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Statistical Analysis Plan

A Phase 2, Multicenter Study to Evaluate the Efficacy and Safety of Autologous Tumor Infiltrating Lymphocytes (LN-145/LN-145-S1) for the Treatment of Patients with Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck

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LIST OF ABBREVIATIONS AND TERMS

Term	Definition
ACT	Adoptive cell therapy
AE	Adverse Event
BMI	Body mass index
BOR	Best overall response
CI	Confidence Interval
CMO	Contract manufacturing organization
CPS	Combined positive score
CR	Complete response
CRF	Case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DCR	Disease control rate
DOR	Duration of response
EBV	Epstein-Barr virus
ECOG	Eastern Cooperative Oncology Group
EOA	End of Assessment
FAS	Full Analysis Set
FDA	Food and Drug Administration
HNSCC	Recurrent and/or metastatic squamous cell carcinoma of the head and neck
HLGT	High-level group term
HLT	High-level term
HPV	Human papillomavirus
ICF	Informed consent form
IL-2	interleukin-2
KM	Kaplan-Meier
LLT	Low-level term
LTFU	Long Term Follow up
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
NE	Not evaluable
NMA-LD	non-myeloablative lymphodepletion
ORR	Objective response rate
OS	Overall survival

Term	Definition
PD	Progressive disease
PD-1	Programmed cell death protein-1
PD-L1	Programmed death-ligand 1
PFS	Progression-free survival
PR	Partial response
PT	Preferred term
RDI	Relative dose intensity
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Stable disease
SI Units	International System of Units
SOC	System organ class
TEAE	Treatment-emergent adverse event
TIL	Tumor infiltrating lymphocyte
WHO	World Health Organization

1 INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide a comprehensive and detailed description of methods for the data analyses outlined in C-145-03 protocol version 4.0 (dated 25 November 2019). Results obtained from the analyses described in this document will provide the basis of the Clinical Study Report (CSR) for this study. Analysis Sets and methods specified in this document take precedence over those described in the protocol should there be any difference due to timing of finalization of each document.

The final statistical analysis will be carried out when all patients have completed 2-year response assessment unless patients discontinued early, and sufficient survival follow up has been performed. This study has been designed as signal detection; no formal hypothesis testing is planned.

2 DESCRIPTIONS OF THE STUDY

This is a Phase 2, multicenter, multicohort, non-randomized, prospective, open-label, interventional study evaluating patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (HNSCC) who receive adoptive cell therapy (ACT) with LN-145/LN-145-S1 autologous tumor infiltrating lymphocytes (TIL). TIL therapy comprises multiple interdependent phases: tumor resection for production of TIL; ex vivo expansion of TIL; NMA-LD; infusion of TIL; and administration of IL-2.

The study is planned to assess efficacy and safety for approximately 55 patients who receive LN-145/LN-145-S1 in the following cohorts:

Cohort 1: Treatment with LN-145, Generation 1 (Gen 1), non-cryopreserved TIL (closed to enrollment; n=8 patients)

Cohort 2: Treatment with LN-145 Generation 2 (Gen 2), cryopreserved TIL, 22-day manufacturing process (approximately 17 patients)

Cohort 3: Treatment with LN-145 Generation 3 (Gen 3), cryopreserved TIL, 16-day manufacturing process (up to 15 patients)

Cohort 4: Treatment with LN-145-S1 PD-1-selected cryopreserved TIL (up to 15 patients)

Cohort 5: LN-145 cryopreserved/LN-145-S1 PD-1-selected cryopreserved TIL re-treatment

TIL product for re-treatment may vary from initial method of manufacturing. Patients treated in the re-treatment cohort may have a second tumor resection if needed. This is recommended when new lesions are available and feasible for resection. The decision for enrollment into Cohort 5, the re-treatment cohort will be based on a discussion between the Investigator and the Medical Monitor.

The study consists of the following periods:

- **Screening and Enrollment Period:** Up to 28 days from signing the informed consent form (ICF)

- **Manufacturing of LN-145/LN-145-S1 Product**

- **Treatment Period:** up to 12 days, including:
    - NMA-LD regimen (up to 7 days)
    - LN-145/LN-145-S1 infusion (1 day)
    - IL-2 infusion (1 to 4 days)

Treatment is completed once the patient receives his/her last dose of IL-2.

- **Assessment Period**
    - ends upon disease progression, the start of a new anticancer therapy, withdrawal of consent, or after 2 years (Month 24), whichever occurs first. An end-of assessment (EOA) visit should be completed.
- **Long-Term Follow-up Period**
    - Begins after the EOA and stops at the end of study (EOS), where EOS can be due to death, patient lost to follow-up, withdrawal of consent, study termination by Sponsor, or after 3 years, whichever occurs first. Patients who had tumor resection but did not receive LN-145/LN-145-S1 for any reason will perform an EOA visit and transition directly into the Long-Term Follow-up Period (LTFU).

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Study Objectives

3.1.1 Primary Objective

- To evaluate the efficacy of LN-145/LN-145-S1 in patients with recurrent and/or metastatic HNSCC based on the Objective Response Rate (ORR) using RECIST v1.1 as assessed by the Investigator (Eisenhauer, 2009)

3.1.2 Secondary Objectives

- To evaluate the efficacy parameters of LN-145/LN-145-S1 in patients with recurrent and/or metastatic HNSCC such as duration of response (DOR), disease control rate (DCR), and progression free survival (PFS) using RECIST v1.1 as assessed by the Investigator
- To evaluate overall survival (OS) in patients with recurrent and/or metastatic HNSCC
- To characterize the safety profile of LN-145/LN-145-S1 in patients with recurrent and/or metastatic HNSCC

3.2 Study Endpoints

3.2.1 Primary Endpoints

- ORR as assessed by the Investigator

3.2.2 Secondary Endpoints

- DOR using RECIST v1.1 as assessed by the Investigator
- DCR using RECIST v1.1 as assessed by the Investigator
- PFS using RECIST v1.1 as assessed by the Investigator
- OS
- Incidence of treatment-emergent AEs (TEAEs), including serious AEs (SAEs), therapy-related AEs, and AEs leading to early discontinuation of treatment or withdrawal from LTFU.

4 GENERAL METHDOLOGY AND CONVENTIONS

4.1 Analysis Sets

Three analysis sets are defined for the statistical analysis and presentation of the data.

Additional analysis for the primary efficacy endpoint, demographics, baseline disease characteristics, prior therapy and adverse events will be conducted using the Enrolled Set for cohorts 1,2,3 and 4. Analyses for Cohort 5 will depend on data availability.

4.2 Sample Size Determination

The total number of patients who will receive LN-145/LN-145-S1 infusions in this study—Gen 1, Gen 2, Gen 3, and PD-1-selected—is approximately 55. Patients who are re-treated will only be counted once. All cohorts are intended for signal seeking; no formal hypothesis testing is planned.

Cohort 1: Approximately 8 patients are planned to be infused with LN-145 Gen 1 product. The enrollment is closed for this cohort.

Cohort 2: Approximately 17 patients are planned to be infused with LN-145 Gen 2 product. The planned enrollment is closed for this cohort. This sample size will provide an estimated ORR with a half-width 95% confidence interval of < 0.21 by the Clopper-Pearson exact method.

Cohort 3: Up to 15 patients are planned to be infused with LN-145 Gen 3 product. This sample size will provide an estimated ORR with a half-width 95% confidence interval of < 0.23 by the Clopper-Pearson exact method.

Cohort 4: Up to 15 patients are planned to be infused with LN-145-S1 TIL product. This sample size will provide an estimated ORR with a half-width 95% confidence interval of < 0.23 by the Clopper-Pearson exact method.

Cohort 5 (Re-treatment cohort): Patients who have been previously treated in Cohort 1, 2, 3, or 4 of this study may rescreen for a second administration of TIL products. These patients may have a second tumor resection if needed, especially when new lesions are available and feasible for resection.

4.3 Timing of Analysis

The final statistical analysis will be carried out when all patients have completed 2-year response assessment unless patients discontinued early, and sufficient survival follow up has been performed. This study has been designed as signal detection; no formal hypothesis testing is planned.

4.4 General Convention

The statistical analysis will be based on the estimation of efficacy and safety parameters and will be performed by cohort unless otherwise specified. There are no planned statistical comparisons between cohorts. Data from each cohort will be evaluated for efficacy and safety if data permit. The statistical analyses will be based on the use of descriptive methods; no formal hypothesis testing is planned.

For patients who had the second course of LN-145/LN-145-S1 treatment in Cohort 5, their safety and efficacy data that are associated with the second LN-145/LN-145-S1 infusion will be listed separately. For patients who did not receive LN-145/LN-145-S1 treatment following the initial screening with or without initial tumor harvest (due to screen failure, manufacturing failure or other reasons), they may be re-screened, and receive LN-145/LN-145-S1 if they meet eligibility criteria at the second screening. In such case, these patients will be included in the analysis sets of the cohort corresponding to the received LN-145/LN-145-S1 treatment.

5 PATIENT CHARACTERISTICS AND TREATMENT EXPOSURE

5.1 Patient Disposition

The patient disposition will be summarized using frequency and percentage for each of the categories listed below:

- All screened patients and the reason for not enrolling
- [redacted]

A summary of patients enrolled by site will be provided.

5.2 Protocol Deviations

The protocol deviations are identified and assessed by clinical research physician or designee following company standard operational procedure. Patients with important protocol deviations will be listed and summarized by categories of deviations for the FAS. All protocol deviations will be listed. All deviations related to COVID-19 will be documented.

5.3 Demographics, Baseline Disease Characteristics and Prior Therapy

Continuous variables will be summarized descriptively by number of patients, mean, standard deviation, median, minimum, and maximum values. Categorical variables will be summarized by number and percentage of patients in each category. Individual patient listings will be provided to support the summary tables.

[redacted]

5.3.1 Demographics

Demographics will include the following:

1. Age (continuous, median (range)) and age categories (<40, ≥40 to <65, and ≥65; <65 and ≥65)
2. Gender
3. Race
4. Ethnicity
5. Weight

[redacted]

6. Body Mass Index (BMI)

5.3.2 Baseline Disease Characteristics

Baseline disease characteristics will include the following:

1. Baseline and screening Eastern Cooperative Oncology Group (ECOG) (0 versus 1)
2. Distant metastasis at study entry and diagnosis
3. Primary Tumor Location
4. Epstein-Barr virus (EBV) status of the primary tumor
5. Human papillomavirus (HPV) status of the primary tumor
6. HPV sub type (ST16 versus others)
7. Stage at initial diagnosis and study entry
8. Current status at study entry
9. Tobacco Usage (current/ former/never)
10. Tobacco Type
11. PD-L1 expression immunohistochemistry available (yes/no)
12. Target Lesion Sum of Diameter (mm)
13. Number of Baseline Target and Non-target Lesions
14. Number of Baseline Target Lesions
15. Number of Baseline non-Target Lesions
16. PD-L1 status: Combined positive score (CPS) (**CPS >=20 &CPS <20; CPS>=1&CPS<1**) from local and central labs depending on data availability

5.3.3 Prior Therapy

Analyses of prior therapy will be focused on prior systemic anti-cancer therapy, which will include the following:

1. Number of lines of prior systemic anti-cancer therapies (1, 2, 3, >3)
2. Types of prior systemic anti-cancer therapies

3. Percent of patients with progressive disease (PD) for the last prior systemic anti-cancer therapy before study entry
4. Time from last prior systemic anti-cancer therapy to tumor harvest (months)
5. Time from last prior anti-PD1/PD-L1 therapy to tumor harvest (months)
6. Cumulative duration of time on prior anti-PD-1/PD-L1 therapies (months)
7. Time from tumor harvested to LN-145/LN-145-S1 infusion (months)
8. Time from last prior systemic anti-cancer therapy to LN-145/LN-145-S1 infusion (months)
9. Reason for Discontinuation for the last prior systemic anti-cancer therapy, n (%)

5.4 Medical History

A summary of medical history will be presented by system organ class (SOC) and preferred term (PT) using MedDRA Version 24.0 or higher A patient data listing of medical and surgical history will also be provided.

5.5 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Global B3 March 2021 or higher. Prior medications are defined as any medications that are stopped before the first dose of NMA-LD, not including prior anti-cancer therapy. Concomitant medications are defined as medications that are either initiated before and continued after the first dose of NMA-LD or initiated after the first dose of NMA-LD through 30 days post LN-145/LN-145-S1 infusion, not including study regimen. The number and percentage of patients who take prior medications and concomitant medications will be summarized New anti-cancer therapies received during survival follow up will also be summarized similarly. All medications recorded on the case report form (CRF) will be listed.

5.6 Treatment Exposure

Study treatment and extent of exposure summaries will be provided

The exposure to NMA-LD regimen (cyclophosphamide and fludarabine) and IL-2 will be summarized based on number of patients who received the agent, total number of infusions received, total cumulative dose, relative dose intensity of protocol planned dose. Relative dose intensity (RDI) is defined as the actual dose intensity divided by the planned dose intensity where dose intensity refers to accumulative dose of above-described agents divided by the corresponding protocol planned number of doses (i.e. 2 doses for cyclophosphamide, 5 doses for fludarabine, and up to a maximum of 6 doses for IL-2).

6 EFFICACY ANALYSIS

6.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the ORR as assessed by the investigator. It is derived as the number of patients who have the best overall response (BOR) of CR or PR divided by the number of patients in the FAS x 100%. In order for the ORR to be categorized as CR or PR, a confirmatory evaluation is required at least 4 weeks apart after the first CR or PR. To determine BOR, all tumor response assessments up to the first PD per investigator should be considered. Any further tumor response assessments after the first PD or after the start of a new anti-cancer therapy are not considered. Patients without any baseline or any post-baseline measurements are considered not evaluable (NE). Derivation of confirmed BOR based on two consecutive tumor assessment visits at least 4 weeks apart per RECIST v1.1 is provided in Table 1.

ORR is expressed as a binomial proportion and will be summarized using a point estimate and its two-sided 95% confidence intervals based on the Clopper-Pearson exact method.

Additional analysis for the primary efficacy endpoint will be conducted using the Enrolled Set.

Table 1 - General Rule to Drive BOR per RECIST v1.1

Overall Response first timepoint	Overall response subsequent timepoint	BOR per RECIST v1.1
CR	CR	CR
CR	PR	SD, PD or PR [a]

CR	SD	SD provided minimum criteria for SD duration met, otherwise PD
CR	PD	SD provided minimum criteria for SD duration met, otherwise PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise NE
PR	CR [b]	PR
PR	PR	PR
PR	SD	SD
PR	PD	SD provided minimum criteria for SD duration met, otherwise PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise NE
SD	CR [b]	SD
SD	PR [b]	SD
SD	SD	SD
SD	PD	SD provided minimum criteria for SD duration met, otherwise PD
SD	NE	SD provided minimum criteria for SD duration met, otherwise NE
NE	NE	NE
PD		PD

Note: BOR=best overall response. CR=complete response. PR=partial response. SD=stable disease. PD=progressive disease. NE=not evaluable. [redacted]

[a] If a CR is met at first time point, then any disease seen at a subsequent time point, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However, sometimes 'CR' may be claimed when subsequent scans suggest small lesions were likely still present and in fact the patient had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

[b] Subsequent assessments should be conducted to confirm the CR/PR of that specific time point.

6.2 Seconday Efficacy Endpoints

For time-to-event endpoints such as DOR, PFS, OS, the Kaplan-Meier (KM) product limit method will be used to estimate the survivorship function. The landmark event-free rates for appropriate time points including Months 6, 12, 18, and 24 will be provided for PFS and OS depending on the maturity of study data at the time of planned analysis.

DOR is measured from the time point at which the initial measurement criteria per RECIST v1.1 are met for a CR or PR (if response is a confirmed response), whichever response is observed first, until

the first date that PD is objectively documented, or the patient expires. Patients not experiencing PD or who have not died prior to the time of data cut or the database lock will have their event times censored at the last adequate tumor assessment. For patients who received new anticancer therapies, DOR will be censored at the date of last tumor response assessment prior to the start of new anticancer therapies. Patients with PD or death immediately after two or more consecutive missing tumor assessment visits, the DOR will be censored at the last adequate tumor assessment prior to the missing tumor assessments.

DOR (day) = Date of PFS event (PD or death) or censoring – Date of first overall response + 1

The median DOR and its 95% confidence interval (CI) will be obtained using the Kaplan-Meier method for patients achieving a response (CR or PR).

DCR is defined as the proportion of patients who have the BOR of CR or PR or stable disease (SD). The BOR of SD must be at least 4 weeks from LN-145/LN-145-S1 infusion. DCR is expressed as a binomial proportion and will be summarized using a point estimate and its two-sided 95% confidence intervals based on the Clopper-Pearson exact method.

PFS is defined as the time (in months) [redacted] to PD or death due to any cause, whichever occurs earlier. Patients not experiencing PD or not having died at the time of the data cut or the database lock will have their event times censored at the last adequate tumor assessment. The PFS censoring rules and definition of progression date follow the Food and Drug Administration (FDA) "Guidance for Industry Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (2018)". For patients who received new anticancer therapies, the PFS will be censored at the date of last tumor response assessment prior to the start of new anticancer therapies. Patients with PD or death immediately after two or more consecutive missing tumor assessment visits, the PFS will be censored at the last adequate tumor assessment prior to the missing tumor assessments.

PFS (day) = [redacted] Date of LN-145/LN-145-S1 infusion + 1

The median PFS with its 95% confidence interval and PFS at landmark time points will be obtained using the Kaplan-Meier method.

OS is defined as the time (in months) [redacted] due to any cause. Patients not having died at the time of data cut or the database lock will have their event times censored on the last date of their known survival status. The date of last known alive will be

derived as the latest among dosing records, safety and any other assessment dates indicating that a patient is alive. The median OS with its 95% confidence interval and OS at landmark time points will be obtained using the Kaplan-Meier method.

OS (day) = Date of death or Last known alive – [redacted] + 1

6.3 Other Planned Efficacy Analyses

The following efficacy analyses will be performed for FAS patients unless otherwise specified.

- The response rates for appropriate time points including Months 6, 12, 18 and 24 will be calculated for investigator assessments and summarized descriptively.
- Time to first response will be calculated and summarized descriptively based on patients with a confirmed CR or PR as assessed by investigators.

7 SAFETY ANALYSIS

[redacted] The assessment of safety data will be descriptive and based on the summarization of adverse events, vital signs, and clinical laboratory tests.

7.1 Adverse Events

The adverse event will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.0 or later. System Organ Class (SOC), High-level Group Term (HLGT), High-level Term (HLT), Preferred Term (PT), and Lower-level Term (LLT) will be provided in the AE dataset. The severity of each adverse event will be graded by the Investigator using Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 or higher, unless otherwise specified in the protocol.

Related AEs are based on 3 out of the 5 categories of causal relationship to study drug reported by investigators: “Definite”, “Probably”, and “Possible”. The causal relationship of “Not Likely” and “Not Related” will categorize AEs as “unrelated”. Adverse events will be identified and captured as SAEs if they meet the definition for SAE.

[redacted]

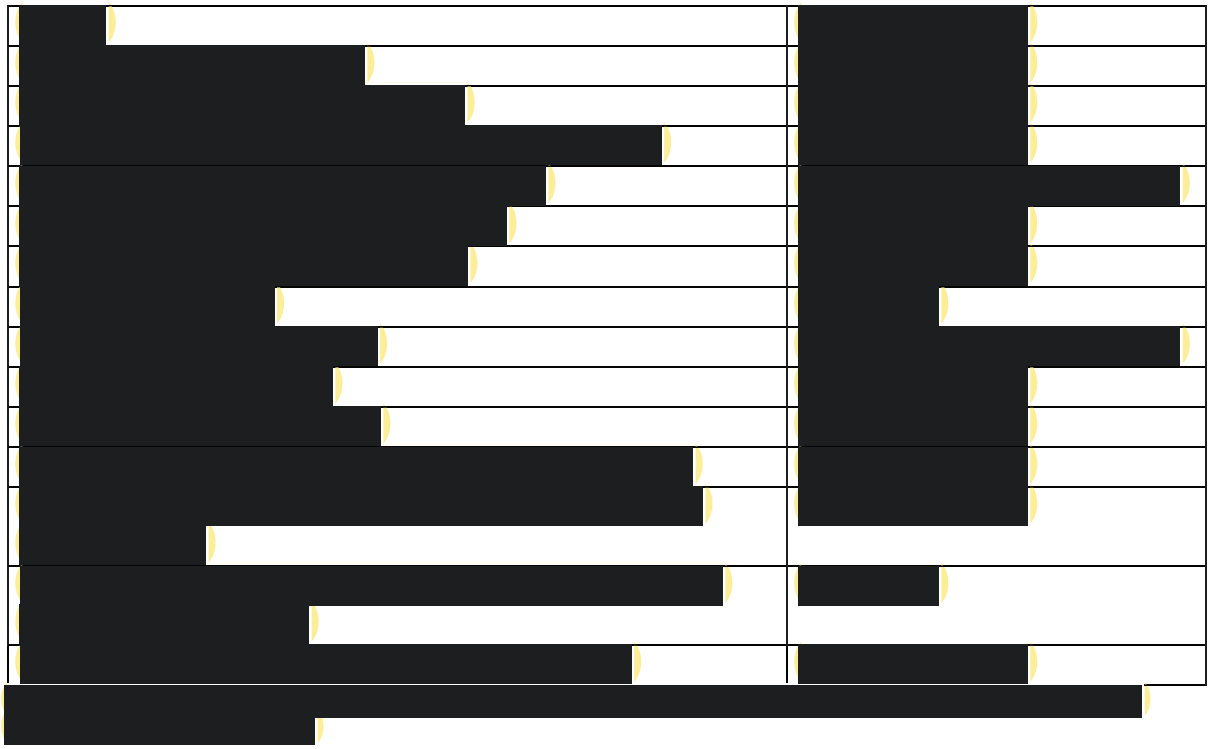
7.1.2 Summary of Adverse Event

Tabular summaries including numbers and percentages of the following adverse events will be presented by SOC and PT and/or presented by PT only in order of descending incidence, as appropriate. All grade AEs, Grade 3/4 AEs and Grade 5 AEs will be presented in separate columns. The most severe grade will be used for those AEs that occur more than once in an individual patient.

For AE summaries by PT, cytopenia AEs will be grouped based on PTs and presented as leukopenia (including white blood cell count decreased and leukopenia), lymphopenia (including lymphocyte count decreased and lymphopenia), neutropenia (including neutrophil count decreased and neutropenia), and thrombocytopenia (including platelet count decreased and thrombocytopenia). These grouped cytopenia PTs belong to different SOCs: Blood and lymphatic system disorders or Investigations. For AE summaries by SOC and PT, for analysis purpose, they will be summarized under SOC of Blood and lymphatic system disorders.

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]



above, a histogram plot of AE frequency overtime will be provided with different colors for different toxicity grades. All occurrences will be counted if a patient experience the same AE, but multiple records are reported on the CRF due to toxicity grade increase. If multiple records are reported on the CRF for the same episode due to toxicity grade decrease when the event is resolving, it will be counted once with the highest grade displayed on the histogram plot.

Patient data listings for the corresponding AE and death summary will also be provided.

7.2 Laboratory Evaluations

The laboratory assessments are conducted by local laboratory. All laboratory values will be converted to and reported in the International System (SI) of units and classified as low, normal, or high based on the reference ranges provided by the local laboratory. All laboratory data will be listed with a variable indicating whether the event is treatment emergent.

7.2.1 Analysis Period for Laboratory Abnormalities

Three analysis periods are defined below for the laboratory abnormality analysis.

7.2.2 Graded Laboratory Results

Applicable hematology and clinical chemistry laboratory data will be graded according to National Cancer Institute (NCI)-CTCAE, Version 4.03 severity grade. Grade 0 includes all non-missing values that do not meet criteria for an abnormality of at least Grade 1. Some laboratory tests have criteria for both increased and decreased levels; analyses for each direction (i.e., increased, decreased) will be presented separately.

The baseline CTCAE severity grade, and the maximum grade during each analysis period will be summarized using number and percentage of patients in each category. Patients will be categorized according to the most severe abnormality grade.

Number and percentage of patients with Grade 3 or 4 laboratory toxicity will be summarized for baseline, and each post-baseline visit.

Shift tables will be presented by showing the change in CTCAE severity grade from baseline to each analysis period. For parameters for which a CTCAE severity scale does not exist, shift tables will be presented showing change in results from the baseline value (low, normal, and high) to each analysis period (low, normal, and high). Summary of laboratory abnormalities worsening at least 2 grades from baseline to worst post-baseline by analysis period will also be provided.

7.2.3 Numeric Laboratory Results

Summaries of numeric laboratory data will be based on observed data and will be reported using SI units. Baseline, measurements after baseline, and changes from baseline at each post-treatment visit will be summarized using descriptive statistics for each laboratory parameter.

7.3 Vital Signs

Descriptive statistics for vital signs parameters (i.e., body weight, heart rate, respirations, blood pressure, and temperature) and changes from baseline will be presented by visit.

8 OTHER PLANNED ANALYSES

8.1 Impact of the COVID-19 Pandemic

The protocol deviations and missing data related to COVID-19 will be identified and documented. Additionally, the following analyses will be performed to assess the impact of COVID-19 pandemic:

- Number and percentage of patients with radiological response assessment performed at outside facility due to COVID-19

9 DEFINITONS AND DATA HANDLING CONVENTIONS

9.1 Definitions and Computations

Patients without any baseline or any post-baseline measurements are considered not evaluable (NE) for BOR.

For time-to-event efficacy endpoint, the interval is calculated as:

- Time to event (in days) = event date or censoring date - start date + 1, or
- Time to event (in months) = (event date or censoring date - start date + 1)/30.4375, or
- Time to event (in years) = (event date or censoring date - start date + 1)/365.25

Calculation of follow-up time for time-to-event endpoints (e.g., OS, DOR) will be performed using the reverse Kaplan-Meier method.

9.2 Missing Data Handling

As a principle, no imputation of missing values for safety data will be performed. For missing or partial start date for AEs, concomitant medications, and subsequent anti-cancer therapies, a conservative approach is taken to perform the relevant analyses. If the available information of a date is not enough to judge whether an event occurred on or after initiation of the study treatment, it will be conservatively taken as a treatment-emergent event.

An intermediate imputation of partial dates may be taken as described below to calculate the study day for AEs and concomitant medications:

- If only day is missing, the 15th of that month will be used.
- If only year is present, June 30th will be used.

If an imputed AE start date is in the same month and year as the first dose date of lymphodepletion but on an earlier date, the first dose date will be used. If an imputed AE start date is after the AE end date, the AE end date will be used.

9.3 Imputation Rules for Laboratory Values Reported with Symbols

Laboratory values that are reported with "<" or "≤" in the database will be imputed by the numeric values x 0.99, and laboratory values that are reported with ">" or "≥" in the database will be imputed by the numeric values x 1.01 for reporting purposes. The original laboratory value will be listed.

9.4 Visit Window

For summarizing data by visit, all scheduled and unscheduled assessments will be assigned to analysis visits according to a visit window schema. Visit windows for laboratory, vital signs and other assessments are defined as shown in Table 2. If more than 1 assessment is within a given visit window, the assessment closest to the target date will be used. If 2 assessments are equally close to the target day, the earlier assessment will be used. By visit analysis will not be conducted after Month 24 due to expected small sample size.

Table 2 - Visit Windows for laboratory and vital sign Assessments

Nominal Visit	Target Study Day	Start (Study Day)	End (Study Day)
Day -7	-7	-7	-7
Day -6	-6	-6	-6
Day -5	-5	-5	-5
Day -4	-4	-4	-4
Day -3	-3	-3	-3
Day -2	-2	-2	-2
Day -1	-1	-1	-1
Day 0	0	0	0
Day 1	1	1	1
Day 2	2	2	2
Day 3	3	3	3
Day 4	4	4	5
Day 14	14	6	20
Day 28	28	21	41
Day 56	56	42	70
Day 84	84	71	105
Day 126	126	106	155
Month 6	183	156	229
Month 9	274	230	320
Month 12	365	321	410
Month 15	456	411	502

Month 18	548	503	594
Month 21	639	595	685
Month 24	730	686	775

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Originator Approval

Name/Signature	Title	Date	Meaning/Reason
[redacted]	Director, Biostatistics	22 Jul 2022, 08:51:31 AM	Approved

Functional Approval

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[redacted]	Senior Medical Director	22 Jul 2022, 08:59:54 AM	Approved
[redacted]	Vice President, Biometrics	22 Jul 2022, 09:07:19 AM	Approved

Quality Approval

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[redacted]	Director, Clinical Quality Assurance	22 Jul 2022, 10:35:13 AM	Approved

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