges will be left missing in those cases.

Clinical chemistry and hematology assessments will be graded according to NCI CTCAE criteria, Version 5.0 or later. The determination of CTCAE grade for each measurement will be based on the collected laboratory values and will not involve clinical judgement. For laboratory parameters that CTCAE toxicity grade are not available, they will not be included in the analyses in which toxicity grades are reported. Instead, these parameter results will be classified and reported by the low/normal/high based on the laboratory normal reference ranges.

Abnormal Hepatic Laboratory Values

Abnormal hepatic laboratory values are defined in the following categories including any occurrence among all on-treatment, post-baseline assessments including scheduled and unscheduled values.

- Hy's Law:
  - Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 3x the upper limit of normal (ULN), alkaline phosphatase (ALP) < 2xULN, and total bilirubin ≥ 2xULN
  - Preexisting baseline ALT, AST, OR total bilirubin values above the upper limit of normal, and the patient subsequently presents with:
    - AST or ALT ≥2 times the baseline values and ≥3 × ULN, or ≥8 × ULN (whichever is smaller)
    - **concurrent** with total bilirubin ≥ 2 times the baseline value OR ≥3 × ULN (whichever is smaller)
- AST: > 3 and ≤ 5x ULN, > 5 and ≤ 8x ULN, > 8 and ≤ 10x ULN, > 10 and ≤ 20x ULN, and > 20x ULN; AST > 5x ULN for more than 5 weeks.
- ALT: >3 and ≤ 5x ULN, > 5 and ≤ 8x ULN, > 8 and ≤ 10x ULN, > 10 and ≤ 20x ULN, and > 20x ULN; ALT > 5x ULN for more than 5 weeks.
- Total bilirubin > 1.5xULN and < 2xULN, ≥ 2xULN

9.3.2. Analysis for Laboratory Parameters

Laboratory data from all central and local laboratories will be included in analyses. Different laboratories are likely using slightly different normal reference ranges, which should not affect the planned analysis since they are all categorical and reported based on CTCAE toxicity grade or relationship to the normal ranges. The default convention for reporting of laboratory units will be standard international (SI) units. If a lab value is reported using an inequality symbol e.g., less than (<) a certain value, or greater than (>) a certain value, the given numeric value will be used in the summary. Data will be presented in listings with their inequality symbol.

For each parameter in the clinical chemistry and hematology laboratory group, respectively, CTCAE toxicity grading is used to classify patients into a toxicity grade from 1 to 5 (where

applicable) for each timepoint assessment. The number and percentage of patients with highest grade during the treatment period will be summarized for each grade from 1 to 4 and Grade 3-4, along with such summary for the value collected at baseline.

For the laboratory parameters that cannot be classified by CTCAE grade, the number and percentage of patients in the categories of treatment-emergent low or treatment-emergent high based on the normal reference range associated with the parameter will be summarized.

The number and percentage of patients in each category of abnormal hepatic laboratory values will be summarized.

Laboratory parameters will be listed by the group of chemistry, hematology, and urinalysis. In the data listing, flags that indicate the corresponding CTCAE grades and the classifications relative to the laboratory reference ranges will be included. In addition, a separate listing will be prepared for patients who met Hy's law, if any.

9.4. Vital Signs

9.4.1. Vital Sign Parameters

Vital signs including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), weight, height, and body temperature will be measured according to Schedule of Assessments in Appendix 1.

Baseline vital signs refers to the most recent measurements taken prior to the first dose (pre-dose C1D1). Post-baseline assessments refer to the measurements taken after the first dose of any study drug and during treatment period. Change from baseline to the highest/lowest value across all post-baseline measurements for each vital sign parameter will be calculated. Patients with a non-missing baseline and at least one non-missing measurement post-first dose for a given parameter will be included in the calculation.

Patients are classified with respect to the criteria of potentially clinically significant (PCS) findings of vital signs, which are defined by the highest/lowest value among post-baseline assessments and/or the change from baseline to the highest/lowest observed value. Details of PCS criteria for vital signs can be found in Table 10.

Table 10 Criteria for Potentially Clinically Significant Vital Signs

Parameter	Direction	Highest/Lowest Observed Value	Change from Baseline to the Highest/Lowest Observed Value
SBP	High	≥180 mmHg	Increase ≥40 mmHg
	Low	≤ 90 mmHg	Decrease ≥40 mmHg
DBP	High	≥105 mmHg	Increase ≥ 20 mmHg
	Low	≤ 50 mmHg	Decrease ≥20 mmHg
Heart Rate	High	≥ 120 bpm	Increase ≥40 bpm
	Low	≤ 50 bpm	Decrease ≥40 bpm
Weight	High	--	Increase ≥10%
	Low	--	Decrease ≥10%

bpm=beats per minute; DBP=diastolic blood pressure; SBP=systolic blood pressure

9.4.2. Analysis for Vital Signs

Number and percentage of patients who meet any PCS criteria for each vital sign parameter as well as for each criterion will be summarized.

All observed vital sign values, change from baseline at each post-first dose assessment, and PCS flag will be listed.

9.5. 12-lead Electrocardiograms

9.5.1. Electrocardiograms Parameters

The standard 12-lead Electrocardiogram (ECG) will collect heart rate, PR interval, QRS interval, RR interval, and QT interval at the frequency according to Schedule of Assessments in Appendix 1. Investigator's clinical interpretation of 12-lead ECG results by normal or abnormal will also be collected.

Since either QTcF or QTcB could be collected by different study sites, QTcF (using Fridericia's method) will be calculated from the QT and RR (converted from collected ms to sec) intervals based on the formula:

QTcF = Uncorrected QT/ (RR Interval)^1/3, if QT and/or RR are missing, the QTcF will be left as missing.

Change from baseline to the highest/lowest value across all post-baseline measurements for QTcF will be calculated. Patients who had a non-missing baseline and at least one non-missing measurement post-first dose will be included in the calculation.

The potentially clinically significant ECG findings are defined by the highest/lowest value across all post-baseline assessments while during the treatment period for all parameters except for QTcF, for which both observed values and change scores are used to define the PCS findings (Table 11). For QTcF, a total of 5 different criteria are defined; some criteria are mutually exclusive and some cumulative (denoted by Criterion Index in Table 11).

Table 11 Criteria for Potentially Clinically Significant ECG Findings

ECG Parameter	Direction or Criterion Index	Highest/Lowest Observed Value	Change from Baseline to the Highest/Lowest Observed Value
RR Interval	High	> 1200 ms	--
	Low	< 500 ms	--
PR Interval	High	≥ 210 ms	--
QRS Interval	High	≥ 120 ms	--
	Low	≤ 50 ms	--
QT Interval	High	≥ 500 ms	--
	Low	≤ 300 ms	--
QTcF	Index 1 (mutually exclusive)	≥ 500 msec	--
		≥ 480 and < 500 msec	--
		≥ 450 and < 480 msec	--
		≤ 300 msec	--
	Index 2	≥ 480 msec	--
	Index 3	≥ 450 msec	--
	Index 4 (mutually exclusive)	--	Increase ≥ 60
		--	Increase ≥ 30 and < 60 ms
	Index 5	--	Increase ≥ 30 ms

9.5.2. Analysis for Electrocardiograms Parameters

For each ECG parameter in Table 11, the number and percentage of patients who met each potentially clinically significant criterion will be summarized.

Investigator's clinical interpretation of the 12-lead ECG results (normal or abnormal) will be tabulated to present shift from baseline to the worst case post-dose during the treatment period. Similarly, a shift table from baseline to the last post-baseline assessment during the treatment period will be generated.

All ECG parameters as collected along with corrected values of QTcF will be included in the data listing. In the listing, the flag of meeting a PCS criterion and the flag indicating investigator's determined abnormality are also included.

10. CHANGES FROM THE PROTOCOL

- Approximately 45 patients were planned to be enrolled per Protocol Version 2.0. The sponsor decided to close enrollment to this study on February 14, 2023 in order to reallocate resources to other ongoing trilaciclib clinical trials. The final total number of patients enrolled in this study is 30.
- The protocol has defined two planned analyses. The first planned analysis, analyses for progression free survival, tumor response endpoints, and myeloproctection endpoints, were to be conducted when approximately 80% of the patients have radiographically determined disease progression or have died. The final planned analysis is to be conducted when approximately 70% of patients have died. The first planned analysis was not officially conducted as planned and was combined with the the final planned analysis (see Section 2.1).
- The following secondary objectives, intended to evaluate the myeloprotective effects of Trilaciclib when administered prior to SG, were not conducted as part of the final analysis as they were not deemed critical for the aCSR:
    - Occurrence and number of RBC transfusions on/after Week 5
    - Occurrence of ESA administration
    - Occurrence of Grade 3/4 decrease of platelets
    - Occurrence and number of platelet transfusions
    - Occurrence of serious infections
    - Use of IV antibiotics
- The protocol mentions the collection of ECOG performance status information. The summary and listing of these data was deemed non-critical and will not be included for the aCSR.
- The change from baseline summaries for laboratory assessment will not be included for the aCSR.

11. REFERENCES

Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2021;384(16):1529-41.

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics. 1982;29-41.

Kalbfleisch JD, Prentice RL. The Statistical Analysis of Failure Time Data. New York: John Wiley & Sons. 1980.

Wu, Jianrong. Sample size calculation for the one-sample log-rank test. Pharmaceutical Statistics. 2015;Volume 14:26-33.

12. APPENDICES

APPENDIX 1. SCHEDULE OF ASSESSMENTS

Table 12 Schedule of Assessments

Assessment	Screening	Treatment Phase (1 cycle = 21 days)				Follow-Up Phase	See Protocol Section for Additional Details
		Every Cycle		End of Treatment Visit	Safety Follow-up	Survival Follow-Up	
	30 days prior to enrollment	Day 1	Day 8	14 days after last dose of study treatment (±7d)	30 days after last dose (+7d)	Every 3 months post-Safety Follow-up	
Informed Consent	X						Section 13.3
Enrollment		X [Cycle 1 (-7d)]					Section 11.1.2
Inclusion/Exclusion Criteria	X						Section 7
Demographics	X						Section 11.1.3
Medical History and Surgical History	X						Section 11.1.4
Concomitant Medications	X	X					Section 11.1.4
Complete Physical Examination (include weight and height)	X						Section 11.3.2
Symptom-directed Physical Examination (with weight only)		X					Section 11.3.2
Vital Signs	X	X		X			Section 11.3.1
ECOG Performance Status	X	X		X			Section 11.3.3
Adverse Event Reporting		X			X		Section 11.3.6
Laboratory Assessments and Procedures							
Hematology	X	X	X	X			Section 11.3.5

Assessment	Screening	Treatment Phase (1 cycle = 21 days)				Follow-Up Phase	See Protocol Section for Additional Details
		Every Cycle		End of Treatment Visit	Safety Follow-up	Survival Follow-Up	
	30 days prior to enrollment	Day 1	Day 8	14 days after last dose of study treatment (±7d)	30 days after last dose (+7d)	Every 3 months post-Safety Follow-up	
Chemistry	X	X [a]		X			Section 11.3.5
Pregnancy Test (WOCBP only)	X	X		X			Section 11.3.5
12-lead Electrocardiogram (in triplicate)	X	X [Cycle 1]	X [Cycle 1]				Section 11.3.4
Study Treatment							
Trilaciclib		X	X				Section 9.1
Sacituzumab govitecan-hziy		X	X				Section 9.1
Disease Assessment							
Tumor Assessments (CT/MRI)	X	X [b]					Section 11.2.1
Survival Follow Up and Subsequent Anti-Cancer Treatments						X	Section 11.7

CR=complete response; CT=computed tomography; d=day; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; FDG=[^{18}F]-fluorodeoxyglucose; MRI=magnetic resonance imaging; NaF=sodium fluoride; PET=positron emission tomography; MRI=magnetic resonance imaging; Q6=every six; Q9=every 9; WOCBP=women of childbearing potential

[a] Chemistry samples will be collected every cycle during Cycles 1-4 and every other cycle (Cycle 6, Cycle 8, etc.) if results are stable, per Investigator discretion.

[b] CT/MRI of chest/abdomen/pelvis Q6 weeks (± 7d) through Week 36 relative to Cycle 1 Day 1 and Q9 weeks (± 7d) thereafter relative to Cycle 1 Day 1 until documented disease progression or subsequent anticancer therapy. Brain scan (MRI preferred) during screening is not required and should be performed per Investigator discretion based on clinical signs and symptoms. Additional brain MRI should be conducted if there are new clinical signs and symptoms suggestive of brain metastases. Bone metastases identified at baseline via a bone scan or PET (such as FDG-PET, NaF-PET, or other locally available PET options) to be followed at scheduled visits using localized CT or MRI as clinically indicated. If bone metastases cannot be seen on CT or MRI scans, bone scans or PET should be repeated, using the same diagnostic procedure bone metastases were at baseline, when CR is identified in target disease or when progression in bone is suspected.

APPENDIX 2. CUSTOMIZED MedDRA QUERIES FOR TRILACICLIB AESIs

AESI Categories	Preferred Terms	
Injection Site Reaction/ Phlebitis/ Thrombophlebitis	Administration site phlebitis Application site phlebitis Catheter site phlebitis Chemical phlebitis Infusion site phlebitis Infusion site thrombosis Injection site phlebitis Injection site thrombosis	Periphlebitis Phlebitis Phlebitis deep Phlebitis infective Septic phlebitis Thrombophlebitis Thrombophlebitis septic Thrombophlebitis superficial Vascular access site thrombosis
	Administration related reaction Administration site dermatitis Administration site hypersensitivity Administration site pain Administration site rash Administration site recall reaction Administration site urticaria Administration site vasculitis Application site dermatitis Application site hypersensitivity Application site pain Application site rash Application site recall reaction Application site urticaria Application site vasculitis Catheter site dermatitis Catheter site hypersensitivity Catheter site pain Catheter site rash Catheter site urticaria Catheter site vasculitis Immediate post-injection reaction Infusion-related reaction Infusion site dermatitis	Infusion site erythema Infusion site hypersensitivity Infusion site pain Infusion site rash Infusion site reaction Infusion site recall reaction Infusion site urticaria Infusion site vasculitis Injection related reaction Injection site dermatitis Injection site erythema Injection site hypersensitivity Injection site pain Injection site rash Injection site reaction Injection site recall reaction Injection site urticaria Injection site vasculitis Installation site urticaria instillation site hypersensitivity instillation site pain instillation site rash Skin reaction Vessel puncture site rash Vessel puncture site vesicles

AESI Categories	Preferred Terms	
Acute drug hypersensitivity reaction	Allergic bronchitis	Laryngitis allergic
	Allergic cough	Laryngospasm
	Allergic eosinophilia	Laryngotracheal oedema
	Allergic oedema	Lip edema
	Allergic pharyngitis	Lip swelling mast cell degranulation present
	Allergic reaction to excipient	Mouth swelling
	Allergic respiratory disease	oedema mouth
	Allergic respiratory symptom	Oropharyngeal oedema
	Anaphylactic reaction	Oropharyngeal spasm
	Anaphylactic shock	Oropharyngeal swelling
	Anaphylactic transfusion reaction	Palatal oedema
	Anaphylactoid reaction	Palatal swelling
	Anaphylactoid shock	Periorbital oedema
	Anaphylaxis treatment	Periorbital swelling
	angioedema	Pharyngeal oedema
	Bronchospasm	Pharyngeal swelling
	Circulatory collapse	Pruritus allergic
	Circumoral oedema	Reaction to excipient
	Circumoral swelling	Shock
	Distributive shock	Shock symptom
	Documented hypersensitivity to administered product	Swelling face
	Drug hypersensitivity	Swelling of eyelid
	Drug reaction with eosinophilia and systemic symptoms	Swollen tongue
	Epiglottic oedema	Therapeutic product cross-reactivity
	Eye oedema	Tongue oedema
	Eye swelling	Tracheal oedema
	Eyelid oedema	Type I hypersensitivity
	Face oedema	Urticaria
	Hypersensitivity	Urticaria contact
	Immune-mediated adverse reaction	Urticaria popular
	Infusion related hypersensitivity reaction	Urticarial dermatitis
	Laryngeal oedema	Urticarial vasculitis

AESI Categories	Preferred Terms	
Hepatotoxicity	Acute hepatic failure	Hepatitis acute
	Acute on chronic liver failure	Hepatitis cholestatic
	Acute yellow liver atrophy	Hepatitis chronic active
	Allergic hepatitis	Hepatitis chronic persistent
	Autoimmune hepatitis	Hepatitis fulminant
	Cholestatic liver injury	Hepatitis toxic
	Chronic hepatic failure	Hepatocellular foamy cell syndrome
	Chronic hepatitis	Hepatocellular injury
	Coma hepatic	Hepatotoxicity
	Drug-Induced Liver Injury	Immune-mediated hepatitis
	Hepatic failure	Liver disorder
	Hepatic infiltration eosinophilia	Liver injury
	Hepatic necrosis	Mixed liver injury
	Hepatic steato-fibrosis	Non-alcoholic steatohepatitis
	Hepatic steatosis	Steatohepatitis
	Hepatitis	Subacute hepatic failure
Interstitial Lung Disease (ILD) /Pneumonitis	Acute interstitial pneumonitis	Idiopathic interstitial pneumonia
	Acute lung injury	Idiopathic pneumonia syndrome
	Acute respiratory distress syndrome	Idiopathic pulmonary fibrosis
	Alveolar lung disease	Immune-mediated pneumonitis
	Alveolitis	Interstitial lung disease
	Alveolitis necrotizing	Necrotizing bronchiolitis
	Autoimmune lung disease	Obliterative bronchiolitis
	Diffuse alveolar damage	Pneumonitis
	Eosinophilic pneumonia	Pneumonitis chemical
	Eosinophilic pneumonia acute	Progressive massive fibrosis
	Eosinophilic pneumonia chronic	Pulmonary fibrosis
	Granulomatous pneumonitis	
	Hypersensitivity pneumonitis	Pulmonary toxicity
		Restrictive pulmonary disease

AESI Categories	Preferred Terms	
Embolic and thrombotic events, venous	Axillary vein thrombosis	Pulmonary thrombosis
	Brachiocephalic vein occlusion	Pulmonary vein occlusion
	Brachiocephalic vein thrombosis	Pulmonary veno-occlusive disease
	Deep vein thrombosis	Pulmonary venous thrombosis
	Embolism venous	Subclavian vein occlusion
	Iliac vein occlusion	Subclavian vein thrombosis
	Obstructive shock	Superior vena cava occlusion
	Pelvic venous thrombosis	Thrombosis
	Peripheral vein occlusion	Vena cava embolism
	Peripheral vein thrombus extension	Vena cava thrombosis
	Phlebectomy	Venous occlusion
	Pulmonary embolism	Venous thrombosis
	Pulmonary microemboli	Venous thrombosis limb