TRANSLATIONAL STATISTICAL ANALYSIS PLAN
KT-US-482-0137

Sponsor:	Kite Pharma, Inc. 2400 Broadway Santa Monica, CA 90404 United States of America
Product Name:	Axicabtagene Ciloleucel
Protocol:	Phase 2 Open-Label, Multicenter Study Evaluating the Safety and Efficacy of Axicabtagene Ciloleucel Concomitant with Prophylactic Steroids in Subjects with Relapsed or Refractory Large B-Cell Lymphoma in the Outpatient Setting
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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AE	adverse event
Axicabtagene ciloleucel KTE-C19	Autologous T cells transduced with retroviral vector containing CD28/CD3 zeta chimeric antigen receptor
AUC	area under the curve
CAR	chimeric antigen receptor
CR	complete response / complete Remission
CRS	cytokine release syndrome
CSF	cerebrospinal fluid
ddPCR	droplet digital polymerase chain reaction
ECOG	eastern cooperative oncology group
IHC	immunohistochemistry
LLOQ	lower limit of quantitation
MRD	minimal residual disease
NE	neurologic event
NHL	non-Hodgkin lymphoma
ORR	objective response rate
PBMC	peripheral blood mononuclear cells
PD	progressive disease
PR	partial response
RCR	replication competent retrovirus
SAE	serious adverse event
SD	stable disease
SOA	schedule of assessments
TSAP	translational statistical analysis plan

1. INTRODUCTION

This translational statistical analysis plan (TSAP) provides the specification and details for the statistical analyses for translational data to support the protocol KT-US-482-0137 Amendment 2, A Phase 2 Open-Label, Multicenter Study Evaluating the Safety and Efficacy of Axicabtagene Ciloleucel Concomitant with Prophylactic Steroids in Subjects with Relapsed or Refractory Large B-Cell Lymphoma in the Outpatient Setting dated 29 March 2024. The scope of this plan includes the primary and final analyses.

Translational data includes but is not limited to the following data: pharmacokinetic (PK) data, pharmacodynamic (PD) data, and product characteristics.

The clinical safety and efficacy data analysis will be described in a separate document (i.e., clinical SAP).

2. OBJECTIVES

2.1. Objectives

- Characterize the presence, expansion, and persistence of CAR T cell in blood after treatment of axicabtagene ciloleucel (pharmacokinetic [PK] profile)
  - Explore associations between PK profile and clinical efficacy and safety outcomes
- Characterize the levels of serum cytokines at baseline, and before and after treatment of axicabtagene ciloleucel (pharmacodynamic [PD] profile)
  - Explore associations between of serum cytokine profile (peak/area under the curve [AUC]) versus PK and safety outcomes
- Characterize key product attributes
  - Explore association between key product attributes and PK, PD, clinical efficacy, and safety outcomes

2.2. Hypothesis

The analyses outlined in this TSAP are exploratory and no formal pre-specified hypothesis will be test.

3. ENDPOINTS, SUBGROUPS AND COVARIATES

3.1. Datasets to be Included

Table 3-1. Data Overview on Assay Methods and Biomarker Lists

Data Type	Assay Method/ Sample Type	Biomarker Set	Assessment Time Points
PK data	ddPCR/PBMC	Number of CAR T cells (/µL)	Outlined in **Error! Reference source not found.**
PD data	Cytokines assay/serum and CSF samples	CSF and serum levels of the following key cytokines, chemokines, and immune effector molecules will be reported: CRP, Ferritin, Granzyme A, Granzyme B, ICAM-1, IFN-γ, IL-1RA, IL-2, IL-2Rα, IL-6, IL-7, IL-8, IL-10, IL-15, TNF-α, VCAM-1. See complete list of serum and CSF cytokines in Appendix 8.4.	Outlined in **Error! Reference source not found.**
Phenotype data	T Cell Phenotyping with Flow Cytometry Panel	The following tests are included as part of Product Characteristics CD3+/ Viable CD3+ T Cells (%) CD3+CD4+/ Viable CD4+ T Cells (%) CD3+CD8+/ Viable CD8+ T Cells (%) CD3+CD45RA-CCR7+/ Viable Central Memory T Cells (%) CD3+CD45RA+CCR7-/ Viable Effector T Cells (%) CD3+CD45RA-CCR7-/ Viable Effector Memory T Cells (%) CD3+CD45RA+CCR7+/ Viable Naïve T Cells (%)	Not Applicable
Product characteristics		Selected product characteristics are provided in Appendix 8.4.	Not Applicable

Abbreviations: CAR, chimeric antigen receptor; CRP, C-reactive protein; ICAM, intercellular adhesion molecule; IFN, interferon; IL, interleukin; IL-1RA, interleukin-1 receptor antagonist; IL-2Rα, interleukin-2 receptor alpha; PBMC, peripheral blood mononuclear cell; ddPCR, droplet digital polymerase chain reaction; TNF, tumor necrosis factor; VCAM, vascular cell adhesion molecule.

3.2. Endpoints

Only the endpoints for translational data analysis are described in the TSAP. Clinical primary, secondary, and exploratory endpoints are described in a separate clinical SAP.

- Levels of CAR T cells in blood samples measured as CAR T cells/µL by visit, peak, area under the curve (AUC) (from infusion to Day 28 post-infusion), and time-to-peak (details for the derivations are included in the definition Section **Error! Reference source not found.**)

- Levels of cytokines in serum by visit; change from baseline at Day 0, Day 1, Day 3, Day 5 Day 7, Day 10, Week 2, and Week 4; fold change from baseline at Day 0, Day 1, Day 3, Day 5 Day 7, Day 10, Week 2, and Week 4; peak, AUC (from infusion to Day 28 post-infusion), and time-to-peak (details for the derivations are included in the definition Section **Error! Reference source not found.**)

- Product attributes measurements after product manufacturing and prior to dosing

3.3. Outcomes, Subgroups, and Covariates

- Efficacy endpoints:

  — Objective response: Responders (complete response [CR] + partial response [PR]) vs Nonresponders (stable disease [SD] + progressive disease [PD])

  — Best overall response: CR vs PR vs Nonresponders

  — Ongoing response: Responder and Ongoing vs Responder and Relapsed vs Nonresponders

  — Progression-free survival (PFS)

  — Even-free-survival (EFS)

  — Overall survival (OS)

- Safety endpoints:

  — Worst grade of neurologic event (NE): Grade 3 or higher vs Grade 2, Grade 1, or None

  — Worst grade of cytokine release syndrome (CRS) event: Grade 3 or higher vs Grade 2, Grade 1, or None

- Subgroups/baseline covariates for PK summaries

  — Eastern Cooperative Oncology Group (ECOG) performance status at baseline (0, 1)

  — Age (in years) at baseline (< 65, ≥ 65)

  — Sex (Male, Female)

  — Disease type

  — Disease stage

Covariate levels that are sparse may be collapsed for purposes of statistical modeling.

Additional associative analyses of covariates with subject outcomes may be explored.

4. DEFINITIONS

The definitions related to translational data analysis included in the TSAP are described below. For the definitions related to efficacy or safety analysis, please refer to the clinical SAP.

4.1. General

Study enrollment date: Study enrollment date is defined as the day when a subject commences leukapheresis.

Study Day 0: Study Day 0 is defined as the day the subject received the first axicabtagene ciloleucel infusion. The day before Study Day 0 will be Study Day −1. The day of enrollment and any days after enrollment and before Study Day −1 will be sequential and negative integer valued.

Baseline: The baseline value is defined as the last non-missing value taken prior to conditioning chemotherapy. For subjects without conditioning chemotherapy date, the baseline value is taken as the last non-missing value on the study. Baseline of cytokines is defined in Section 4.3.

Retreatment period: (defined only for subjects who undergo retreatment with axicabtagene ciloleucel): the retreatment period starts on the earliest date of the re-leukapheresis, the lymphodepleting chemotherapy for retreatment, and the retreatment of axicabtagene ciloleucel.

Retreatment baseline: Baseline for retreatment is defined as the last assessment taken before the earliest of the re-leukapheresis, the lymphodepleting chemotherapy for retreatment, and the retreatment of axicabtagene ciloleucel.

Actual follow-up time: Actual follow-up time among all subjects treated with axicabtagene ciloleucel is calculated as the time from the first infusion of axicabtagene ciloleucel to the date of death or last date known to be alive, whichever is later.

Potential follow-up time: Potential follow-up time is defined as the time from the first infusion of axicabtagene ciloleucel to the data cutoff date for the analysis.

Study therapy: Study therapy includes bridging chemotherapy, conditioning chemotherapy and axicabtagene ciloleucel infusion.

4.2. Pharmacokinetic: CAR T Cells Levels over Time

The expansion and persistence of CAR T cells in peripheral blood will be measured by droplet digital polymerase chain reaction (ddPCR) assay. Calculation of number of CAR T Cells in blood is described in Appendix 8.7.

Scheduled blood draw for CAR T cells
This TSAP will focus on the CAR T cells data collected as per planned assessment. The schedule of assessments and the analytic visit windows are defined in Appendix 8.1.

Baseline number of CAR T cells (cells/µL) is defined as 0 since the axicabtagene ciloleucel infused in Day 0, and number of CAR T cells will not be derived.

Peak of CAR T cells (cells/uL) is defined as the maximum absolute number of CAR T cells in serum attained after Day 0.

Time-to-Peak of CAR T cells (days) is defined as "peak date – axicabtagene ciloleucel infusing date + 1".

Area-Under-Curve (AUC) of level of CAR T cells (cells/ uL ▪ days) is defined as the area under the curve in a plot of levels of CAR T cells against scheduled visits from Day 0 to Day 28. This AUC measures the total levels of CAR T cells overtime. Given the CAR T cells is measured at certain discrete time points, the trapezoidal rule as described in Appendix 8.6 will be used to estimate the AUCs.

4.3. Pharmacodynamic: Serum Cytokines over Time

Scheduled blood draw for serum cytokines: Blood draws for cytokines will be collected at

- Within approximately 5 days of eligibility confirmation (Enrollment/Leukapheresis) as baseline,
- Day 0, Day 1, Day 3, Day 5, Day 7, Day 10, Week 2 (± 2 days), Week 4 (± 3 days).

The Schedule of Assessment and analytic visit window is defined in Appendix 8.2.

Baseline of cytokines is defined as the value measured on Enrollment/Leukapheresis.

Fold change from baseline at Day X is defined as

$$\frac{\text{Cytokine level at Day X}}{\text{Cytokine level at Baseline}}$$

Peak of cytokine post baseline is defined as the maximum level of cytokine in serum attained after baseline up to Day 28.

Time-to-Peak of cytokine post axicabtagene ciloleucel infusion is defined as "peak date – axicabtagene ciloleucel infusing date + 1".

Area-Under-Curve (AUC) of cytokine levels from baseline to Day 28: is defined as the area under the curve in a plot of levels of cytokine against scheduled visits from baseline to Day 28. This AUC measures the total levels of cytokine between baseline and day 28. Given the cytokine is measured at certain discrete time points, the trapezoidal rule will be used to estimate the AUCs.

4.4. Pharmacodynamic: CSF Cytokines

Scheduled blood draw for CSF cytokines: Blood draws for cytokines will be collected at

- Within approximately 5 days of eligibility confirmation (Enrollment/Leukapheresis) as baseline,
- Week 4 (± 3 days),
- Disease progression as needed.

4.5. Product Characteristics

Selected product characteristics as defined in Table 3.1 and Appendix 8.4 will be summarized individually and also analyzed for the correlative analysis with CAR T levels in blood and clinical outcome endpoints.

5. ANALYSIS SETS

Only analysis sets that will be used for translational data analysis included in the TSAP are described below.

Generally, this TSAP will utilize the same efficacy analysis strategies, including analysis sets and outcome definitions, as described in the clinical Statistical Analysis Plan.

5.1. Full Analysis Set

The Full analysis set consists of all enrolled subjects.

5.2. Safety Analysis Set

The Safety Analysis Set consists of all subjects who were treated with any dose of axicabtagene ciloleucel.

The Safety Analysis Set will be the primary analysis set used to summarize the translational data among evaluable samples and to explore the association between translational data and clinical efficacy and safety outcomes covered in this TSAP.

6. STATISTICAL ANALYSIS

6.1. General Statistical Methods

The following methods will be applied to the data analysis when applicable. All p-values generated will be descriptive.

- **Summary statistics** will be generated in frequency (n, %) and quartile range (minimum, 1st quartile [Q1], median, 3rd quartile [Q3], maximum) overall and by appropriate subgroups and covariates (Section **Error! Reference source not found.**)

- **Simple linear regression (SLR)** will be conducted to explore relationships between biomarkers with continuous values {Gelman 2006}. The estimated slope and its 95% confidence interval (CI) with the unadjusted p-value will be reported.

- **Nonparametric Wilcoxon rank sum tests**
  Nonparametric Wilcoxon rank sum tests {Siegel 1956, Wilcoxon 1945} will be utilized to explore the associations between CAR T pharmacokinetics/pharmacodynamics, product characteristics, and outcomes. Unadjusted p-values will be reported. The multiplicity adjustment (Holm-Bonferroni step-down method) {Holm 1979, Hommel 1988} may be implemented when further characterization of potential associations are identified, and adjusted p-values will be reported. Median fold change will be utilized to describe the differences in the outcome.

- **Nonparametric Kruskal-Wallis test**
  Nonparametric Kruskal-Wallis test {Kruskal 1952} will be conducted for comparison of three or more groups followed by pairwise comparisons using Dunn's test with Holm's adjustment method {Dunn 1964}

- **Clopper Pearson Method** will be used to calculate exact 95% CIs for objective response rate (ORR) and complete response rate {Brown 2002}

6.2. Handling for Limit of Quantification Values (LOQ)

For cytokines with values below the lower limit of quantifications (LLOQs) reported as "<LLOQ" will be assigned to LLOQ/2.

For cytokines with multiple upper limit of quantifications (ULOQs) reported as ">ULOQ1", ">ULOQ2" etc., minimum ULOQ value denoted as MINULOQ = min(ULOQ1, ULOQ2,…) will be assigned to all values above the min(ULOQ1, ULOQ2, …). This can include text values (reported as >ULOQ) or numeric values that fall between multiple set of ULOQs.

6.3. Pharmacokinetics and Pharmacodynamics Analysis

6.3.1. Characterize the CAR T Cell Expansion (PK) and Serum Cytokine (PD) Profiles

- The safety analysis set will be used.
- A median line plot over time with interquartile range (IQR) will be produced.
- The CAR T cell profile (PK) over time, AUC, Peak, and Time-to-Peak will be summarized using summary statistics described in Section **Error! Reference source not found.**.
- The CAR T cell profile (PK) over time, AUC, Peak, and Time-to-Peak, by subgroup and baseline covariates specified in Section 3.3 will be summarized using summary statistics described in Section **Error! Reference source not found.**.
- The serum cytokine PD profile as measured by serum cytokine levels over time, AUC, Peak, and Time-to-Peak will be summarized using summary statistics described in Section **Error! Reference source not found.**.

6.3.2. Explore the Association Between PK Profile and Clinical Response Outcomes

- The safety analysis set will be used to analyze the correlation between CAR T cells and clinical response outcomes.
- The Wilcoxon rank sum test and Kruskal-Wallis test will be used to compare the PK profile among the categorical clinical outcomes. Following a significant Kruskal-Wallis test, a pairwise comparisons through Dunn's test with Holm's adjustment method will be conducted. See Table 6-1 for details.
- The Cox proportional hazard (PH) model (unstratified) will be conducted to estimate the hazard ratios and 2-sided 95% CIs with the associated p-values for time-to-event outcomes (e.g., EFS, PFS, DoR, and OS) and PK profile. See Table 6-1 for details.

Table 6-1. Associations Between PK Profiles and Clinical Response Outcomes

Outcome	Method	Key Measurements	
		CAR T Cell Expansion in Blood	Cytokine Levels in Serum
Objective Response		AUC Peak	NA
Responders (CR+PR) vs Nonresponders (SD+PD)	Wilcoxon rank sum test		
Durability of Response			
Responder and Ongoing vs Responder and Relapsed vs Nonresponders	Kruskal-Wallis test		
Responder and Ongoing vs Responder and Relapsed	Wilcoxon rank sum test		

Outcome	Method	Key Measurements	
		CAR T Cell Expansion in Blood	Cytokine Levels in Serum
Responder and Ongoing vs Nonresponders	Wilcoxon rank sum test		
Responder and Relapsed vs Nonresponders	Wilcoxon rank sum test		
Best Ovearll Response			
CR vs PR vs Nonresponders	Kruskal-Wallis test	AUC Peak	NA
CR vs PR	Wilcoxon rank sum test		
CR vs Nonresponders	Wilcoxon rank sum test		
PR vs Nonresponders	Wilcoxon rank sum test		
Time-to-Event Outcome			
EFS	Cox PH model (unstratified)	AUC Peak	NA
PFS	Cox PH model (unstratified	AUC Peak	NA
OS	Cox PH model (unstratified)	AUC Peak	NA
DoR	Cox PH model (unstratified)	AUC Peak	NA

Abbreviations: AUC, area under the curve; CAR, chimeric antigen receptor; CR, complete response; EFS, event-free survival; PFS, progression-free survival; OS, overall survival; NA, Not Applicable; PR, partial response; SD, stable disease; vs, versus.

6.3.3. Explore the Association Between PK Profile, PD Profile, and Safety Outcomes

- The safety analysis set will be used to explore the association between PK profile, PD (serum cytokines only) profiles and safety outcomes.
- Safety outcomes in this TSAP refer to the following:
  - Worst grade of NE
    - Grade 3 or higher vs Grade 2, Grade 1, or None
    - Grade 2 or higher vs Grade 1, or None
  - Worst grade of CRS event
    - Grade 3 or higher vs Grade 2, Grade 1, or None

- Grade 2 or higher vs Grade 1, or None

- The Wilcoxon rank sum test will be used to compare PK and PD (serum cytokines only) profiles by safety outcomes (Table 6-2).

Table 6-2. Associations Between PK/PD Profiles and Safety Outcomes

Outcome	Subgroups	Method	Key Measurements	
			CAR T Cell Expansion in Blood	Cytokine Levels in Serum
Worst Grade of CRS Event	Grade 3 or higher vs Grade 2, Grade 1 or None Grade 2 or higher vs Grade 1 or None	Wilcoxon rank sum test	AUC Peak	Baseline, Day 0, AUC Peak
Worst Grade of Neurologic Event	Grade 3 or higher vs Grade 2, Grade 1 or None Grade 2 or higher vs Grade 1 or None	Wilcoxon rank sum test	AUC Peak	Baseline, Day 0, AUC Peak

Abbreviations: AUC, area under the curve; CRS, cytokine release syndrome

6.4. CSF Cytokine Analysis

- CSF cytokines analytes are the same as serum cytokine analytes.

- CSF cytokine analytes will be listed only.

6.5. Product Characteristics Analysis

6.5.1. Characterize Product Attributes

- The safety analysis set will be used to summarize the product attributes data.

6.5.2. Explore the Association between Product Attributes and PK Profile

- The safety analysis set will be used to explore the association between product attributes and CAR T cells.

- Quartile analysis, correlation analysis (e.g., Spearman correlation), and the simple linear regression model will be used to summarize the association between product attributes versus peak/AUC of CAR T-cell levels.

- Scatter plots with fitted line will also be generated.

6.5.3. Explore the Association Between Product Attributes and Clinical Efficacy and Safety Outcomes

- The safety analysis set will be used to explore the association between product attributes and clinical and safety outcomes.
- Quartile descriptive analysis will be used to summarize the observed rates of following clinical and safety outcomes by quartiles and medians of product analytes:
  - Objective response: Responders (CR+PR) vs Nonresponders (SD+PD)
  - Best overall response: CR vs PR vs Nonresponder (SD+PD)
  - Ongoing response: Responder and Ongoing vs Responder and Relapsed vs Nonresponder (SD+PD)
  - Worst grade of NE: Grade 3 or higher vs Grade 2, Grade 1, or None
  - Worst grade of CRS event: Grade 3 or higher vs Grade 2, Grade 1, or None

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8. APPENDIX

8.1. Definition of Analytic Visit Windows for CAR T Cells in Blood

Table 8-1. Analytic Visit Windows for CAR T Cells in Blood

Analytic Visit	Baseline	Day 1	Day 3	Day 7	Day 10	Week 2	Week 4	Month 3
Target Day	0	1	3	7	10	14	28	90
Analysis Visit Window	<= 0	[1]	[2, 5]	[6, 8]	[9, 12]	[13, 21]	[22, 59]	[60, 135]

Analytic Visit	Month 6	Month 9	Month 12	Month 18	Month 24
Target Day	180	270	360	540	720
Analysis Visit Window	[136, 225]	[226, 315]	[316, 450]	[451, 630]	>= 631

8.2. Definition of Analytic Visit Windows for Serum Cytokines

Table 8-2. Analytic Visit Windows for Serum Cytokines

Analytic Visit	Baseline	Day 0	Day 1	Day 3	Day 5	Day 7	Day 10	Week 2
Target Day	Baseline	0	1	3	5	7	10	14
Analysis Visit Window	<= -5	0	[1, 2]	[3, 4]	[5, 6]	[7, 8]	[9, 12]	[13, 21]

Analyti Visit	Week 4
Target Day	28
Analysis Visit Window	>=22

8.3. Serum and CSF Cytokines

Table 8-3. List of Serum and CSF Cytokine Analytes

Analytes	Label
Angiopoietin-1 (pg/mL)	ANG-1 (pg/mL)
Angiopoietin-2 (pg/mL)	ANG-2 (pg/mL)
CD95 Ligand Ella (pg/mL)	CD95 Ligand Ella Assay (pg/mL)
C Reactive Protein (mg/L)	CRP (mg/L)
Cytotoxic T-lymphocyte-associated protein 4 (pg/mL)	CTLA-4 (pg/mL)
Chemokine (C-X-C Motif) Ligand 10 (pg/mL)	CXCL10 (pg/mL)
Ferritin (ng/mL)	Ferritin (ng/mL)
Granulocyte Macrophage Colony Stm Factor (pg/mL)	GM-CSF (pg/mL)
Glycoprotein 130 (pg/mL)	GP 130 (pg/mL)
Granzyme A Ella (pg/mL)	Granzyme A Ella Assay (pg/mL)
Granzyme B Ella (pg/mL)	Granzyme B Ella Assay (pg/mL)
Intercellular Adhesion Molecule 1 (ng/mL)	ICAM-1 (ng/mL)
Interferon Gamma (pg/mL)	IFN-gamma (pg/mL)
Interleukin 1 Receptor Antagonist (pg/mL)	IL-1 RA (pg/mL)
Interleukin 1 Alpha (pg/mL)	IL-1 alpha (pg/mL)
Interleukin 1 Beta (pg/mL)	IL-1 beta (pg/mL)
Interleukin 10 (pg/mL)	IL-10 (pg/mL)
Interleukin 12+23 p40 (pg/mL)	IL-12 P40 (pg/mL)
Interleukin 12 (pg/mL)	IL-12 P70 (pg/mL)
Interleukin 13 (pg/mL)	IL-13 (pg/mL)
Interleukin 15 (pg/mL)	IL-15 (pg/mL)
Interleukin 16 (pg/mL)	IL-16 (pg/mL)
Interleukin 17 (pg/mL)	IL-17 (pg/mL)
Interleukin 18 (pg/mL)	IL-18 (pg/mL)
Interleukin 2 (pg/mL)	IL-2 (pg/mL)
Interleukin 2 Receptor Alpha (ng/mL)	IL-2 R alpha (ng/mL)
Interleukin 4 (pg/mL)	IL-4 (pg/mL)
Interleukin 5 (pg/mL)	IL-5 (pg/mL)
Interleukin 6 (pg/mL)	IL-6 (pg/mL)
Interleukin 6 Receptor Alpha (pg/mL)	IL-6 RA (pg/mL)
Interleukin 7 (pg/mL)	IL-7 (pg/mL)
Interleukin 8 (pg/mL)	IL-8 (pg/mL)
Lymphocyte-activation gene 3 (pg/mL)	LAG-3 (pg/mL)
Monocyte Chemotactic Protein 1 (pg/mL)	MCP-1 (pg/mL)
Monocyte Chemotactic Protein 4 (pg/mL)	MCP-4 (pg/mL)
Macrophage-Derived Chemokine (pg/mL)	MDC (pg/mL)

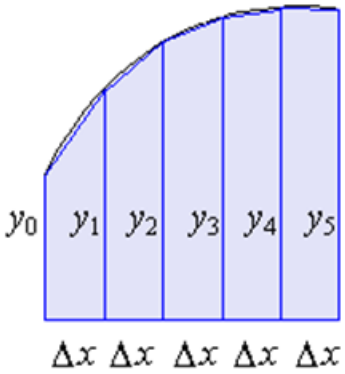
Analytes	**Label**
Macrophage Inflammatory Protein 1 Alpha (pg/mL)	MIP-1 alpha (pg/mL)
Macrophage Inflammatory Protein 1 Beta (pg/mL)	MIP-1 beta (pg/mL)
Programmed Death Ligand 1 (pg/mL)	PDL1 (pg/mL)
Perforin (ng/mL)	Perforin (ng/mL)
Regulated upon Activation, Normal T Cell Expressed and Persumably Secreted (pg/mL)	RANTES (pg/mL)
Amyloid A (pg/mL)	SAA (pg/mL)
Chemokine (C-C Motif) Ligand 17 (pg/mL)	TARC (pg/mL)
TEK Tyrosine Kinase (pg/mL)	TIE-2 (pg/mL)
Tumor Necrosis Factor Alpha (pg/mL)	TNF alpha (pg/mL)
Tumor Necrosis Factor Beta (pg/mL)	TNF beta (pg/mL)
TNF-related apoptosis-inducing ligand (pg/mL)	TRAIL (pg/mL)
Vascular Cell Adhesion Molecule 1 (ng/mL)	VCAM-1 (ng/mL)
Vascular Endothelial Growth Factor (pg/mL)	VEGF (pg/mL)

8.4. Product Characteristics

Table 8-4. List of Product Characteristics

Data Source	Analytes	Label
phenotyp_prod	CD3+	Viable CD3+ T Cells (%)
phenotyp_prod	CD3+CD4+	Viable CD4+ T Cells (%)
phenotyp_prod	CD3+CD8+	Viable CD8+ T Cells (%)
phenotyp_prod	CD3+CD45RA-CCR7+	Viable Central Memory T Cells (%)
phenotyp_prod	CD3+CD45RA+CCR7-	Viable Effector T Cells (%)
phenotyp_prod	CD3+CD45RA-CCR7-	Viable Effector Memory T Cells (%)
phenotyp_prod	CD3+CD45RA+CCR7+	Viable Naïve T Cells (%)
Derived		Number of CD3+ T Cells (10^6)
Derived		Number of CD4+ T Cells (10^6)
Derived		Number of CD8+ T Cells (10^6)
Derived		Number of Central Memory T Cells (10^6)
Derived		Number of Effector T Cells (10^6)
Derived		Number of Effector Memory T Cells (10^6)
Derived		Number of Naïve T Cells (10^6)
pct	Viability	Viability (%)
pct	Transduction Efficiency	Transduction (%)
pct	Actual Patient Weight	Patient Weight (kg)
pct	Manufacturing Dose Produced	Manufacturing Dose Produced (10^6 cells/kg)
pct	Interferon Gamma by Co-culture	IFN-Gamma by Co-culture (pg/mL)
pct	Fold Expansion per Day	Fold Expansion per Day
pct	Total CAR+ Cells in the Final Product	Total CAR+ T Cells (10^6)
Derived		Total T Cells (10^6)
Derived		VCN of Product Normalized by Transduction Rate (copies per Td cells)
Derived		Total Cells (10^6)

8.5. Trapezoidal Rule for AUC Estimation



$$\text{AUC} \approx \frac{1}{2}(y_0 + y_1) \cdot \Delta x + \frac{1}{2}(y_1 + y_2) \cdot \Delta x + \frac{1}{2}(y_2 + y_3) \cdot \Delta x + \ldots$$

8.6. Number of CAR T in Blood (cells/µL)

Table 8-5. Derivation of Number of CAR T in Blood

Variable	Formula	Data Source
Alpha	Vector Copy Number in PBCM (ddPCR)	P:\stat_prog\KTE-C19\KT-US-482-0137\analysis\Biomarker_live\data\raw_cdms\ddpcr.sas7bdat where SPEC= 'ddPCRbld' and TESTNAME= 'VCN'
Beta	Vector Copy Number of product (ddPCR) / Transduction of product (%)	P:\stat_prog\KTE-C19\KT-US-482-0137\analysis\Biomarker_live\data\raw_cdms\ddpcr.sas7bdat where SPEC= 'Product' and TESTNAME= 'VCN' P:\stat_prog\KTE-C19\KT-US-482-0137\analysis\Biomarker_live\data\raw_cdms\pct.sas7bdat where BATTNAM= 'Transduction Efficiency'
% CAR+PBMC	Alpha/Beta	Derived
nCART (/µL)	1000*(WBC[10^9/L])*(MONOLE[%]+LYMLE[%])/100*CAR+PBMC[%]/100	Central lab: WBC, MONOLE, LYMLE