STATISTICAL ANALYSIS PLAN

Open-label Rollover Study to Evaluate Long-term Safety in Subjects with Metastatic Solid Tumors that are Benefiting from Continuation of Therapy with Sacituzumab Govitecan

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APPROVAL SIGNATURE PAGE

IMMU-132-14 Statistical Analysis Plan

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REVISION HISTORY

Version Number	Version Date	Summary and Rational of Revision(s)
1.0	20May2020	Initial version

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
ADaM	Analysis Data Model
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BUN	Blood Urea Nitrogen
CI	Confidence interval
CRF	Case report form
CTCAE	Common Terminology Criteria for Adverse Events
FDA	Food and Drug Administration
IND	Investigational New Drug Application
LDH	Lactate Dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
PD	Disease Progression /Progressive Disease
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical analysis plan
SG	Sacituzumab govitecan
TEAE	Treatment-emergent adverse event
WHO	World Health Organization

1. INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to describe the procedures and the statistical methods that will be used to analyze, and report results for study IMMU-132-14: "Open-label Rollover Study to Evaluate Long-term Safety in Subjects with Metastatic Solid Tumors that are Benefiting from Continuation of Therapy with Sacituzumab Govitecan". This SAP incorporates the original version of the protocol, dated as 16Dec2019. The focus of this SAP is for the final analysis specified in the study protocol.

This SAP provides a comprehensive and detailed description of the objectives, definitions of endpoints, statistical and analytical methods used to evaluate the specified safety endpoints. There is no efficacy analysis for this study.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Primary Objectives and Endpoints

The primary objective is to evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan.

The corresponding endpoints are:

- Safety evaluated on adverse events and serious adverse events, laboratory assessments, study drug exposure and concomitant medications

3. STUDY OVERVIEW

3.1. Study Design

This is an open-label, longitudinal cohort, rollover study designed to evaluate long-term safety in subjects with metastatic solid tumors that are benefiting from continuation of therapy with sacituzumab govitecan. Only subjects who continue to receive clinical benefit from continuation of sacituzumab govitecan therapy and are tolerating therapy at the time of enrollment are eligible for this study. Subjects enrolled may continue to receive sacituzumab govitecan at the dose that they were receiving in the Immunomedics-sponsored parent study at the time of consenting to participate in this rollover study. No dose escalation beyond the dose the subject was receiving in the Immunomedics-sponsored parent study at the time of consenting to participate in this rollover study is permitted. No subject will receive more than 10 mg/kg dose of sacituzumab govitecan. Subjects may continue to receive sacituzumab govitecan until they experience toxicity, disease progression or withdrawal of consent, lost to follow-up, loss of clinical benefit, or sponsor termination of the study is documented. Subjects who continued to receive sacituzumab govitecan in the parent study after disease progression (PD), may continue to receive sacituzumab govitecan until there is no clinical benefit per treating physician's assessment.

3.2. Determination of Sample Size

The sample size of up to approximately 200 subjects assumes that 10-15% of subjects in any of the ongoing sacituzumab govitecan parent studies will rollover to this study upon closure of the parent study.

4. ANALYSIS POPULATION

The following analysis population will be used for analyses:

- All Treated Subjects: defined as all subjects who have received at least one dose of study drug. This analysis population will be used as the basis for essentially all safety analyses.

5. STATISTICAL METHODS AND ANALYSIS

5.1. General Statistical Considerations

Endpoints and analyses pertaining to the study's primary objectives will be conducted as prescribed in respective sections of this SAP. Any notable analyses, adjustments to analyses, or analyses not conducted due to lack of data or due to other technical constraints will be noted.

All safety analyses will be analyzed in the All Treated Subjects population and presented by a single arm. When deemed appropriate, it may also be presented by dose level, cancer types and histology. Same for subgroup analysis, it may also be conducted.

Continuous data will be summarized using descriptive statistics: n (number of subjects), mean, median, standard deviation, upper and lower quartiles, and range (minimum and maximum), unless otherwise specified. Categorical data will be summarized using counts and percentages. For summary statistics, the tables will be presented by a single arm sacituzumab govitecan. In general, individual subject listings will be provided to support the tables.

All calculations and analyses will be conducted using SAS version 9.2 or higher.

5.2. Previous Immunomedics (Parent) Study Information

A by-subject listing will be provided for all subjects enrolled into the study, including previous study protocol number, previous subject number, previous site number, last cycle received while on parent study, last dose of sacituzumab govitecan in parent study and date of last dose of sacituzumab govitecan in parent study. If available, the date of first dose of sacituzumab govitecan in parent study, number of dose reduction and each dose reduction date and reason in parent study will also be listed.

5.3. Subject Disposition

Disposition in terms of number of subjects enrolled into the study, treated, permanently discontinued from treatment and discontinued from study, and reasons for treatment or study discontinuation will be summarized for All Treated Subjects.

A by-subject listing for disposition will be provided for all subjects, including their Informed Consent dates, Protocol Number the subject is consented under, study discontinuation date, and whether they meet inclusion/exclusion eligibility.

For All Treated Subjects, a listing is provided to include the following: treatment status, treatment start/end date, reason for treatment discontinuation, study completion status, study end date and reason for study discontinuation.

5.4. Demographics

Demographics for All Treated Subjects will be summarized using descriptive statistics.

Individual subject listings will be provided to support the summary tables.

5.4.1. Demographics

Baseline demographic data summaries will include age, age by categories (<50, 50-65 and >65 years; <=65 vs >65 years), sex, race, ethnicity.

5.5. Prior, Concomitant Medications and Non-protocol Specific Procedures/Surgeries

5.5.1. Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary. Prior medications include medications with a start and end date prior to first administration of study drug. Concomitant medications are those medications that were taken at any time while on study treatment, including medications that were started before first dose of study therapy but were ongoing at the time of first dose of study drug or that were initiated after first dose but prior to last dose. If an end date is missing or the medication is ongoing during sacituzumab govitecan treatment, the medication will be included as concomitant medications. Prior and concomitant medications will be summarized separately for All Treated Subjects by following the WHO Drug Anatomical Therapeutic Chemical (ATC) Classification and listed for All Treated Subjects.

A by-subject listing will be provided for All Treated Subjects.

5.5.2. Non-protocol Specific Procedures/Surgeries

A by-subject listing will be provided for All Treated Subjects, including but not limited to procedure/surgery name, date of procedure/surgery and indication.

6. SAFETY ANALYSIS

Safety analyses will be conducted in All Treated Subject.

Safety data will be presented in terms of study drug exposure, AEs, clinical laboratory data.

6.1. Exposure to Study Drug and Compliance

Treatment exposure will be summarized for All Treated Subjects using the following measures:

- Number of doses administered
- Descriptive statistics of duration of treatment (months), along with number of subjects with treatment duration longer than or equal to 3 months, 6 months, 12 months and 24 months; Duration of treatment (in days) will be calculated as (date of the last dose - date of the first dose + 1) and converted to months by dividing by 30.4375
- Number and percentage of subjects with dose reduction according to percentage of dose reduction and reasons for dose reduction
- Descriptive statistics of time to first dose reduction.
- Number and percentage of subjects with dose delays
- Number and percentage of subjects with infusion interruptions
- Descriptive statistics of duration of interruptions
- Relative dose intensity will be calculated as described below and summarized. Cumulative dosage and relative dose intensity will be summarized by descriptive statistics, and relative dose intensity will be additionally summarized by the category of <50%, 50% to < 70%, 70% to <90%, 90% to <110%, >=110%.

Delivered dose (mg) for each infusion is calculated per CRF form from ("Total dose to be administrated" x "Actual volume administered"/"Total volume prepared ").

Delivered dosage (mg/kg) of each infusion in a cycle is calculated by dividing the delivered dose (in mg) by body weight (in kg) at the beginning of the cycle (the body weight according to which the prescribed dose is calculated and prepared per the Protocol).

Cumulative dosage (mg/kg) received for each subject is defined as the sum of all delivered doses (mg/kg) of all infusions the subject received in the study.

Total assigned dosage (mg/kg) for each subject is defined as the product of the assigned dose of sacituzumab govitecan ("planned dose" per CRF form) and number of doses the subject was scheduled to receive during the subject's treatment period (number of infusions actually received by the subject plus the number of infusions the subject missed between the first and last infusion).

Relative dose intensity (in %) for each subject is calculated: dividing the subject's cumulative dosage received (in mg/kg) by the total assigned dosage (in mg/kg) as defined above.

6.2. Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as any AEs that begin or worsen on or after the start of study drug through 30 days after the last dose of study drug. All AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA). The severity will be graded based on the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Only TEAEs will be summarized and will be referred to as AEs hereafter.

The frequency and severity of AEs, classified by MedDRA, will be summarized using MedDRA Preferred Term (PT) and System Organ Class (SOC). An AE that occurs more than once within each subject will be counted only once in the summaries, i.e., where a subject has the same adverse event, based on preferred terminology, reported multiple times, the subject will only be counted once at the preferred terminology level in adverse event summary tables. Where a subject has multiple adverse events within the same system organ class, the subject will be counted only once at the system organ class level in adverse event summary tables. When reporting adverse events by NCI-CTCAE grade, summary tables will be provided using the worst NCI-CTCAE grade.

The following AE summary tables will be provided:

- Overall Summary of Treatment-Emergent Adverse Events
- Summary of Treatment-Emergent Adverse Events by SOC and PT
- Summary of Treatment-Emergent Adverse Events Reported >=10% by Preferred Term
- Summary of Treatment-related Treatment-Emergent Adverse Events by SOC and PT
- Summary of Treatment-Emergent Serious Adverse Events by SOC and PT
- Summary of Treatment-Emergent Serious Adverse Events Reported >=2% by Preferred Term
- Summary of Treatment-related Treatment-Emergent Serious Adverse Events by SOC and PT
- Summary of Treatment-Emergent Adverse Events by Worst NCI-CTCAE Grade, SOC and PT
- Summary of Treatment-related Treatment-Emergent Adverse Events by Worst NCI-CTCAE Grade, SOC and PT
- Summary of NCI-CTCAE Grade 3 or Higher Treatment-Emergent Adverse Events by SOC and PT
- Summary of NCI-CTCAE Grade 3 or Higher Treatment-Emergent Adverse Events Reported >=5% by Preferred Term
- Summary of Treatment-related Treatment-Emergent Adverse Events with NCI-CTCAE Grade 3 or Higher by SOC and PT

- Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction by SOC and PT
- Summary of Treatment-related Treatment-Emergent Adverse Events Leading to Dose Reduction by SOC and PT
- Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by SOC and PT
- Summary of Treatment-related Treatment-Emergent Adverse Events Leading to Dose Interruption by SOC and PT
- Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by SOC and PT
- Summary of Treatment-related Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by SOC and PT
- Summary of Treatment-Emergent Adverse Events Leading to Death by SOC and PT
- Summary of Treatment-related Treatment-Emergent Adverse Events Leading to Death by SOC and PT

The following AE listings will be provided:

- Listing of All Adverse Events
- Listing of All Treatment-Emergent Adverse Events
- Listing of All Treatment-related Treatment-Emergent Adverse Events
- Listing of Serious Treatment-Emergent Adverse Events
- Listing of Serous Treatment-related Treatment-Emergent Adverse Events
- Listing of Treatment-Emergent Adverse Events with NCI-CTCAE Grade 3 or Higher
- Listing of Treatment-related Treatment-Emergent Adverse Events with NCI-CTCAE Grade 3 or Higher
- Listing of Treatment-Emergent Adverse Events Leading to Dose Reduction
- Listing of Treatment-related Treatment-Emergent Adverse Events Leading to Dose Reduction
- Listing of Treatment-Emergent Adverse Events Leading to Dose Interruption
- Listing of Treatment-related Treatment-Emergent Adverse Events Leading to Dose Interruption
- Listing of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation
- Listing of Treatment-related Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation
- Listing of Treatment-Emergent Adverse Events Leading to Death

- Listing of Treatment-related Treatment-Emergent Adverse Events Leading to Death

6.3. Adverse Events of Special Interest (AEOSI)

In addition to analyses of AEs, adverse events of special interest (AEOSI) will be assessed. Definitions of AEOSI, as currently defined, are provided in Table 1, including but not limited to the listed. For AEOSI, frequency tables will be generated, showing overall summary of AEOSI, Summary of AEOSI by SOC and PT, Serious AEOSI by SOC and PT, AEOSI leading to study drug discontinuation by SOC and PT, AEOSI leading to dose modification by SOC and PT, Grade 3 or higher AEOSI by SOC and PT, treatment-related AEOSI (by a worst CTCAE grade of 3, 4, or 5, >=3 and any grade) by SOC and PT. Corresponding listings will also be produced. Please see the lists at the end of this section for details.

Table 1: Definitions of Adverse Events of Special Interest

Adverse Event of Special Interest	Definition
Diarrhea	Preferred term: diarrhea
Neutropenia+	Preferred terms: neutropenia, neutrophil count decreased, febrile neutropenia
Febrile neutropenia	Preferred term: febrile neutropenia
Infections	SOC: infections and infestations
Neuropathy+	Preferred term: gait disturbance, hypoesthesia, muscular weakness, neuropathy peripheral, paresthesia, and peripheral sensory neuropathy
Hypersensitivity+*	Hypersensitivity SMQ (broad) and Anaphylactic Reactions SMQ (broad)*
Pulmonary events+	Interstitial lung disease SMQ (narrow)

All definitions based on MedDRA vs 20.0 or higher, SMQ=Standard MedDRA Query
+ Grouped AE terms
* For the category of Hypersensitivity+, only events whose onset dates are on the day of or 1 day after an infusion are included.

The following AEOSI tables will be provided:

- Overall Summary of Adverse Events of Special Interest
- Summary of Adverse Events of Special Interest by SOC and PT
- Summary of Serious Adverse Events of Special Interest by SOC and PT
- Summary of Adverse Events of Special Interest with NCI-CTCAE Grade 3 or Higher by SOC and PT
- Summary of Treatment-related Adverse Events of Special Interest with NCI-CTCAE Grade 3 or Higher by SOC and PT
- Summary of Adverse Events of Special Interest Leading to Dose Reduction by SOC and PT

- Summary of Treatment-related Adverse Events of Special Interest Leading to Dose Reduction by SOC and PT
- Summary of Adverse Events of Special Interest Leading to Dose Interruption by SOC and PT
- Summary of Treatment-related Adverse Events of Special Interest Leading to Dose Interruption by SOC and PT
- Summary of Adverse Events of Special Interest Leading to Study Drug Discontinuation by SOC and PT
- Summary of Treatment-related Adverse Events of Special Interest Leading to Study Drug Discontinuation by SOC and PT
- Summary of Adverse Events of Special Interest Leading to Death by SOC and PT
- Summary of Treatment-related Adverse Events of Special Interest Leading to Death by SOC and PT

The following AEOSI listings will be provided:

- Listing of Adverse Events of Special Interest
- Listing of Adverse Events of Special Interest with NCI-CTCAE Grade 3 or Higher by SOC and PT
- Listing of Treatment-related Adverse Events of Special Interest with NCI-CTCAE Grade 3 or Higher by SOC and PT
- Listing of Adverse Events of Special Interest Leading to Dose Reduction by SOC and PT
- Listing of Treatment-related Adverse Events of Special Interest Leading to Dose Reduction by SOC and PT
- Listing of Adverse Events of Special Interest Leading to Dose Interruption by SOC and PT
- Listing of Treatment-related Adverse Events of Special Interest Leading to Dose Interruption by SOC and PT
- Listing of Adverse Events of Special Interest Leading to Study Drug Discontinuation by SOC and PT
- Listing of Treatment-related Adverse Events of Special Interest Leading to Study Drug Discontinuation by SOC and PT
- Listing of Adverse Events of Special Interest Leading to Death by SOC and PT
- Listing of Treatment-related Adverse Events of Special Interest Leading to Death by SOC and PT

6.4. Death

All-cause deaths will be summarized (including presentation of causes of death), and deaths within 30 days of the last dose of study drug will be summarized. A listing of all death information will be generated.

6.5. Clinical Laboratory

Routine safety laboratories, based on hematology (including but not limited to hemoglobin, platelets, leukocytes, lymphocyte, neutrophils, monocytes, basophils and eosinophils) and routine serum chemistry data (including but not limited to glucose, creatinine, BUN, total bilirubin, AST, ALT, LDH, alkaline phosphatase, serum albumin, total protein, potassium, calcium, chloride, magnesium and phosphate), will be summarized using values at each visit and change from baseline using descriptive statistics. Laboratory test results for lab parameter including but not limited to platelets, neutrophils, white blood count, lymphocytes and hemoglobin will be graded according to NCI-CTCAE v5.0 severity grade. A shift table from baseline to the worst NCI-CTCAE grade observed on-treatment will be tabulated for each lab parameter. For parameters whose CTCAE scales do not exist, the proportion of subjects with abnormal values will be summarized.

Clinical laboratory data results will be reported in standard international units. Baseline is defined as the last observation occurring prior to the first treatment administration of sacituzumab govitecan.

If a lab value is reported using a non-numeric qualifier (e.g., less than [<] a certain value, or greater than [>] a certain value), the given numeric value will be used in the summary statistics, ignoring the non-numeric qualifier. Any other manipulation related to lab data and not documented here will be specified in the ADaM specification.

All lab values will be summarized by the single arm sacituzumab govitecan. If applicable, it may also be presented by dose level, cancer types and histology. Subgroup analysis may also be conducted for the lab parameters. The lab listings will be generated to support the lab tables.

7. METHODS FOR HANDLING MISSING DATA

The imputation for missing data in adverse events, concomitant medications and other prior therapies/procedures will be provided in a separate file.

8. CHANGES TO ANALYSIS SPECIFIED IN PROTOCOL

Not applicable at this point.

9. REFERENCES

[1] Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, published November 27, 2017

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