Adaptimmune LLC

STATISTICAL ANALYSIS PLAN

Protocol Title:	A PHASE 2 OPEN-LABEL CLINICAL TRIAL OF ADP-A2M4CD8 IN SUBJECTS WITH ADVANCED ESOPHAGEAL OR ESOPHAGOGASTRIC JUNCTION CANCERS (SURPASS-2 STUDY)
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SIGNATURE PAGE

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We, the undersigned, have reviewed and approved this Statistical Analysis Plan:

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List of Abbreviations and Definition of Terms

Abbreviation	Description
aCSR	Abbreviated Clinical Study Report
ADaM	Analysis Data Model
AE	Adverse Event
BMI	Body Mass Index
BOR	Best Overall Response
CI	Confidence Interval
CR	Complete Response
CRS	Cytokine Release Syndrome
CTCAE	Common Toxicity Criteria for Adverse Events
DoR	Duration of Response
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EQ-5D-3L	EuroQOL Group EQ-5D 3 Level Version
GEJ	Gastroesophageal Junction
HLA	Human Leukocyte Antigen
ICANS	Immune Effector Cell-Associated Neurotoxicity Syndrome
ICE	Immune Effector Cell-Associated Encephalopathy
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IO	Insertional oncogenesis
IRAC	Independent Radiological Assessment Committee
ITT	Intent-To-Treat
IVD	In-vitro Diagnostic
LIMS	Laboratory Information Management System
LTFU	Long-Term Follow-Up
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
MUGA	Multiple-grated Acquisition Scan
NE	Not Evaluable
OR	Objective Response
ORR	Overall Response Rate
OS	Overall Survival
PD	Progressive Disease
PFS	Progression-Free Survival
PP	Per-Protocol
PR	Partial Response
PT	Preferred Term
RCL	Replication Competent Lentivirus
RECIST	Response Evaluation Criteria in Solid Tumors

Abbreviation	Description
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Stable Disease
SOC	System Organ Class
TEAE	Treatment-emergent Adverse Event
TTR	Time to Response
WBC	White blood cell
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

1 Introduction

The purpose of this statistical analysis plan (SAP) is to document technical and detailed specifications for the analyses of data collected for study protocol ADP-0055-002. This SAP only contains analyses of limited baseline, efficacy and safety data as the study stopped early with a total of three subjects enrolled. Results of the analyses in this SAP will be included in the abbreviated Clinical Study Report (aCSR). In addition, the planned analyses identified in this SAP will be included in regulatory submissions or future manuscripts. This SAP is to be finalized prior to the database lock. After which, any post-hoc, deviations from the SAP or unplanned analyses performed to provide results for inclusion in the aCSR will be clearly identified in the aCSR.

This SAP is based upon Section 9 (Statistical Considerations) of the trial protocol and is prepared in compliance with International Council for Harmonisation (ICH) E9.

2 Study Objectives

The following objectives are stated in the protocol:

2.1 Primary Objective

To evaluate the efficacy of autologous genetically modified specific peptide enhanced affinity receptor (SPEAR) T-cells (ADP-A2M4CD8) in HLA-A*02 positive subjects with MAGE-A4 expressing advanced esophageal or esophagogastric junction (GEJ) cancers.

2.2 Secondary Objectives

- To evaluate the safety and tolerability of autologous genetically modified T-cells (ADP-A2M4CD8) in HLA-A*02 positive subjects with MAGE-A4 expressing advanced esophageal or GEJ cancers.
- To evaluate the efficacy of autologous genetically modified T-cells (ADP-A2M4CD8) in HLA-A*02 positive subjects with MAGE-A4 expressing advanced esophageal or GEJ cancers.
- Development and validation of an in vitro diagnostic (IVD) assay for the screening of tumor antigen expression for regulatory approval.
- Characterize the surrogates of treatment effect.

2.3 Exploratory Objectives

- To evaluate changes in health-related outcomes following treatment with ADP-A2M4CD8.
- To characterize the tumor and tumor microenvironment pre- and post-T- cell infusion to understand tumor-driven determinants of response and resistance to ADP-A2M4CD8 therapy.
- To characterize subject peripheral blood, which includes, but is not limited to, transduced T-cells (ADP-A2M4CD8), non-transduced T-cells, as well as serum and/or plasma pre- and

post-T-cell infusion to understand factors that can influence response or resistance to ADP-A2M4CD8 therapy.

3 Study Overview

3.1 Study Design

This is a phase 2, open-label study of genetically engineered ADP-A2M4C8 in HLA-A*02 subjects with MAGE-A4 expressing metastatic or inoperable (advanced) esophageal or GEJ cancer.
All subjects will be enrolled into one treatment cohort based upon their tumor type and histology. Subjects with advanced esophageal or GEJ cancers will be enrolled in this study. Based on the tumor histology, this cohort of subjects will have either adenocarcinoma or squamous cell carcinoma type of disease. Approximately 45 subjects were planned to be enrolled according to a Chen's three-stage design, however only 3 subjects were enrolled into the study. This study is now closed for further recruitment. Please refer to Section 4 of study protocol for further details.

3.2 Treatments

3.2.1 Premedication

Please refer to Section 6 of the study protocol for details on leukapheresis and lymphodepleting chemotherapy.

3.2.2 T-cell Infusion

Please refer to Section 6.3.2 of the study protocol for details.

3.3 Determination of Sample Size

In the protocol, it is stated that approximately 45 subjects will be enrolled using Chen's three-stage design, however only 3 subjects were enrolled, and were also dosed in the study. This study is now closed for further recruitment.

Please refer to section 9.2 of the protocol for details of sample size determination.

4 Study Endpoints and Covariates

4.1 Study Endpoints

Below endpoints are stated in the protocol but not all endpoints will be analyzed and reported due to the number of subjects actually enrolled. Definitions and methods of summary will be detailed in section 10.9 and section 10.10.

4.1.1 Primary Endpoint

ORR per RECIST v1.1 by independent radiological assessment committee.

4.1.2 Secondary Endpoints

- Adverse events (AEs) including serious adverse events (SAEs)
- Incidence, severity, and duration of the AEs of special interest
- Replication competent lentivirus (RCL)
- T-cell clonality and insertional oncogenesis (IO)
- Time to response (TTR) per RECIST v1.1 by independent radiological assessment committee (IRAC), and by investigator radiological assessment
- Duration of response (DoR) per RECIST v1.1 by the IRAC, and by investigator radiological assessment
- Best overall response (BOR) per RECIST v1.1 by the IRAC, and by investigator radiological assessment
- PFS per RECIST v1.1 by the IRAC, and by investigator radiological assessment
- Overall Survival (OS)
- ORR per RECIST v1.1 by investigator radiological assessment
- Retention of additional tumor tissue during Pre-screening to enable development and validation of the MAGE-A4 antigen expression companion diagnostic assay
- Peak expansion (i.e., maximum persistence) and time to peak expansion by responder status and overall

4.1.3 Exploratory Endpoints

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

4.2 Covariates

No statistical modelling is planned to be carried out for this study.

5 Hypothesis and/or Estimations

No hypothesis testing is planned due to low numbers of subjects recruited into the study and the study is now closed to further recruitment. This is considered as a change from protocol stated analysis.

6 Definitions

6.1 General Definitions

The definitions of baseline and study visit will supersede any definitions of the following items provided in the protocol.

6.1.1 Baseline Definitions

Baseline is defined as the last non-missing assessment (including unscheduled assessments) prior to lymphodepleting chemotherapy. An exception to this definition of baseline is listed in table 1.

Table 1. Exceptions to pre-lymphodepletion chemotherapy baseline

Assessment/Test	Visit
Immune Effector Cell-Associated Encephalopathy (ICE) Score	Collected daily from the first T-cell infusion (Day 1) to Day 8. Baseline is defined as the day of T-cell infusion.

6.1.2 Study Day Definition

Nominal study day is relative to T-cell infusion. There will be no study day 0. T-cell infusion day is the study day 1. Study Days are in Table 2 below.

Table 2. Definition of Study Day 1 and Study Day

Day 1	The day of the first T-cell infusion
Study Day	(Date of Interest - Date of first T-cell infusion) + 1, if Date of Interest is >= T-cell infusion date
	Date of Interest - Date of T-cell infusion, if Date of Interest is <Date of T-cell infusion

6.1.3 Treatment Group Definition

There is only one treatment arm in the study. Summary tables, figures and listings will be presented by tumor type.

6.2 Definition for Safety Endpoints

6.2.1 AEs

Please refer to Section 8.5 of the protocol for relevant information.

7 Analysis Population

7.1 Intent-to-Treat (ITT) population

This is the population of all subjects who were enrolled in the trial. The ITT population will be used to assess the safety of the end-to-end autologous T-cell therapy procedure.

7.2 Modified Intent-to-Treat (mITT) population

This is the population of all ITT subjects who received T-cell infusion. The mITT population is the primary analysis population for safety and efficacy evaluations following T-cell infusion.

7.3 Per-protocol (PP) population:

A PP population may be included if there are subjects in the mITT population who have protocol violations that are expected to affect efficacy assessments (e.g., subjects enrolled who do not meet key eligibility criteria) during the trial. Protocol violators resulting in exclusion from the PP population will be identified and documented prior to database lock.

PP population will not be used in reporting any of the endpoints stated in the SAP. This is considered as a change from protocol stated analysis.

8 Interim Analysis and Data Review

8.1 Interim Analysis

No Interim analysis will be performed.

8.2 Data Review

No independent Data Safety Monitoring Board (DSMB) will conduct interim monitoring of safety data throughout the treatment period of the study.

9 General Analysis Conventions

Data collected in this study will be analyzed using summary tables, and subject data listings.

Unscheduled assessments (laboratory data, scans, ECG, vital signs, etc. associated with non-protocol clinical visits or obtained while investigating or managing adverse events) will be included in listings, but not summaries.

Continuous variables will be summarized using descriptive statistics (Number of subjects, Mean, Median, Standard deviation, Minimum, and Maximum). Continuous data that are expected to be skewed will be presented in terms of the maximum, upper quartile, median, mean, lower quartile, minimum, standard deviation, and number of observations. The minimum and maximum will be reported to the same number of decimal places as the raw data recorded in the database. The mean, median, lower quartile and upper quartile will be reported to one more decimal place than the raw data recorded in the database. The standard deviation will be reported to two more decimal places than the raw data recorded in the database. In general, the maximum number of decimal places reported shall be four for any summary statistic. Confidence intervals (CI) will be presented to one more decimal place than the raw data. If the confidence intervals are calculated for proportions, then they will be presented to three decimal places.

Categorical variables will be summarized using frequencies and percentages. Adverse events, medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA), Version 25.0 or higher. Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary version (2022).

All tables, listings, and figures will be programmed using SAS Version 9.4 or higher.

9.1 Study Periods

Please refer to Section 8.5 of protocol for collection of AE / SAE information through the study.

For the purposes of reporting, adverse events/serious adverse events will be summarized using the below periods.

- During Pre-screening period, only SAEs related to protocol-specified procedures will be listed.
- From the time of signing the treatment Informed Consent Form (ICF) until day before lymphodepletion starts, only SAEs related to study design/procedures or AEs leading to withdrawal from study will be listed.
- From start of lymphodepleting chemotherapy, defined as starting on the first day of lymphodepleting chemotherapy until the subject has discontinued the Interventional Phase of the study, all AEs and SAEs will be listed.
- From the end of interventional phase to end of study (LTFU)

9.2 Visit Windows

Study visits are expected to occur according to the protocol schedule. All data will be tabulated per the evaluation visit as recorded on the eCRF, even if the assessment is outside of the visit window. No imputation of data will be performed for missed assessments unless otherwise noted. In data listings, the relative study day of all dates will be presented.

10 Statistical Methods of Analysis

10.1 Handling of Dropouts or Missing Data

In general, imputed partial dates will not be used to derive study day, duration (e.g., duration of adverse events), or elapsed time variables. In addition, imputed dates are not used for deriving the last contact date in the overall survival analysis dataset.

Imputed dates will not be displayed in listings unless otherwise stated.

The partial date imputation will follow ADaM conventions. The ADaM approach is to populate the numeric date variables with the imputed date and add a flag variable to the dataset that indicates the level of imputation. The flag variable can contain the values: blank, 'D', 'M', 'Y'.

- blank: indicates that no imputation was done
- D='Day': indicates that the day portion of the date is imputed
- M='Month': indicates that the month and day portions of the date are imputed
- Y='Year': indicates that the entire date (year, month, and day) is imputed

Imputing partial AE, medical history, initial diagnosis partial dates, and prior/concomitant medication start dates:
a) If the year is unknown, the date will not be imputed and will be assigned a missing value.

b) If only year is present, and month and day are unknown, then:

1.If the year matches the first date of lymphodepleting chemotherapy:
- If the stop date is available and complete, and is on or after the first lymphodepleting chemotherapy date, then impute to the month and day of the first lymphodepleting chemotherapy date.
- If the stop date is available and complete, and is before the first lymphodepleting chemotherapy date, then impute to the first day of the month of the stop date.
- If the stop date is missing (and unable to be imputed) or no stop date is applicable, then impute to the month and day of the first lymphodepleting chemotherapy date.

2. Otherwise, assign 'January 01'.

c) If month and year are preset and the day is unknown, then:

1. If the month and year match the first lymphodepleting chemotherapy date, then impute to the day of the first lymphodepleting chemotherapy date.

2. Otherwise, assign '01' of the month.

Imputing partial AE, medical history, and prior/concomitant medication stop dates:

a) If the year is unknown, the date will not be imputed and will be assigned a missing value.

b) If the month is unknown, then assign 'December 31'.

c) If the day is unknown, then impute to the last day of the month.

Note: After imputation, if the imputed date is later than the date of death or the date that the subject ends the study, then the date of death or date of end of the study will be used, whichever is earlier. If AE is ongoing but the subject discontinues the study, then the stop date will be resolved to the date that the subject discontinues the study.

If a period determination cannot be made for an adverse event, it will be attributed to the post-lymphodepletion period interventional phase.

For cytokine parameters with character values, following guidelines will apply:
- Characters such as "Fail QC" "Fail Std" "CV>25%" "TNP" "DNR" "CV>30%" "std" "std Fail" "<##.#" or ">##.#" will set to missing (i.e., ".").

10.2 Pooling of Centers in Multi-Center Studies

Data will not be summarized by study center.

10.3 Multiple Comparisons/Multiplicity

No adjustments for multiple comparisons or multiplicity are planned.

10.4 Examination of Subgroups

Safety summaries will be displayed by tumor type (advanced esophageal or esophagogastric junction cancers), and overall.

10.5 Subject Disposition

A clear accounting of the disposition of all subjects who enter the study will be provided, from screening to study completion. Summaries of subject disposition by tumor type (esophageal, and esophagogastric Junction) and overall, in the ITT population, may be provided as follows if data is permitted:

- Number and percentage of subjects in the analysis populations (ITT, mITT)
- Number and percentage of subjects who received leukapheresis
- Number and percentage of subjects who underwent lymphodepleting chemotherapy
- Number and percentage of subjects who received T-cell infusion
- Number and percentage of subjects who completed/discontinued the Interventional Phase as well the reason for discontinuing the interventional phase
- Number and percentage of subjects who entered the LTFU phase.
- Number and percentage of subjects who withdrew/discontinued early from the study (including reasons for early withdrawal)
- Number and percentage of subjects completed the study

By-subject listings of infusion dates, and withdrawal details (including reason for discontinuation and days on study) will also be provided for ITT population.

10.6 Protocol Deviations

The reporting of protocol deviations will be handled outside of this SAP (clinical activity) but will be discussed within the aCSR

10.7 Demographic and Baseline Characteristics

Demographic and baseline characteristics at study entry will be summarized by tumor type and overall for the ITT population.

Variables to be summarized are:

- Age at time of informed consent (in years, as a continuous variable)
- Age Categorization (<65, ≥65 years)
- Gender (Male, Female)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, Unknown)
- Race (White, Black/African American, Asian, American Indian/Alaska Native, Hawaiian Native/Other Pacific Islander)
- Height at baseline (in meters)
- Weight at baseline (in kilograms)
- BMI at baseline (BMI=kg/m2) of weight and height at baseline

- Histological Grade [G1- Well differentiated (Low Grade), G2- Moderately differentiated (Intermediate Grade), G3- Poorly differentiated (High Grade), GX- Grade cannot be assessed (Undermined Grade), Unknown]
- Baseline Eastern Cooperative Oncology Group (ECOG) performance
- Current Cancer Stage (0, I, II, III, IIIA, IIIB, IV, IVA, IVB, Unknown)
- Prior Lines of Systemic Therapy (as a continuous variable)
- Prior Lines of Systemic Therapy categorization (0, 1, 2, 3, 4+)
- Bridging therapy (Yes, No)
- Time since initial diagnosis to enrollment (months)
- Time from initial diagnosis to T-cell infusion (months)

Since age is part of the inclusion criteria, age will be reported as the number of complete years at the date of informed consent.

Additionally, MAGE-A4 expression at pre-screening is collected in Clinical Laboratory Information Management System (LIMS) database and, as data permits, may be summarized for subjects in the mITT by tumor type and overall. Expression will be summarized by P Score and H score at pre-screening, each calculated as below:

P score is defined as: % 2+ tumor cells staining intensity + % 3+ tumor cells staining intensity...

H score is defined as: % 1+ tumor staining intensity + 2 x % 2+ tumor staining intensity + 3 x % 3+ tumor staining intensity

A by-subject listing will also be provided for the ITT population.

In case of multiple records, the following record selection criteria will be applied:

a. Select the record with latest analysis date in Clinical LIMS data.
b. If there are duplicates after applying step a then select the record with maximum ‘HE Estimated nr of cancer cells’ in Clinical LIMS data.
c. If one record has a value ‘100-500’ and another record has a value ‘>500’ then select the record with value ‘>500’.
d. If there are still duplicates, then select the one with highest H Score/ P Score.

10.8 Medical History

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 25.0 or higher.

A supportive listing of medical history data by subject will also be created for the ITT population.

10.9 Prior Systemic Cancer Therapy

Prior systemic cancer therapy from screening to leukapheresis, and from leukapheresis to start of lymphodepletion (i.e., bridging therapy) will be listed by subject in a data listing for the ITT population.

10.10 Efficacy Analysis

Only following efficacy data listings will be provided.

10.10.1 Best Overall Response (BoR) by Investigator Radiological Assessment

The best overall response is defined as the best response from the date of first T-cell infusion until disease progression. Response categories from best to worse are: confirmed CR, confirmed PR, SD, PD, and NE based on investigator assessment of overall response (per RECIST v1.1) at each visit.

To confirm CR or PR, changes in tumor measurements must be confirmed by repeat assessments that should be no less than 4 weeks (28 days) after the criteria for response are first met, excluding the day of the initial assessment of CR or PR.

The determination of stable disease must be at least 4 weeks (Day 29) from the T-cell infusion to qualify a SD as the BOR. If a subject did not have confirmed CR or PR and had stable disease for less than 4 weeks, BOR will depend on the subsequent assessments. For example, if SD is followed by a PD as the second assessment and does not meet the minimum duration (4 weeks), then the BOR should be PD. Subjects who lost to follow-up after the first SD that is obtained less than 29 days from the T-cell infusion should be considered not evaluable (NE) for BOR. A missing assessment at a time point will be assigned a value of NE.

To take into account potential pseudo progression, no tumor assessments prior to the 29 day window from T-cell infusion will be considered for BOR determination, unless there is unequivocal progression of existing non-target lesions and/or the appearance of new malignant lesions.
In the absence of unequivocal progression of existing non-target lesions and/or the appearance of new malignant lesions:

- Overall response for any tumor assessment on or after 29 days window will be presented.
- If a subject only has tumor assessments prior to 29 days, or does not have any tumor assessments, window as of data cut date, then BOR=NE

A by-subject listing will be provided to include, but not limited to, tumor assessment date, lesion ID, lesion type, lesion location, diameters, sum of diameters of target lesions (mm), new lesion, Investigator's overall response, and BOR. This listing for tumor assessment of Target Lesion, Non-Target Lesion, and New Lesion should be in accordance with records from the eCRF pages.

10.10.2 Progression- Free Survival (PFS)

Progression-Free Survival (PFS) is defined as the time from the T-cell infusion to the date of the first documentation of PD or death due to any cause, whichever occurs first. PFS (in weeks) will be calculated as: (first event date – first T-cell infusion date + 1) / 7.

PFS data will only be listed by subject; reason for progression will be included in listing.

The details regarding the handling of missing assessments and censoring for primary PFS analysis are presented as follows:

• If a subject has an inadequate baseline scan, PFS will be censored and have a duration set to 1.

• If there are no adequate post baseline tumor assessments after T-cell infusion or date of death recorded, PFS will be censored and have a duration set to 1.

• If a subject is known to be alive and progression-free, PFS will be censored on the day of the last adequate tumor assessment.

• Note per Section 6.5.1 of the protocol, use of active curative anticancer therapy post T-cell infusion (i.e. prior to disease progression) will also be considered as meeting the PD criterion.

• If a subject discontinues the interventional phase prior to PD, PFS will be censored on the date of the last adequate tumor assessment.

• If a subject misses 2 or more consecutive post-baseline tumor assessments and the following assessment is a PD, or if a subject misses 2 or more consecutive postbaseline tumor assessments and then dies, PFS will be censored on the date of the last adequate tumor assessment.

When determining PFS, the recorded date of progression (defined as first time at which progression can be declared) will be used. For progression due to the presence of a new lesion, the date of progression is the first date that the new lesion was observed. If multiple assessments based on the sum of target lesion measurements are done at different times, the date of progression is the date of the first observation or radiological assessment of target lesions that shows a predefined increase in the sum of the target lesion measurements. PFS data will be listed by subject.

10.10.3 Overall Survival (OS)

OS is defined as the time from the date of first T-cell infusion to the date of death (due to any cause). OS in weeks will be calculated as: (death date – first T-cell infusion date + 1) /7. The details regarding the handling of missing assessment and censoring for OS analysis are presented as follows:

- If there is no documentation of death occurring, OS will be censored on the date the subject is last known to be alive, or the data cutoff date, or the end of study date, whichever is earlier.

OS data will be listed by subject; reason for censoring will be included in listing.

10.11 Safety Analysis

This section, as well as its subsections, include specifications for definitions and statistical rationales to summarize safety endpoints such as study drug exposure, adverse events, clinical laboratory tests, vital signs, and electrocardiogram (ECG) measurements. Safety data will either be summarized as observed with descriptive statistics by tumor type and overall for the mITT population, and/or listed.

Safety data will be listed for mITT population.

10.11.1 Study Drug Exposure

T-cell dose is based on the total number of transduced cells reported on the T-cell infusion eCRF page in units 10^6. Cell dose will be reported as stated in the protocol in units of 10^9. The total number

of transduced cells will be summarized for the T cell infusion in the mITT population by tumor type and overall using descriptive statistics.

All dose administration data including Cyclophosphamide (mg), Fludarabine (mg), Mesna (mg), G-CSF data available and T-cell infusion ($\times 10^6$) may be presented by subject in a data listing as data is available.

10.11.2 Adverse Events

Adverse events (AEs) will be monitored from the time the patient signs the interventional informed consent and throughout the study. AE terms will be coded by system organ class (SOC) and preferred term (PT) using the MedDRA v25.0 or higher, and graded according to NCI Common Toxicity Criteria for Adverse Events (CTCAE v5.0).

A treatment-emergent adverse event (TEAE) in the interventional phase is defined as an AE (identified by PT) that:

- Has an onset date on or after the start of lymphodepleting chemotherapy
  Or
- For an ongoing AE which started prior to the start of lymphodepleting chemotherapy, the AE subsequently worsened (in severity grade/relationship or seriousness) after starting lymphodepleting chemotherapy.

The end of the interventional phase (when considering AE onset or AE worsening for defining TEAE) is the discontinuation from the interventional phase or 30 days after T cell infusion, which ever date is later.

Treatment-related TEAEs are those with reasonable causality to a study drug:

- TEAEs related to T-cell therapy are defined as any TEAEs with an Investigator relationship of “definitely related”, “probably related”, or “possibly related” to T-cell therapy in the eCRF, or with relationship missing.
- TEAEs related to Cyclophosphamide are defined as any TEAEs with an Investigator relationship of “definitely related,” “probably related,” or “possibly related” to Cyclophosphamide in the eCRF, or with relationship missing .
- TEAEs related to Fludarabine are defined as any TEAEs with an Investigator relationship of “definitely related,” “probably related,” or “possibly related” to Fludarabine in the eCRF, or with relationship missing.
- TEAEs with fatal outcome are defined as any TEAEs with a toxicity Grade of 5, an outcome of “fatal”, or result in death.

An AE in the long-term follow-up (LTFU) period is defined as an AE that starts or worsens after discontinuation from the interventional period or 30 days after T cell infusion, which-ever is later, until discontinuation from the long-term follow-up period. If an AE or AE from the interventional period is ongoing at the start of the long-term follow-up period, but does not then worsen, it will not be defined as an emergent AE in the long-term follow-up period. LTFU AE will be collected in a separate LTFU AE eCRF page and reported in a separate listing from the other adverse event data.

10.11.2.1 Overview of Adverse Events

Summary tables will be presented for AE and TEAEs by tumor type and overall. An overall summary table of all adverse events will be presented, which will summarize the number and percentages of subjects of the following categories:

- Subjects with Any AEs
- Subjects with Any TEAEs
- Subjects with at least one treatment-related TEAE
    - Any TEAEs Related to Cyclophosphamide
    - Any TEAEs Related to Fludarabine
    - Any TEAEs Related to T-cell Therapy
- Subjects with Any TEAEs of Grade 3 or higher
- Subjects with Any treatment-related TEAE of Grade 3 or higher
    - Any TEAEs of Grade 3 or higher and Related to Cyclophosphamide
    - Any TEAEs of Grade 3 or higher and Related to Fludarabine
    - Any TEAEs of Grade 3 or higher and Related to T-cell Therapy
- Subjects with Any TESAEs
- Subjects with Any treatment-related TESAEs
    - Any TESAEs Related to Cyclophosphamide
    - Any TESAEs Related to Fludarabine
    - Any TESAEs Related to T-cell Therapy
- Subjects with Any TEAEs with Fatal Outcome

10.11.2.2 Adverse Events

Adverse events (AEs) will be summarized by tumor type and overall for the mITT population, and by different study period where applicable. All counts will be by subject, not by event, and subjects are only counted once within each SOC or PT. For tables categorized by maximum CTCAE grade, subjects with multiple events within a particular SOC or PT will be counted under the category of their most severe event within that SOC or PT. Unless otherwise stated, AEs terms will be displayed in the frequency of overall counts from high to low, and then sorted by the frequency of the primary SOC and PT. In case when multiple PTs have the same overall number of subjects, they will be displayed in alphabetical order.

The following summaries will be provided:

- Number and percentage of subjects for each TEAE, categorized by PT, and maximum CTCAE grade
- Number and percentage of subjects for each treatment-related (to T-cell) TEAE, categorized by PT, and maximum CTCAE grade

A listing of long-term follow-up AEs will also be provided. Please refer to Table 2 for summaries by reporting periods.

A by-subject listing of all AEs (including non-treatment-emergent events) will be provided. This listing will be presented by tumor type and will include: subject identifier, age, gender, race, adverse event (SOC, PT, and verbatim term), AE date of onset, AE date of resolution, duration, CTCAE grade, seriousness, and relatedness.

For missing or partially missing dates, imputation will be done according to Section 10.1. In general, however, adverse events will be assumed to be treatment-emergent unless there is clear evidence (through comparison of partial dates) to suggest that the adverse event started prior to the date of first lymphodepletion therapy and did not get worse post lymphodepleting therapy.

Number and percentage of subjects with serious TEAEs will be provided. A by-subject listing of all serious AEs (including non-treatment-emergent events) will also be provided for mITT population.

If data is permitted, a listing of LTFU AE may be listed for mITT population.

Table 3. Summary of AEs by Reporting Period

	AEs (from ICF up to first day of LD)	Interventional Period TEAEs (All Events)	LTFU Period
AEs by PT and Maximum Toxicity Grade		X	
T Cell Related AEs and Maximum Toxicity Grade by PT		X	
Serious AEs by PT		X	

10.11.2.3 Adverse Events of Special Interest

Prolonged Cytopenia

Prolonged Cytopenia is defined as Grade 3 or higher Anemia, Thrombocytopenia, Neutropenia or WBC decreased (Leukopenia) that persists for ≥ 4 weeks from receiving T-cell therapy. The severity is assessed using CTCAE v5.0 criteria Grade 3 or higher. The following summaries are to be produced:

- Incidence of Anemia: Hgb < 8 g/dL, Thrombocytopenia: Platelets < $50x10^9$/L, Neutropenia: ANC < 1.0 x 10^9/L), WBC decreased (Leukopenia): WBC < 2.0 x 10^9/L

Listing of Lab data for Hemoglobin (g/dL), Platelets (10^9/L), ANC (10^9/L) and WBC (10^9/L) between and inclusive of Week 4 and Week 12 will be provided. Data from all scheduled and unscheduled visits included between Week 4 and Week 12 will be mapped to Week 4, Week 8 and Week 12 based on the following reporting window:

- Visit windowing for Week 4 is based on worst value from Day 24 to Day 41 post T-cell infusion inclusive.
- Visit windowing for Week 8 is based on worst value from Day 42 to Day 69 post T-cell infusion inclusive.
- Visit windowing for Week 12 is based on worst value from Day 70 to Day 98 post T-cell infusion inclusive.

If there are more than one value at the same post-baseline visit, the worst laboratory value will be displayed. If there are more than one record with the same worst laboratory value, only the first one would be selected.

A table to summarize the number and percent of subjects who have cytopenia, as well as the laboratory components, at week 4, 8, 12 will be provided. A by subject listing will also be provided.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

The Immune Effector Cell-Associated Encephalopathy (ICE) neurological assessment is used to monitor subjects for ICANS and these results will be listed by subject at T-cell infusion and each scheduled post-infusion visits.

Cytokine Release Syndrome (CRS)

Time to resolution of Cytokine release syndrome (CRS) will be reported in standard CRS listing:

- If a subject has only one occurrence of Cytokine Release Syndrome, then Time to resolution of CRS (in days) = [Stop date of CRS – Start date of CRS + 1]
- If a subject has multiple occurrences of Cytokine Release Syndrome, then Time to resolution of CRS (in days) is the number of days from the first onset of CRS syndrome to the last stop date of CRS, with the non-event date in between subtracted

  [stop date of last CRS – Start date of first CRS +1] – number of non-event days in between.

10.11.2.4 On-study Deaths

A by-subject listing of on-study deaths will be provided for the ITT population

10.11.3 Replication Competent Lentivirus

A listing of subject status for replication competent lentivirus (RCL) over time will be provided mITT population.

10.11.4 T-cell Persistence and Insertional Oncogenesis

Persistence data will be displayed by subject listings for mITT population. Insertional Oncogenesis (IO) data will not be available to present due to early closure of the study.

10.11.5 Clinical Laboratory Data

The list of all clinical laboratory tests is provided in Section 10.3 of the protocol. Local laboratories will be used for laboratory safety evaluations in this study. Laboratory normal ranges will be provided by the local laboratory. For parameters where an NCI CTCAE v.5.0 scale exists, laboratory results will be graded according to the NCI CTCAE v.5.0 severity grade. For parameters where an NCI CTCAE v.5.0 scale does not exist, an indicator of whether the value is below, within, or above the normal range will represent severity instead.

All laboratory values will be reported in SI units unless an alternative convention is more commonly used.

By-subject listings of laboratory data for Hematology and Chemistry, with abnormal values flagged, will be provided by tumor type for the mITT population. This listing will include subject identifier, visit and laboratory reference ranges for each parameter.

10.11.6 Vital Signs

Vital signs will be listed by subject for the mITT population.

10.11.7 Electrocardiograms

ECG parameters will be listed, for the mITT population, by subject for each tumor type and time point.

10.11.8 Eastern Cooperative Oncology Group (ECOG) Performance Status

ECOG performance status will be listed by subjects.

10.11.9 Prior and Concomitant Medications

All medications will be collected from the time the subject signs the informed consent form and throughout the subject's participation in the interventional phase. Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD) version (2022).

Medications will be assigned to a time period (prior and/or concomitant) as follows:

• If both the start and stop date exist and are before the first lymphodepleting therapy date, the medication will be counted as prior.

• If the start date is on or after the first lymphodepleting therapy date, the medication will be counted as concomitant.

• If the start date is before the first lymphodepleting therapy date and the stop date is after the first lymphodepleting chemotherapy or the medication is continuing, the medication will be counted as prior and concomitant.

• If the start date is missing and the stop date is before the first lymphodepleting chemotherapy, the medication will be counted as prior.

• If the start date is missing and the stop date is after the first lymphodepleting therapy date or the medication is continuing, the medication will be counted as concomitant.

• If the start and stop dates are missing and the subject gets lymphodepletion the medication will be counted as concomitant, otherwise the medication will be counted as prior.

If data permits, following by-subject listings will be provided for the ITT population:

- Prior and concomitant medication data
- Prior radiotherapies

- Prior cancer surgeries

11 Changes to Protocol Specified Analysis

There are numerous changes to the protocol specified analysis. Due to the small number of subjects enrolled resulting from early closure of the study, no hypotheses will be tested. In addition, the primary, and some secondary and exploratory endpoints that are stated in the protocol will not be reported. In particular, data relating to ORR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by independent radiological assessment committee (primary efficacy endpoint) will not be reported, nor will any presentations based on the PP population. Only limited baseline, efficacy and safety endpoints that are covered in this SAP will be analyzed and reported in the aCSR.

12 References

None.