STATISTICAL ANALYSIS PLAN

An Open-Label Phase 1B/2 Study to Evaluate the Safety and Efficacy of Tabelecleucel in Combination with Pembrolizumab in Subjects with Platinum-pretreated, Recurrent/Metastatic Epstein-Barr Virus-Associated Nasopharyngeal Carcinoma

Study Number ***ATA129-NPC-202***

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition/Explanation
AE	adverse event
BOR	best overall response
CBR	clinical benefit rate
CI	confidence interval
CR	complete response
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
EBNA	EBV nuclear antigen
EBV	Epstein-Barr virus
EBV-CTLs	Epstein-Barr virus cytotoxic T lymphocytes
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EWB	emotional well-being
FWB	functional well-being
GvHD	graft-versus-host disease
HLA	human leukocyte antigen
IPD	important protocol deviation
IR	indeterminate response
iRECIST	immune response evaluation criteria in solid tumors
IRR	independent radiographic review
IV	intravenous
LMP	latent membrane protein
MTD	maximum tolerated dose
NE	not evaluable
NPC	nasopharyngeal carcinoma
ORR	objective response rate
OS	overall survival
RP2D	recommended phase 2 dose
PD-1	programmed cell death protein-1
PD-L1	programmed death-ligand1
PD-L2	programmed death-ligand2
PFS	progression-free survival

Abbreviation	Definition/Explanation
PK	pharmacokinetics
PR	partial response
PTLD	post-transplant lymphoproliferative disease
PWB	physical well-being
RP2D	recommended phase 2 dose
SAE	serious adverse event
SD	standard deviation
SOP	standard operating procedure
SWB	social/family well-being
TEAE	treatment-emergent adverse event
TESAE	treatment-emergent serious adverse event
TTR	time to response

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide details of the statistical analyses that have been outlined within the protocol for tabelecleucel Study ATA129-NPC-202 entitled, "An Open-Label Phase 1B/2 Study to Evaluate the Safety and Efficacy of tabelecleucel in Combination with Pembrolizumab in Subjects with Platinum-pretreated, Recurrent/Metastatic Epstein-Barr Virus-Associated Nasopharyngeal Carcinoma", amendment 1, dated 9 August 2018.

Upon Atara's decision, this study was terminated by Phase 1B with 12 subjects enrolled, and all analysis will be performed for Phase 1B only.

2 STUDY OVERVIEW

2.1 Study Objectives

2.1.1 Primary Objective

The primary objectives of the study are:

- Phase 1B: To characterize the incidence of dose-limiting toxicities (DLTs) of tabelecleucel in combination with pembrolizumab in subjects with platinum-pretreated, recurrent/metastatic NPC

- To identify the maximum tolerated dose (MTD), or in the absence of an MTD, the recommended phase 2 dose (RP2D) of tabelecleucel when administered in combination with pembrolizumab

- Phase 2: To evaluate the objective response rate (ORR), defined as a CR or PR confirmed ≥ 28 days from the initial response assessment showing a response obtained following administration of the combination of tabelecleucel and pembrolizumab, where the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 response is determined using an independent radiographic review (IRR)

- For both phase 1B and phase 2: To characterize the safety profile of tabelecleucel in combination with pembrolizumab in the NPC subject population

2.1.2 Secondary Objectives

The secondary objectives are as follows:

- To evaluate additional clinically relevant outcomes in subjects with NPC treated with tabelecleucel in combination with pembrolizumab, as measured by CR rate, duration of response (DOR; ie, CR + PR), progression-free survival (PFS) and OS

- To evaluate the immune response rate (iRR; ie, immune CR [iCR] + immune PR [iPR] rate) and duration of immune response (DOiR)

2.1.3 Exploratory Objectives

2.2 The exploratory analyses will be conducted adhoc upon request and are not described in this analysis plan.Study Design

This is a multicenter, open-label, single-arm study in subjects with platinum-pretreated, recurrent/metastatic EBV+ NPC (also referred to as NPC in this protocol). The study was originally planned to be conducted in 2 parts as following: Cohort 1 will be enrolled as the phase 1B portion to determine the phase 2 dose; Cohort 2 will be enrolled as the phase 2 portion to examine the clinical benefits of combined T cell and checkpoint inhibitor immunotherapies for the treatment of subjects with NPC. The study will enroll 48 to 60 subjects in total. Phase 1B (Cohort 1) will enroll 12 to 24 subjects. For each dose level explored in Cohort 1, at least 6 subjects must have had disease that is refractory to PD-1 or PD-L1 monoclonal antibody. All other subjects enrolled to Cohort 1 will be checkpoint inhibitor naïve subjects (have never received pembrolizumab or other anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, anti-OX40 [CD134] or anti-CTLA-4 products). Dose de-escalation is permitted in Cohort 1 only. Cohort 2 will enroll 36 subjects who are checkpoint inhibitor naïve. Tabelecleucel was selected for each subject from the bank of available tabelecleucel cell products based on matching ≥ 2 HLA alleles, at least one of which is a restricting HLA allele, ie, shared between the tabelecleucel source material (donor) and the subject.

The overall treatment schema is shown in Figure 1 and the planned dose cohorts are provided in Table 2. In Cohort 1, tabelecleucel was to be administered initially to 12 subjects at a dose of 2 x 10^6 cells/kg IV on Day 1, Day 8, and Day 15 of a 21-day cycle. Pembrolizumab was administered to adult subjects (≥ 18 years of age) at a dose of 200 mg IV Q3W (ie, on Day 1 of each 21-day cycle) and to pediatric (adolescent) subjects (12 to < 18 years of age) at a dose of 2 mg/kg IV Q3W. If ≥ 2 of the initial 6, or ≥ 4 of the initial 12, Cohort 1 subjects experience a DLT in the first 21 days, the dose of tabelecleucel would have been reduced to 1 x 10^6 cells/kg/dose, and an additional 12 subjects would have been treated with the combination of tabelecleucel at 1 x 10^6 cells/kg/dose and pembrolizumab at the recommended dose level (Table 3). Otherwise, all 12 subjects in Cohort 1 were planned to receive tabelecleucel at 2 x 10^6 cells/kg/dose and pembrolizumab at the recommended dose level.

A Safety Data Review Committee (SDRC) composed of representatives from the sponsor and the principal investigators or designated sub-investigators from all sites enrolling subjects in Cohort 1 was planned to review reported DLTs and cumulative safety data to determine further enrollment. The data review occurred as soon as possible after Cycle 1 Day 21 of the last subject in Cohort 1. Upon positive feedback from the SDRC review, 36 subjects were planned to be enrolled in Cohort 2 and treated with the combination at the recommended dose level.

Table 2 Dose Cohorts

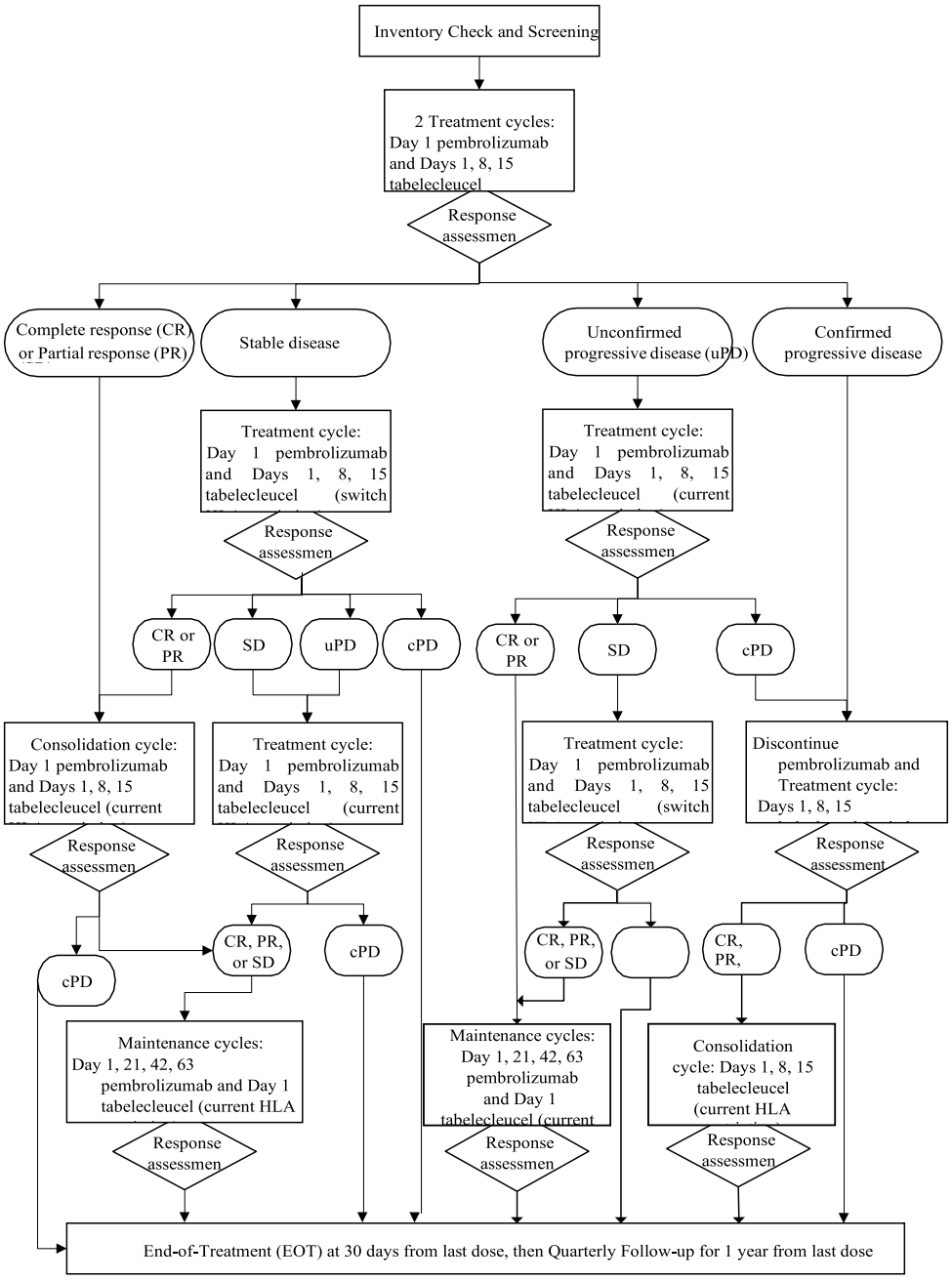
Cohort	Number of Subjects	Prior Therapy
1	12 to 24	Checkpoint inhibitor naïve [a] or PD-1/PD-L1 failures (ie, refractory to or relapsed after PD-1/PD-L1 treatment) At least 6 of the 12 subjects must have disease that is refractory to an anti-PD-1 or anti-PD-L1 monoclonal antibody for each dose level explored
2	36	Checkpoint inhibitor naïve [a] subjects

[a] Checkpoint inhibitor naïve have never received pembrolizumab or other anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, anti-OX40 or anti-CTLA-4 antibodies

Table 3 Initial Dose and Dose De-escalation Levels

	Tabelecleucel Dose (cells/kg)	Pembrolizumab Adult Dose (mg)	Pembrolizumab Pediatric Dose (mg/kg)
Dose level 1	2×10^6 on Day 1, Day 8 and Day 15	200 on Day 1	2 on Day 1
Dose level 2	1×10^6 on Day 1, Day 8 and Day 15	200 on Day 1	2 on Day 1

2.3 Figure 1Overall Study Design Schema (Cohorts 1 and 2)



NOTE: A maximum of 4 treatment/consolidation cycles and 1 switch of tabelecleucel to a different HLA restriction (Switch Therapy) is permitted if an appropriately matched product is available.

* For a clinically stable subject with first radiographic evidence of progressive disease by RECIST 1.1 (ie, unconfirmed PD [uPD]), it is at the discretion of the investigator not continue treating the subject with the assigned treatment per protocol until cPD at least 28 days from the date of the scan first suggesting progressive disease. If radiographic progression is not confirmed by immune (i)RECIST per the

investigator, then the subject may continue treatment as described above in consultation with the sponsor's medical monitor.

During the Treatment Phase, subjects will receive two 21-day treatment cycles of combination immunotherapy and then undergo a response assessment at the Observation Visit (refer to Figure 1). Based on the subject's response to the initial 2 cycles s/he may receive one additional consolidation cycle with the same tabelecleucel product or additional treatment cycles with tabelecleucel with the same or a different HLA restriction, if an appropriately matched product is available. At any time during the Treatment Phase if a subject has a confirmed progressive disease (cPD), it is at the investigator's discretion to continue treatment with tabelecleucel with a different HLA restriction (Switch Therapy), if available without pembrolizumab. A maximum of 4 treatment/consolidation cycles and 1 Switch Therapy, if available will be permitted.

During the Maintenance Phase, subjects will receive tabelecleucel on Day 1 and pembrolizumab on Day 1, Day 21, Day 42, and Day 63 of 84-day maintenance cycles, which will continue until disease progression, unacceptable toxicity, or a total of 35 pembrolizumab infusions (including for treatment, consolidation, and maintenance) have been given. After completing the End-of-Treatment (EOT) Visit 30 days after the last dose of investigational product, subjects will enter quarterly follow-up until 12 months after the last dose of investigational product or until disease progression. During this last phase, survival and disease status will be collected. The end-of-study is defined as the date of the last quarterly follow-up.

2.4 Sample Size

The sample size for cohort 1 was planned to be 12-24. This is based on a 6+6 design with dose de-escalation.

The sample size for cohort 2 was estimated as 36. The estimated ORR for treatment with the combination of tabelecleucel and pembrolizumab is ≥ 45%. The comparator ORR deemed uninteresting is 20%. Based on the exact binomial test at the 1-sided alpha = 0.025 significance level, a sample size of 36 subjects would provide 90% power to detect a true ORR of at least 45%.

3 STUDY ENDPOINTS

NPC disease response and progression were to be assessed via protocol-specific criteria by the study site per RECIST 1.1. Response-related endpoints assessed by investigators per iRECIST was planned to be used for supportive analyses.

3.1 Primary Endpoints

The primary endpoints are:

- The incidence of DLTs in Cohort 1

- The MTD, or in the absence of an MTD the RP2D, of tabelecleucel when administered in combination with pembrolizumab

- The ORR of tabelecleucel in combination with pembrolizumab

- The characterization of the safety profile of tabelecleucel in combination with pembrolizumab in subjects with NPC.

3.2 Secondary Endpoints

• CR rate, DOR, PFS, and OS
• iRR (ie, iCR + iPR rate) and DOiR

As study terminated, not all endpoints will be analyzed in final CSR. Incidence of DLTs will summarized as part of the safety section, efficacy summary will be limited to ORR only, Subject survival information will be provided by listing and swimmer plot.

4 ANALYSIS SETS AND SUBGROUPS

4.1 Analysis Set

Full Analysis Set consists of all subjects who have received at least 1 dose of IP (tabelecleucel or pembrolizumab). Safety Analysis Set will be identical to the full analysis set. All efficacy and safety analyses will use the Full Analysis Set.

4.2 Subgroups

Per data limitation, no subgroup analysis is planned for CSR.

4.3 Subject cohorts

Cohort 1, subjects enrolled in phase 1B part is called Cohort1 with sub-cohort of checkpoint inhibitor naïve and sub-cohort of PD-1/PD-L1 failures (ie, refractory to or relapsed after PD-1/PD-L1 treatment).

5 INTERIM ANALYSIS AND EARLY STOPPING GUIDELINES

No interim analysis is planned for this study.

6 GENERAL PRINCIPLES

6.1 General

The Full Analysis Set will be used for all the safety analyses unless otherwise specified.

Unless otherwise specified, all continuous variables will be summarized using descriptive statistics, which will include the number of subjects with a valid measurement (n), mean,

standard deviation (SD), median, 25th percentile (Q1) and 75th percentile (Q3), and minimum and maximum. All categorical variables will be summarized using frequencies and percentages.

The following terms may be used for tables, figures and listings (TFLs):

- **Investigational product (IP):** Investigational product refers to tabelecleucel (Atara IP) or pembrolizumab (non-Atara IP) in this study.
- **Study treatment**: Study treatment refers to all the protocol-specified treatments administrated to subjects. In this combination therapy study, study treatment refers to tabelecleucel and/or pembrolizumab.
- **Enrolled subjects**: Enrolled subjects are those who signed informed consent and met the inclusion/exclusion criteria.
- **Enrollment date**: Enrollment date is the date the subject was enrolled
- **Study day**: Study Day 1 is defined as the day of the earlier of the first administration of tab-cel or pembro. Study day is defined as the date of interest minus Study Day 1 + 1 if the date is on or after the first dose date. If the date is before Study Day 1, study day is defined as the date of interest minus Study Day 1. There is no Study Day 0.
- **Baseline:** Baseline in general refers to Study Day 1. The baseline value of a parameter (eg, vital signs, laboratory tests and efficacy endpoints) is defined as the last value on or prior to the day of the first IP administration.
- **Duration of treatment:** The duration of IP treatment is defined for tabelecleucel and pembrolizumab separately as the date of the last dose of IP minus the date of the first dose of IP + 1.
- **Treatment exposure period**: The treatment exposure period is defined for tabelecleucel and pembrolizumab together as the time from Study Day 1 through 30 days after the last administration of IP.
- **Year**: A year consists of 365.25 days
- **Month**: A month consists of 365.25/12 days
- **Week**: A week consists of 365.25/52 days

6.2 Hypothesis and/or Estimation

No hypothesis or estimation is planned on treatment efficacy endpoint for phase 1B section.

6.3 Missing Data Handling

In general, missing data will not be imputed; however, missing or partially missing start/end dates for events, such as AEs, concomitant medication use, and initial diagnosis date, will be imputed according to the rules outlined in Table 1. If an event is ongoing, the end date will not be imputed.

Table 1 Missing Imputation Rules

Missing variables	Missing Dates	Imputation method
Event start date	Only day is missing	If the month and year of the event start date are the same as those for Study Day 1, the imputed start date will be the same as that for Study Day 1. Otherwise, the imputed start date will be the first day of the known month.
	Both month and day are missing, but year is available	If the year of the event start date is the same as that for Study Day 1, the imputed event start date will be the same as that for Study Day 1. Otherwise, the imputed start date will be Jan 1st.
	Year, month, and day are missing, or only year is missing	No imputation
Event end date	Only day is missing	Impute the last day of the known month. If an event stop day is missing and the event stop month and year are the same as the death month and year, the imputed event stop date will be the date of death.
	Both month and day are missing, but year is available	Impute with min (the date of end of study, December 31 of the known year).
	Year is missing	No imputation
Initial diagnosis date	Only day is missing	Impute the first day of that month
	Both month and day are missing	Impute Jan 1st
	Year is missing	No imputation

6.4 Visit Window

6.5 Nominal visits will be used in the analysis, unless specified otherwise.Data Handling and Electronic Transfer of Data

Analysis Data Model (ADaM) data sets will be prepared for statistical analysis. ADaM data are derived from the Study Data Tabulation Model (SDTM) data. SDTM data are derived from raw data. Raw data consist of data from the electronic case report form (eCRF) and other external data (central/vendor laboratory generated data; imaging and laboratory data). Atara Clinical Data Management is responsible for the collection and receipt of eCRF and central vendor data. The Atara data management standard operating procedure (SOP) will be followed.

6.6 Validation of Statistical Analysis

The statistical analysis validation will follow the Atara's validation SOP.

7 STUDY SUBJECTS

7.1 Study Disposition

7.2 Subject disposition data will be summarized by sub cohort and overall (ie, all Phase 1B subjects combined); the summary table will include: the number of subjects screened, the number of subjects who failed screening, the number of subjects enrolled, the number of subjects enrolled but not treated, and the number of subjects treated. Treatment status (completed or discontinued) with reasons for treatment discontinuation and end of study status (completed vs. did not complete) with reasons for not completing the study will also be summarized by cohort and overall. Important Protocol Deviations

Important protocol deviations (IPDs) categories are defined by the study team before the first subject's visit and updated during the IPD reviews throughout the study. The categories will be finalized prior to database lock. IPD categories, deviation codes, and descriptions will be used during the course of the study. Subjects with IPDs will be listed with IPD categories, deviation codes, and descriptions.

7.3 Demographic and Baseline Characteristics

The following demographic and baseline characteristics will be summarized for the Full Analysis Set by sub-cohort and overall.

- Age at baseline: descriptive statistics and n (%) for Age categories such as < 16, ≥ 16 years and Age <18, ≥ 18 years
- Gender
- Ethnicity
- Race
- Eastern Cooperative Oncology Group (ECOG) performance status descriptive statistics and n (%)
- Time from initial diagnosis to first dose of tabelecleucel (months)
- NPC history factors will be also summarized in this table by n (%) on Lines of systemic treatment, overall disease stage; Distant metastasis; Tumor burden at baseline; Lesion location at baseline.

7.4 Prior therapy

Prior therapy will be summarized on Type of therapy, Chemotherapy category, Best Response to Prior therapies.

7.5 Extent of Exposure

Summary statistics will be provided for the exposure of pembrolizumab and tabelecleucel, including the total dose of pembrolizumab and the weight-adjusted dose of tabelecleucel, total number of doses administered, number of lots subjects received, number of cycles and duration of treatment, number of restriction switch will be summarized for tabelecleucel.

8 EFFICACY ANALYSES

The Full Analysis Set will be the primary analysis set for efficacy analyses.

Efficacy analyses will be conducted separately for subjects who are checkpoint inhibitor naïve or PD-1/PD-L1 failures. The disease assessments will be performed by the investigators.

The exact binomial 2-sided 95% CI will be provided for binary endpoints, ORR.

If any anti-NPC therapy other than specified in the protocol, is initiated, disease assessment data after the initiation date will be censored for the purpose of the efficacy analysis.

Subjects may have post-cycle 1 response of indeterminate response (IR). In the event that a subject with an IR assessment has discontinued the study and has not proceeded to a subsequent assessment (eg, subject is lost to follow up or dies), then the IR response will be considered as progressive disease. If a subject is still on study and has an IR assessment without a subsequent assessment, then the IR response will be considered as not evaluable (NE).

8.1 Analysis of the Primary Endpoint

8.1.1 Primary Analysis

The incidence of DLTs (defined in section 5.2.3 of the protocol) will be evaluated for phase 1B part of the study from the subjects in Cohort 1 (by dose level if applicable).

The primary endpoint is ORR (overall response rate), responder is defined as the proportion of subjects who achieved Best Overall Response (BOR) of CR or PR after administration of up to the first 2 tabelecleucel cell products, clinical benefit is defined as the proportion of subjects who achieved Best Overall Response (BOR) of CR or PR or SD after administration of up to the first 2 tabelecleucel cell products. If any new anti-NPC treatment, other than specified in the protocol,

is initiated, response data after the initiation date will not be considered for the definition of response. Disease assessment during the follow-up stage will not be considered for ORR or CBR definition.

The ORR and CBR (clinical benefit response) and their corresponding 95% CI will be reported.

9 PHARMACOKINETIC/PHARMACODYNAMIC ANALYSIS

No pharmacokinetic/pharmacodynamic analysis is planned.

10 BIOMARKERS

No biomarker analysis is planned.

11 SAFETY ANALYSES

11.1 Summary of Adverse Events

MedDRA version 24.0 or later will be used to code AEs to a system organ class (SOC) and a PT within the SOC. The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 will be used to grade severity of AEs. For certain AEs for which CTCAE does not apply, non-CTCAE grades will be applied. The severity grade of non-CTCAE graded AEs are mapped using the following rules and then summarized together with CTCAE graded AEs: mild (grade 1), moderate (grade 2), severe (grade 3), life-threatening (grade 4), or death (grade 5). In addition, for graft-versus-host disease (GvHD), the Center for International Blood and Marrow Transplant Research (CIBMTR) consensus grading system will be used. CIBMTR grading includes an overall grade and separate grades based on rash status, bilirubin level, diarrhea status, and nausea status.

TEAEs are defined as follows:

- Any AE occurring after initiation of the first dose of study treatment through 30 days after the last administration of study treatment or
- Any pre-existing AE (ie, started prior to the first dose of study treatment) that worsened after the first dose through 30 days after the last administration of study treatment or
- Any related AE on or after first dose.

AEs occurring on the same day of the first dose of study treatment will be counted as TEAEs. AEs with complete or partial missing start/end dates will be all considered as treatment-emergent unless

- The partial start date is clearly after the 30 days of the last dose of study treatment. For example, last dose date + 30 days is in November and the AE start date is in the next January with the day missing.

or

- The partial end date is clearly before the first dose date of study treatment. For example, the first dose date is in March while the AE end date is in February with the day missing.

Imputation rules for partial missing dates may be applied to TEAE start/end dates, as described in Section 7.3.

All the AEs collected in this study (whether or not treatment-emergent) will be listed; TEAEs will be summarized as follows:

- Overall Summary of AE including
  - Any TEAEs
  - TEAEs with worst grade ≥ 3
  - Fatal TEAEs
  - Serious TEAEs
  - TEAEs leading to any study treatment discontinuation
  - TEAEs leading to any study treatment interruption
  - The above summaries will be repeated for TEAEs that are related or possibly related to study treatment pembrolizumab or tabelecleucel respectively.
- By SOC and PT, sorted by alphabetic order of SOC, then by descending order of PT total frequency
  - Subject incidence of all TEAEs
  - Subject incidence of serious TEAEs
- By PT, sorted by descending order of PT frequency and then by alphabetic order of PT.
  - Subject incidence of TEAEs
  - Subject incidence of serious TEAEs
  - Subject incidence of TEAEs leading to death
  - Subject incidence of TEAEs leading to pembrolizumab or tabelecleucel discontinuation
  - Subject incidence of treatment related TEAEs
  - Subject incidence of treatment related serious TEAEs

  - Subject incidence of treatment related TEAEs leading to pembrolizumab or tabelecleucel discontinuation

- By preferred term and worst severity grade
  - Subject incidence of TEAEs
  - Subject incidence of serious TEAEs
  - Subject incidence of treatment related TEAEs
  - Subject incidence of treatment related serious TEAEs
- A summary table of identified and potential risks including TEAEs of special interest (TEAESIs) by PT sorted by risk category and PT in descending order of frequency within a risk category. The Risk categories for tabelecleucel include:
  - infusion-related reactions
  - transmission of infectious disease(s)
  - cytokine release syndrome
  - GvHD event
  - And additional risk of tumor flare.
- A summary table of TEAEs of special interest (TEAESIs) by PT sorted by PT in descending order of frequency for Pembrolizumab include:
  - Overdose- >1000 mg or >/= 5 times the indicated dose
  - Elevated liver values per Pembro label
- A summary table of TEAEs of dose limiting toxicity by PT in descending order of frequency.

The primary cause of all deaths will be summarized.

A listing of all deaths, serious TEAE, and TEAE leading to treatment or study discontinuation, or leading to death will be provided.

11.2 Summary of Laboratory Results

Routine clinical laboratory data (ie, hematology and serum chemistry) will be processed by local laboratories and entered directly into the electronic data capture system by site users. Atara Biotherapeutics will convert the original test results/units to standard and conventional results/units and grade lab test results based on the CTCAE version 5.0 grading and corresponding normal ranges for the lab parameters.

In case the lab test result is less than the lower limit of quantification (LLOQ), a value of half the LLOQ will be used for analysis and summary. If the lab test result is greater than the upper limit of quantification (ULOQ), the ULOQ will be used for analysis and summary. Lab test normal

range from University of California at San Francisco (UCSF) Clinical Laboratories Online Manual standards will be adapted.

11.2.1 General presentation of laboratory data

Descriptive summaries of laboratory data will be provided for the Full Analysis Set and will include only data collected up to the last dose of study treatment plus 30 days.

For selected lab parameters, summaries of actual values, changes from baseline and percent changes from baseline for the postbaseline laboratory data will be presented for each scheduled assessment time point. Minimum and maximum post baseline values will be summarized. In the case of multiple values at the same visit, the assessment closest to the corresponding previous dose date will be used for summary purposes, unless specified otherwise. If either the baseline or post-baseline value is missing, the observation will not be included in the change from baseline summary.

In addition, grade shifts from baseline to the worst on-treatment value will be summarized for selected lab parameters.

For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately.

Laboratory test results at unscheduled visits will be included in the summary of minimum and maximum post baseline values and the worst post baseline grade, but not in the by-visit summary.

11.2.2 Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase by at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study treatment plus 30 days. If the relevant baseline laboratory value is missing, any abnormality of at least grade 1 observed within the time frame specified above will be considered treatment-emergent.

Treatment-emergent laboratory abnormalities will be summarized for the selected laboratory parameters.

11.3 Exposure to Concomitant Medication, and Subsequent anti-NPC Therapy

The number (%) of subjects who received each concomitant medication will be summarized by preferred term as coded by the World Health Organization Drug (WHODRUG) dictionary. The number (%) of subjects who receive subsequent anti-NPC therapies will also be summarized if data are available.

Concomitant medication: A concomitant medication is any medication except study treatment taken during the treatment period. All medications will be considered as concomitant medication unless

- The complete or partial medication start date is clearly after the last dose of study treatment

or

- The complete or partial medication end date is clearly before the first dose date of study treatment

11.4 Other Safety Summaries

The results of the screening serum pregnancy test will be listed. In the event of any pregnancy reported while on-treatment or during follow-up, the relevant dates and outcome will be listed.

Descriptive statistics for vital signs will be summarized with observed value, change from baseline and percentage change from baseline by scheduled assessment time points. A listing will be provided for all vital signs data collected during the study.

ECOG performance status scores will be summarized by baseline score and worst postbaseline score.

APPENDIX: SUMMARY OF LAB TESTS

Lab Test	Lab Test with CTCAE Grading	Summary of Abnormality & Shift Table	Summary of Lab Test Value by visit
LEUKOCYTES	decreased	Y	Y
PLATELETS	decreased	Y	Y
ABSOLUTE NEUTROPHIL	decreased	Y	Y
ABSOLUTE LYMPHOCYTE	increased and decreased	Y	Y
LACTATE DEHYDROGENASE (LDH)			Y
HEMOGLOBIN	decreased	Y	Y
ABSOLUTE MONOCYTES			Y
ABSOLUTE EOSINOPHILS			Y
ABSOLUTE BASOPHILS			Y
CREATININE	increased	Y	Y
TOTAL BILIRUBIN	increased	Y	Y
ASPARTATE AMINOTRANSFERASE (AST)	increased	Y	Y
ALANINE AMINOTRANSFERASE (ALT)	increased	Y	Y
ALKALINE PHOSPHATASE (ALK)	increased	Y	Y