Sponsor:	Kite Pharma, Inc. 2400 Broadway Santa Monica, CA 90404 United States of America
Product Name:	**Axicabtagene ciloleucel**
Protocol	**A Phase 2 Multicenter Study Evaluating the Efficacy and Safety of Axicabtagene Ciloleucel as First-Line Therapy in Subjects with High-Risk Large B-Cell Lymphoma (ZUMA-12)**
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CONFIDENTIALITY NOTICE

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
ADaM	Analysis data model
AE	Adverse event
ASCT	Autologous stem cell transplant
BOR	Best overall response
BSA	Body surface area
CAR	Chimeric antigen receptor
CI	Confidence Interval
CNS	Central nervous system
CR	Complete response
CRF	Case report form
CRS	Cytokine release syndrome
CSF	Cerebrospinal fluid
CSR	Clinical study report
CTCAE	Common terminology criteria for adverse event
DOR	Duration of response
DORR	Duration of response to retreatment
DLBCL	Diffuse large B-cell lymphoma
DSMB	Data safety monitoring board
ECOG	Eastern Cooperative Oncology Group
EFS	Event-free survival
FAS	Full Analysis Set
GVHD	Graft-Versus-Host-Disease
IPI	International Prognostic Index
MedDRA	Medical Dictionary for Regulatory Activities
MST	MedDRA search terms
NCI	National Cancer Institute
ND	Not done
NE	Not evaluable
ORR	Objective response rate
OS	Overall survival
PET-CT	Positron emission tomography-computed tomography

Abbreviation	Definition
PFS	Progression-free survival
PR	Partial response
PT	Preferred term
RCR	Replication-competent retrovirus
SAP	Statistical analysis plan
SCT	Stem cell transplant
SD	Stable disease
SDTM	Study data tabulation model
SMQ	Standardized MedDRA query
SOC	System organ class
SUSAR	Suspected unexpected serious adverse reactions
TEAE	Treatment-emergent adverse event
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) provides the pre-specification and details for the statistical analyses to support the protocol KTE-C19-112 (ZUMA-12) entitled "A Phase 2 Multicenter Study Evaluating the Efficacy and Safety of Axicabtagene Ciloleucel as First-Line Therapy in Subjects with High-Risk Large B-Cell Lymphoma". The scope of this document is to provide details on the planned interim, primary, and final analyses.

2. OBJECTIVES

The primary objective of the analyses outlined herein is to estimate the efficacy of axicabtagene ciloleucel, as measured by CR rate, in subjects with high-risk large B-cell lymphoma, as determined by study investigators.

Secondary objectives are to characterize the safety profile, and to further characterize efficacy with secondary endpoints; further secondary objectives will include pharmacokinetic/pharmacodynamics endpoints.

3. STUDY DESIGN

3.1. Overview

Study KTE-C19-112 is a Phase 2, multicenter, single arm, open-label study evaluating the efficacy and safety of axicabtagene ciloleucel as first-line therapy in subjects with high-risk large B-cell lymphoma.

Approximately 40 subjects with high-risk large B-cell lymphoma, including either high-grade B-cell lymphoma (HGBL) with MYC and BCL2 and/or BCL6 translocations (double-/triple-hit lymphomas), or large B-cell lymphoma with a high-intermediate/ high-risk International Prognostic Index (IPI) score ≥ 3, will be enrolled and treated with cyclophosphamide and fludarabine conditioning chemotherapy, followed by a target dose of 2 x 10^6 anti-CD19 chimeric antigen receptor (CAR) T cells/kg body weight.

Each subject with a positive interim positron emission tomography-computed tomography (PET-CT) per the Lugano Classification (Cheson et al, 2014) (Deauville 5-point scale PET score of 4 or 5) after 2 cycles (PET2+) of standard-of-care chemoimmunotherapy will proceed through the following study periods:

- Screening
- Enrollment/Leukapheresis
- [redacted]
- Conditioning chemotherapy period
- Investigational Product (IP) treatment period
- Post treatment assessment period
- Long term follow-up period

For study requirements assigned to each study period, refer to protocol Section 7 for details.

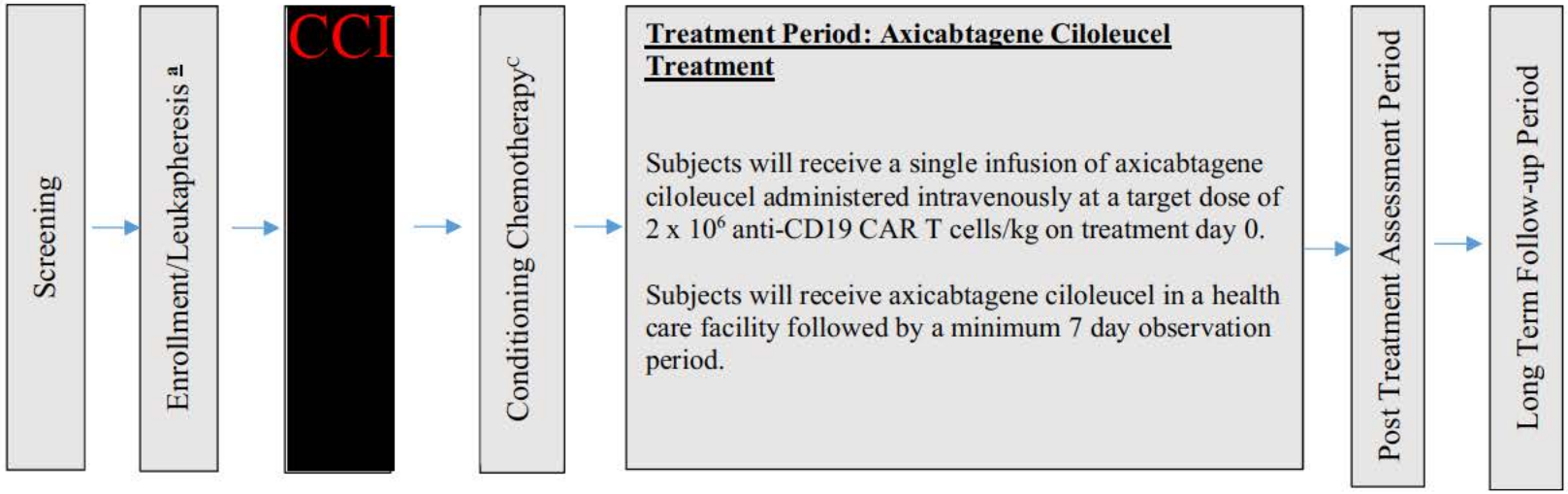
At specific time points as outlined in the schedule of assessments, subjects will undergo the following assessments/procedures: collection of informed consent, general medical history including previous treatments for large B-cell lymphoma, physical exam including vital signs and performance status, neurologic assessments, blood draws for complete blood count, chemistry panels, cytokines, C-reactive protein, lymphocyte subsets, replication-competent retrovirus (RCR) and anti-CD19 CAR T cell analysis. Subjects will also undergo a baseline electrocardiogram, echocardiogram, PET-CT, and leukapheresis. Subjects may also need bone marrow aspirate/biopsy, brain magnetic resonance image, and lumbar puncture.

Routinely throughout the conduct of the study, subjects will be asked to report concomitant medications and adverse events and will have their disease assessed.

The primary endpoint is complete response (CR) rate, defined as the incidence of a CR per the Lugano Classification (Cheson et al, 2014), as determined by study investigators. All evaluable subjects who do not meet the criteria for a CR by the analysis data cutoff date will be considered non-complete responders.

Further details on study procedures may be found in the study protocol. A study schema is present in Figure 1.

Figure 1. Study Schema for Study KTE-C19-112



Approximately 40 subjects who are either double hit/triple hit or have IPI ≥ 3 will be enrolled and treated.

[a] **Enrollment/Leukapheresis:** Subjects who have a positive interim PET per the Lugano Classification {Cheson 2014} (Deauville PET score of 4 or 5) after 2 cycles (PET2+) of an anti-CD20 monoclonal antibody and anthracycline-containing regimen per local standard of care (eg, DA-EPOCH-R) if double hit/triple hit, or an anti-CD20 monoclonal antibody and anthracycline-containing regimen per local standard of care (eg, R-CHOP) if large B-cell lymphoma with IPI score ≥ 3

CCI

[c] **Conditioning Chemotherapy:** Subjects will receive a 3-day conditioning chemotherapy regimen consisting of fludarabine 30 mg/m^2/day and cyclophosphamide 500 mg/m^2/day (Day 5 to Day 3) followed by 2 rest days (Day 2 and Day 1).

3.2. Hypothesis

No formal hypothesis will be tested. This study is designed to estimate the CR rate in subjects with high-risk large B-cell lymphoma. The CR rate targeted in this study is 60%.

3.3. Sample Size Consideration

In the GELA randomized phase 2 study evaluating the efficacy of R-ACVBP or R-CHOP-14 induction, using IWF 2007 criteria in young patients with high-risk DLBCL, the primary objective of achieving a higher than 50% CR rate after 4 cycles of induction regime was not met in both randomization groups (Casasnovas et al, 2017). Accordingly, it is postulated that a CR rate of 60% would represent a clinically meaningful improvement over standard chemoimmunotherapy in a high-risk large B-cell lymphoma patient population. Although there is no formal hypothesis testing, the sample size has been determined in part with descriptive analysis described below.

The trial uses a single-arm design to estimate the CR rate in subjects with high-risk large B-cell lymphoma treated with axicabtagene ciloleucel. A CR rate of 60% with axicabtagene ciloleucel treatment is targeted. With a total sample size of 40 subjects, an observed CR rate of 60% will yield an 80% confidence interval (CI) for the response rate with a maximum half-width of less than or equal to 11%, corresponding to a lower limit of at least 48.6%. This target CR rate, and the lower limit of the 80% CI for the CR rate, is meaningful because it would represent a significant improvement in the response rate for the subjects with high-risk large B-cell lymphoma and would likely offer an improvement over existing therapies in patients with high-risk large B-cell lymphoma (Table 1).

Table 1 provides the estimated CR rate, and the lower and upper limits of 80/95% CIs based on the Clopper-Pearson method for a range of possible CR rate for a sample of 40 subjects.

Table 1. Lower and upper limits of 80/95% CIs for CR rates from 60% to 100% for a sample of 40 subjects

Number (%) of CRs	24 (60)	28 (70)	32 (80)	36 (90)	40 (100)
Lower and Upper Limits of 80% CI (%, %)	48.6, 70.6	58.8, 79.5	69.6, 88.0	81.0, 95.6	94.4, 100
Lower and Upper Limits of 95% CI (%, %)	43.3, 75.1	53.5, 83.4	64.4, 90.9	76.3, 97.2	91.2, 100

One planned interim analysis will be performed. Interim Analysis 1 will be conducted after 15 subjects have been enrolled and treated with axicabtagene ciloleucel, and have had an opportunity to be followed for 3 months after axicabtagene ciloleucel infusion. This analysis will be for efficacy and safety, and will be descriptive.

4. STUDY ENDPOINTS AND COVARIATES

4.1. Endpoints

4.1.1. Primary Endpoint

- CR rate, defined as the incidence of a CR per the Lugano Classification (Cheson et al, 2014) as determined by study investigators.

4.1.2. Secondary Endpoints

- Objective response rate (ORR), defined as the incidence of either a CR or a partial response (PR) per the Lugano Classification (Cheson et al, 2014) as determined by the study investigators

- Duration of response (DOR), defined only for subjects who experience an objective response after axicabtagene ciloleucel infusion and is the time from the first objective response to disease progression per the Lugano Classification (Cheson et al, 2014) or death from any cause.

- Event-free survival (EFS), defined as the time from the axicabtagene ciloleucel infusion date to the earliest date of disease progression per the Lugano Classification (Cheson et al, 2014), commencement of subsequent new anti-lymphoma therapy including SCT, or death from any cause.

- Progression-free survival (PFS), defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression per the Lugano Classification (Cheson et al, 2014) or death from any cause.

- Overall survival (OS), defined as the time from axicabtagene ciloleucel infusion to the date of death from any cause.

- Incidence of adverse events (including grade ≥3, serious, fatal, and adverse events of interest) and clinically significant changes in safety lab values.

- Relapse with central nervous system (CNS) disease, defined only for subjects who experience CNS relapse and defined as the time from the axicabtagene ciloleucel infusion date to the earliest date of CNS involvement with lymphoma as determined by typical symptoms, CSF evaluation, and/or diagnostic imaging.

Additional secondary endpoints include pharmacokinetic/pharmacodynamic endpoints such as evaluation of levels of anti-CD19 CAR T cells in blood and levels of cytokines in serum in relationship with clinical outcome.

4.2. Covariates and Subgroups

The following covariates at screening/baseline or on the study may be used to examine CR, ORR and other efficacy and safety endpoints in covariate or subgroups analyses:

- Age (< 65, ≥ 65 years)
- Gender
- Race
- Ethnicity
- ECOG status
- IPI score
- Diagnosis category (double-hit lymphomas vs triple-hit lymphomas vs non double-/triple-hit with IPI score ≥3), by both local and central pathology
- Levels of cytokines
- Levels of CAR T Cells
- CR achieved on the study

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

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

5. DEFINITIONS

5.1. General

Study enrollment: Study enrollment occurs at the commencement of leukapheresis.

Study Day 0: Study Day 0 is defined as the day the subject received the first axicabtagene ciloleucel infusion. The day prior to 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 value taken prior to first dose of conditioning chemotherapy; if enrolled subjects do not receive conditioning chemotherapy, the baseline value is defined as the last value taken prior to enrollment/leukapheresis.

Study therapy: Study therapy is defined as conditioning chemotherapy or axicabtagene ciloleucel.

On-study: Time from enrollment to the last date of contact.

End of study: This will occur after all subjects treated with axicabtagene ciloleucel have been followed for 15 years post axicabtagene ciloleucel infusion, have withdrawn consent, been lost to follow-up, or have died.

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

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

Follow-up time for response: Follow-up time for response is derived as the time from the axicabtagene ciloleucel infusion date to the last disease assessment or censoring date. Follow-up time for response is derived using the reverse Kaplan-Meier approach in which the censoring times and event times are reversed to derive the median follow-up time.

5.2. Safety

Treatment-emergent adverse event (TEAE): Any adverse event with onset on or after the axicabtagene ciloleucel infusion. For subjects who receive retreatment with axicabtagene ciloleucel, TEAEs after retreatment may be summarized separately.

Deaths: All deaths that occur after leukapheresis up through the end of study.

Adverse events of interest: Adverse events of interest for axicabtagene ciloleucel treatment include adverse events in the categories of:

Important Identified risks:

- Cytokine-release syndrome (CRS)
- Neurologic toxicity
- Cytopenias, including

  neutropenia

  thrombocytopenia

  anemia
- Hypogammaglobulinemia
- Infections

Important Potential risks:

- Secondary malignancies
- Tumor lysis syndrome
- Bone marrow failure
- Graft-Versus-Host-Disease (GVHD)
- Replication competent retrovirus (RCR)
- Immunogenicity (anti-axicabtagene ciloleucel antibodies)

Cytokine release syndrome (CRS): CRS as a syndrome (i.e. a collection of individual symptoms) is identified via collection of the syndrome on a case report form specifically designed to collect CRS. Individual symptoms of CRS are separately collected on the adverse events log and are linked to the CRS syndrome. CRS syndrome severity is graded according to a modification of the grading system proposed by Lee and colleagues (Lee et al, 2014). In the modified grading scale, neurologic AEs are not reported as part of the CRS syndrome; rather, they are reported on the AE log form separately based on specific symptoms per Common Terminology Criteria for Adverse Events (CTCAE).

Neurologic toxicity (Neurotoxicity): Neurologic adverse events will be identified with Medical Dictionary for Regulatory Activities (MedDRA) search terms (MST) search strategy based on known neurologic toxicities associated with anti-CD19 immunotherapy (Topp et al, 2015). The search strategy focuses on central nervous system (CNS) toxicity, without regard to temporal relationship and concomitant conditions (e.g. CRS). MedDRA system organ classes (SOCs) of Psychiatric Disorders and Nervous System Disorders will be reviewed for additional events.

These events will then be evaluated for potential inclusion as neurologic AEs. Neurologic toxicity will be reported separately from CRS.

Cytopenias (including aplastic anemia): Cytopenias (neutropenia or thrombocytopenia or anemia including aplastic anemia and bone marrow failure) are identified as:

- Thrombocytopenia will be identified using the standardized MedDRA query (SMQ) for haematopoietic thrombocytopenia (narrow search)
- Neutropenia will be identified using Kite-specified MedDRA search terms (MST)
- Anemia (including aplastic anemia) will be identified using the SMQ haematopoietic erythropenia (broad search)

Subjects with cytopenias (neutropenia or thrombocytopenia or anemia) present on or after Day 30 post axicabtagene ciloleucel infusion will be summarized separately by cell lineage.

Hypogammaglobulinemia: Hypogammaglobulinemia will be identified using a MST search strategy defined by Kite.

Infections: Infections are identified as adverse events within the system organ class (SOC) of Infections and Infestations that occur after treatment with axicabtagene ciloleucel and in MedDRA high level group terms (HLGTs) that capture events of:

1) Bacterial infection, encompassing PTs within the MedDRA HLGTs of
    a) bacterial infectious disorders
    b) chlamydial infectious disorders
2) Viral infection, encompassing PTs within the MedDRA HLGTs of viral infectious disorders
3) Opportunistic infections, encompassing PTs within the MedDRA HLGTs of
    a) fungal infectious disorders
    b) mycobacterial infectious disorders
4) Other infections, encompassing PTs within the MedDRA HLGTs of Infections pathogen unspecified

Secondary malignancy: Adverse events that are coded into the SOC of Neoplasms benign, malignant, and unspecified (including cysts and polyps) will be reviewed to identify potential events. Additionally, adverse events that are coded into the SOC of Neoplasms benign, malignant, and unspecified (including cysts and polyps) will be reviewed to identify other potential events.

Tumor Lysis Syndrome: Tumor lysis syndrome will be identified as events with MedDRA PTs in the Tumor Lysis Syndrome SMQ (MedDRA). The narrow version of this SMQ will be used.

Bone marrow failure: Bone marrow failure will be identified using the narrow SMQ of haematopoietic cytopenias affecting more than one type of blood test.

Graft-Versus-Host Disease (GVHD): Graft-Versus-Host-Disease (GVHD) will be identified using a MST search strategy defined by Kite by using subsets of PT from HLGT of procedural related injuries and complications NEC and high level term (HLT) of immune and associated conditions NEC.

Immunogenicity (Anti-axicabtagene ciloleucel antibody): Immunogenicity will be identified for subjects who have treatment emergent anti-axicabtagene ciloleucel antibodies and have developed any AE belonging to the SMQ of anaphylactic reaction and the SMQ of hypersensitivity. The narrow version of these two SMQs will be used.

Time to Onset of Event/Syndrome: Time to onset of an event/syndrome is defined as the time from study day 0 to the day of the first occurrence of the event/syndrome. Time to Onset of Grade 3 or Higher Events/Syndromes are defined in the same way, but restricted to Grade 3 or higher events/syndromes.

Duration of Event/Syndrome: The duration across all events is the last day of the last event first day of the first event +1, regardless of whenever the events are consecutive, overlapping, or neither.

Durations of events will not be calculated for events that are ongoing at the time of the data cutoff date or subject death. For events defined by laboratory criteria, time to onset and duration will not be calculated. For events defined by both laboratory criteria and adverse events, only the adverse event component will be used to define time to onset and duration.

5.3. Efficacy

CR rate: CR rate is defined as the incidence of a CR per the Lugano Classification (Cheson et al, 2014) as determined by study investigators. All evaluable subjects who do not meet the criteria for a CR by the analysis data cutoff date will be considered non-complete responders. The derivation of this endpoint will only include response assessments obtained after the initial axicabtagene ciloleucel infusion and up to progressive disease (PD)/death due to any cause or the disease assessments prior to any subsequent anti-lymphoma therapy including stem cell transplant (SCT) or retreatment with axicabtagene ciloleucel.

ORR: ORR is defined as the incidence of either a CR or a PR per the Lugano Classification (Cheson et al, 2014) as determined by the study investigators. All evaluable subjects who do not meet the criteria for an objective response by the analysis cutoff date will be considered non-responders, including the subjects with nonevaluable assessment data and those without any assessment. The derivation of this endpoint will only include response assessments obtained after the initial axicabtagene ciloleucel infusion and up to PD/death due to any cause or the disease assessments prior to any subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel

DOR: DOR is defined only for subjects who experience an objective response (CR or PR) after axicabtagene ciloleucel infusion and is the time from the first objective response to disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression or death by the analysis data cutoff date will be censored at their last evaluable disease assessment date. The DOR for subjects who receive any subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel in the absence of documented disease progression or death due to any cause will be censored at the last evaluable disease assessment prior to the start date of the subsequent anti-lymphoma therapy. Further details on the derivation of DOR are provided in Appendix 2.

EFS: EFS is defined as the time from the axicabtagene ciloleucel infusion date to the earliest date of disease progression per the Lugano Classification (Cheson et al, 2014), commencement of subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel, or death due to any cause. Subjects alive, in response, and with no new anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel will be censored at the last evaluable disease assessment. Further details on the derivation of EFS are provided in Appendix 2.

PFS: PFS is defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression or death from any cause by the analysis cutoff date will be censored at the last evaluable disease assessment. The PFS for subjects who receive any subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel in the absence of documented disease progression or death due to any cause will be censored at the last evaluable disease assessment prior to the start date of the subsequent anti-lymphoma therapy. Further details on the derivation of PFS are provided in Appendix 2.

OS: OS is defined as the time from the axicabtagene ciloleucel infusion to the date of death due to any cause. Subjects who are alive by the analysis data cutoff date will be censored at their last date known to be alive or the data cutoff date, whichever is earlier. Subjects who die after the data cutoff date will be censored at the data cutoff date. Further details on the derivation of overall survival and the specific data modules that will be used to derive the last date known to be alive are provided in Appendix 2.

Relapse with CNS: relapse with CNS disease is defined only for subjects who experience CNS relapse. It is defined as the time from the axicabtagene ciloleucel infusion date to the earliest date of CNS involvement with lymphoma as determined by typical symptoms, CSF evaluation, and/or diagnostic imaging.

Duration of response to retreatment (DORR): DORR is defined only for subjects who receive retreatment following progression of disease and then go on to experience an objective response to retreatment. It is defined as the time from the first objective response after retreatment to disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression after retreatment or death due to any cause by the analysis data cutoff date will be censored at their last evaluable disease assessment date after retreatment. DORR will be derived using disease assessments obtained on study prior

to the start date of any subsequent anti-lymphoma therapy including SCT. Further details on the derivation of DORR are provided in Appendix 2.

6. ANALYSIS SUBSETS

In this study, subjects are to be dosed at a target of 2 x 10^6 (1.0 x 10^6 to 2.4 x10^6) anti-CD19 CAR T cells/kg. A minimum dose of 1 x 10^6 anti-CD19 CAR T cells/kg may be administered. For subjects weighing ≥ 100 kg, a maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells will be administered. Subjects are considered to have received the target dose if they receive at least 1 x 10^6 anti-CD19 CAR T cells/kg.

6.1. Safety Analysis Set

The safety set is defined as all subjects treated with any dose of axicabtagene ciloleucel. This analysis set will be used for all safety data analyses.

6.2. Full Analysis Set

The full analysis set (FAS) will consist of all enrolled/leukapheresed subjects and will be used for the summary of subject disposition and the listing of deaths.

6.3. Response Evaluable Analysis Set

The response evaluable analysis set will consist of the subjects who are enrolled and treated with axicabtagene ciloleucel at a dose of at least 1 x 10^6 anti-CD19 CAR T cells/kg, and centrally confirmed disease type (double-/triple- hit lymphomas) or IPI score ≥ 3. This analysis set will be used for all efficacy data analyses including CR rate and ORR, and endpoints based on response (DOR, EFS, PFS), relapse with CNS, and OS.

6.4. Safety Retreatment Analysis set

The safety retreatment analysis set will consist of all subjects who undergo retreatment with axicabtagene ciloleucel. This set will be used for all retreatment safety and efficacy analyses.

6.5. Subgroup Analysis Sets

Subgroup analyses of selected efficacy and safety endpoints may be performed for the covariates and subgroups defined in Section 4.2.

7. INTERIM ANALYSIS AND EARLY STOPPING GUIDELINES

The data safety monitoring board (DSMB) will meet and review the serious adverse events (SAEs) and suspected unexpected serious adverse reactions (SUSARs) on at least a semi-annual basis after the first subject has been treated with axicabtagene ciloleucel up through the primary analysis of the study. The DSMB will also review SAEs and SUSARs on a regular basis up through the primary analysis.

One planned interim analysis will be performed. At Interim Analysis 1, the DSMB will meet to review safety data after 15 subjects have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 3 months after axicabtagene ciloleucel infusion.

The DSMB will make trial conduct recommendations on an ongoing basis based on an analysis of risk vs benefit. The DSMB may request additional safety data or may recommend modifying the study conduct if safety concerns are identified. Data submitted to the DSMB may be monitored or unmonitored to facilitate and ensure timely DSMB review.

8. DATA SCREENING AND ACCEPTANCE

8.1. General Principles

The database will be subject to the edit checks outlined in the Data Management Plan and additional manual data reviews defined by the study team. Data inconsistencies will be reviewed and resolved before the database snapshot for the primary analyses and the final database lock. For interim analyses, snapshots may include data that has not passed all data cleaning procedures at the time the data are extracted for snapshot.

8.2. Electronic Transfer and Archiving of Data

The database for this study will be managed and maintained by Kite Pharma. Raw data, Study Data Tabulation Model (SDTM) data, and Analysis Data Model (ADaM) datasets will be generated by Kite Pharma, Inc. and will be archived for all planned analyses. Any additional unplanned analyses that occur after the primary analyses and prior to the final analysis will also be archived.

Data from the central pathology laboratory, the product characteristics central laboratory assessment of subject serum samples (CAR T cell levels in the peripheral blood, antibody assays, RCR testing) will be generated from contract laboratories and Kite Pharma. These data will be transferred to Kite held in a peripheral directory and not built into the clinical trial database. At the time analyses require these data, they may be merged with the SDTM and ADaM datasets.

8.3. Handling of Missing and Incomplete Data

8.3.1. Efficacy

The method for handling missing data is described in the definition for each efficacy endpoint. Every effort will be made to obtain complete dates for deaths. In the event of a partial or missing death date and the corresponding censoring date for survival, the algorithm in Appendix 2 will be used.

8.3.2. Safety

Partial adverse event start dates will be imputed. If dates are missing or incomplete for adverse event start dates, the algorithm defined in Appendix 1 will be used. Completely missing death dates or death dates with only a year reported will not be imputed.

8.4. Detection of Bias

A listing of subjects with important protocol deviations will be generated. The deviations included in this list will include violations of eligibility criteria and use of exclusionary medication during the study. Lack of protocol compliance will be evaluated by summarizing the subject incidence of important protocol deviations. High rates of important protocol deviations may indicate bias.

8.5. Outliers

Descriptive statistics will be used to identify potential outliers in any key variables analyzed. Suspected outliers will be included in all analyses unless there is sufficient scientific justification to exclude them.

8.6. Distributional Characteristics

The goal of the primary statistical analysis is to estimate CR rate. All 80/90/95% confidence intervals will be 2-sided and calculated via the Clopper-Pearson method. This test assumes only the independence of the individual subject responses.

8.7. Validation and Configuration Management

Programs for the development of the SDTM and ADaM datasets and the generation of the tables, figures, and listings will be developed and maintained according to Kite Pharma Standard Operating Procedures. The software and version used to generate analyses will be indicated in the archived documentation.

9. STATISTICAL METHODS OF ANALYSIS

9.1. General Principles

The primary analysis will occur after all treated subjects have an opportunity to be assessed for response 6 months after the Week 4 disease assessment. The clinical study report (CSR) will be written based on the data collected and analyzed from this primary analysis. The final analysis will occur after all subjects complete the study. The primary analysis of CR rate will be based on investigator review of disease assessments in the response evaluable analysis set.

9.2. Subject Accountability

The number of subjects screened, enrolled, leukapheresed, treated with conditioning chemotherapy, treated with axicabtagene ciloleucel, and retreated with axicabtagene ciloleucel will be summarized. The reasons for discontinuing treatment and the disease assessment and survival follow-up periods will be summarized.

Summaries of actual follow up time will be provided.

The number of subjects enrolled by country and site will be summarized.

The number of subjects in each analysis set along with reasons for exclusion will be provided.

9.3. Important Protocol Deviations

The clinical study team will define important protocol deviation categories and review all potential important protocol deviations at minimum, prior to the database snapshot for the primary efficacy analysis. Important protocol deviations will be categorized by deviation type (e.g. entry/eligibility, use of excluded medication, etc). The subject incidence of important protocol deviations will be summarized overall and by deviation category.

9.4. Demographic and Baseline Characteristics

Summary statistics and frequencies for the following demographic and baseline characteristics will be tabulated:

- Age (< 65, ≥ 65)
- Race: white, Asian, other (categories may be collapsed or expanded based on accrual)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Sex (male, female)
- Weight
- Height

- IPI score
- ECOG performance status
- Diagnosis category (double-hit lymphomas vs triple-hit lymphomas vs non double-/triple-hit with IPI score ≥3). Double/triple hit status will be summarized per investigator and per central pathology.
- Disease stage
- Disease extent (presence of B symptoms, splenic involvement, extranodal disease, bulky disease)
- Bone marrow involvement

9.5. Efficacy Analyses

For the primary analysis, the investigator assessment status per the Lugano Classification (Cheson et al, 2014) for CR rate will be used. The investigator reviewer will provide the determination of disease status (CR, PR, stable disease [SD], progressive disease [PD], not evaluable [NE], not done [ND]) at each time point. SAS programs developed by Kite Pharma will derive the best overall response (BOR), DOR, EFS, and PFS based on these assessments.

The primary efficacy analysis will be presented in the response evaluable analysis set.

For subjects retreated with axicabtagene ciloleucel, disease assessments obtained prior to retreatment but not disease assessment obtained after retreatment will be included in the primary summaries of ORR and BOR, DOR, EFS, PFS, and summaries of change in tumor burden (if applicable). For such retreated subjects, disease assessments obtained after retreatment will be included in the summaries of ORR, BOR rate to retreatment with axicabtagene ciloleucel, and DOR after retreatment with axicabtagene ciloleucel.

In the event any subject undergoes any subsequent antilymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel) while on study, the subject's BOR and change in tumor burden will be derived only based on disease outcomes assessed prior to initiation of the subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel), whichever is earlier. For subjects without documentation of disease progression prior to initiation of the subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel), DOR, EFS, and PFS time will be censored at the last disease assessment prior to the initiation of subsequent anti-lymphoma therapy.

9.5.1. CR rate

9.5.1.1. Primary Analyses of CR Rate

The subject incidence of CR will be calculated. The 2-sided 80/90/95% CIs will be provided about the CR rate, calculated with the Clopper-Pearson method.

9.5.1.2. Subgroup Analyses of CR

CR rate, and 95% CIs about CR rate will be generated for subgroups defined in Section 4.2.

A forest plot of the proportion of responders for each of these groups will be generated.

9.5.2. ORR and Best Overall Response (BOR)

9.5.2.1. Primary Analyses of ORR and BOR

The subject incidence of objective response will be calculated. The 2-sided 80/90/95% CIs will be provided about the ORR, calculated with the Clopper-Pearson method.

The incidence of subjects with PR, SD, PD, ND and NE, as BOR to treatment and exact 2-sided 80/90/95% CIs about the incidence will also be generated.

9.5.2.2. Subgroup Analyses of ORR

ORR, and 95% CIs about ORR will be generated for subgroups defined in Section 4.2.

A forest plot of the proportion of responders for each of these groups will be generated.

9.5.3. DOR

Kaplan-Meier plots, estimates, and 2-sided 80/90/95% CIs will be generated for DOR among the subjects who achieve an objective response. Kaplan-Meier estimates of the proportion of subjects alive and progression-free at 3-month intervals will be provided. The number of subjects censored or having events, and the reasons for censoring or type of events (PD or death) will be summarized.

A sensitivity analysis of DOR will be conducted in which disease assessments obtained after SCT (for subjects who undergo SCT while in an axicabtagene ciloleucel-induced response) will be used in the derivation of DOR.

DOR may be evaluated in subgroups defined by the covariates described in Section 4.2.

9.5.4. EFS

Kaplan-Meier plots, estimates, and 2-sided 80/90/95% CIs will be generated for EFS. Kaplan-Meier estimates of the proportion of subjects alive and event-free at 3-month intervals will be provided. The number of subjects censored or having events, and the reasons for censoring or type of events (PD, subsequent anti-lymphoma therapy, or death) will be summarized.

EFS may be evaluated in subgroups defined by the covariates described in Section 4.2.

9.5.5. PFS

Kaplan-Meier plots, estimates, and 2-sided 80/90/95% CIs will be generated for PFS. Kaplan-Meier estimates of the proportion of subjects alive and progression-free at 3-month intervals will

be provided. The number of subjects censored or having events, and the reasons for censoring or type of events (PD or death) will be summarized.

PFS may be evaluated in subgroups defined by the covariates described in Section 4.2.

9.5.6. OS

Kaplan-Meier plots, estimates and 2-sided 80/90/95% CIs will be generated for OS. Estimates of the proportion of subjects alive at 3-month intervals will be provided through 2 years after the final subject has been enrolled and then annually through the completion of the study. The number of subjects censored or having events, and the reasons for censoring or type of events (death) will be summarized.

OS may be evaluated in subgroups defined by the covariates described in Section 4.2.

9.5.7. Relapse with CNS Disease

The number of subjects with CNS relapse and time to relapse with CNS disease among the subjects who experience CNS relapse will be summarized.

Relapse with CNS disease may be evaluated in subgroups defined by the covariates described in Section 4.2.

9.5.8. Tumor Burden

The change in tumor burden, as measured by the sum of the products of the diameters of the selected lesions, from baseline to post-baseline nadir will be summarized in absolute numbers (mm^2) and percentage. A graphical summary of this change will be presented in a vertical bar chart with each subject's change from baseline to nadir displayed as a vertical bar, with color coding that indicates best response attained ("waterfall" plot). Summary statistics will be provided for this change. Additionally, plots over time of the percent change in tumor burden for each subject (superimposed on one graph) will be presented. Data collected after the subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel will not be included for the analyses.

9.5.9. ORR and BOR among Subjects Retreated with axicabtagene ciloleucel

The subject incidence of objective response and BOR (CR, PR, SD, PD, NE) to the retreatment among subjects retreated with axicabtagene ciloleucel will be calculated. Confidence intervals will be provided about the ORR and CR rate to the retreatment.

9.5.10. DORR

The analysis of DORR will use the same methods as the analysis of duration of response.

9.6. Safety Analyses

The primary analysis of safety data will summarize all treatment-emergent adverse events and laboratory values. For subjects who undergo retreatment with axicabtagene ciloleucel, adverse events occurring in the axicabtagene ciloleucel retreatment period may be summarized in an additional separate summary that presents only the AEs occurring during the axicabtagene ciloleucel retreatment period.

Adverse events will be coded with MedDRA. The version of the MedDRA may vary over time as the current version in use is updated. The severity of adverse events will be graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 or above. Cytokine release syndrome (CRS) will be graded using a revised CRS grading scale developed by Lee et al (Lee et al, 2014). The incidence and severity of CRS will be reported as a syndrome with severity per Lee et al. Individual symptoms associated with CRS will be graded per CTCAE version 5.0 or above.

Tables and/or narratives of deaths through the long term follow-up and treatment related SAEs will be provided.

Subjects enrolled but not dosed with axicabtagene ciloleucel will be followed for adverse events for 30 days after the last study procedure. Adverse events reported in these patients will be archived in the study database and available in SDTM and ADaM datasets, but will not be tabulated in adverse event summaries.

The safety summaries by disease diagnosis type (eg, double-hit lymphomas vs triple-hit lymphomas vs non double-/triple-hit with IPI score ≥ 3) may be presented.

9.6.1. Adverse Events

The subject incidence of the following treatment-emergent adverse events will be tabulated by SOC and PT:

- Summary of adverse events (any, worst severity, serious, related)
- All adverse events
- All serious adverse events
- All leukapheresis-related adverse events
- All conditioning-chemotherapy-related adverse events
- All axicabtagene ciloleucel-related adverse events
- All conditioning chemotherapy-related serious adverse events
- All axicabtagene ciloleucel-related serious adverse events
- All Grade 3 or higher adverse events

- All Grade 3 or higher conditioning chemotherapy-related adverse events
- All Grade 3 or higher axicabtagene ciloleucel-related adverse events
- The most common adverse events (incidence ≥20%)
- The most common grade 3 or higher adverse events (incidence ≥10%)
- Fatal adverse events
- Adverse events of interest, including important identified and important potential risks

Summary statistics for the onset time (Kaplan-Meier estimates) and duration of adverse events of interest will be provided.

The subject incidence of deaths will be provided.

A subject listing of deaths and serious adverse events (including narratives) will be provided.

Subgroup analyses of AEs may be generated using the covariates listed in Section 4.2.

Summary of AEs during specific time periods may be conducted to support the safety evaluations.

9.6.1.1. Laboratory Test Results

Laboratory results will be graded according to NCI CTCAE version 5.0 or above. Laboratory data collected at baseline and throughout the axicabtagene ciloleucel treatment period will be summarized. Lab shift tables calculating the shift from baseline to minimum post-baseline and/or maximum post-baseline will be presented for select analytes. The incidence of worst CTCAE grade post-baseline by grade for all analytes will be provided. Additional laboratory shift tables calculating the shift from the last assessment prior to axicabtagene ciloleucel infusion to the worst CTCAE grade post axicabtagene ciloleucel infusion may be generated.

9.6.1.2. Replication Competent Retrovirus (RCR)

The subject incidence of replication competent retrovirus (RCR) detected in blood samples will be tabulated overall and by assessment time. The persistence of RCR over time will be summarized.

9.6.1.3. Exposure to Study Treatment

Summary statistics and subject listings will be provided for the following:

- Total body surface area (BSA)-adjusted dose of cyclophosphamide
- Total BSA-adjusted dose of fludarabine
- Weight-adjusted dose of axicabtagene ciloleucel

- Number and percent of subjects who received a dose of axicabtagene ciloleucel within +/- 10% of the planned dose

The analysis by patient demographics (age, and sex etc.) as well as by tumor burden may be provided.

Separate summaries will be presented for the 2nd administration of conditioning chemotherapy and retreatment of axicabtagene ciloleucel for subjects in the Safety Retreatment Analysis Set.

9.6.1.4. Exposure to Concomitant Medications and Procedures

The subject incidence of concomitant medications will be provided and summarized, including tocilizumab, steroids, vasopressors, and IVIG. In addition, the incidence of dialysis and intubation will be summarized.

9.6.1.5. Schedule of Study Treatment

Summary statistics will be provided for the following durations:

- Days from leukapheresis to commencement of conditioning chemotherapy
- Days from leukapheresis to administration of axicabtagene ciloleucel
- Days from leukapheresis to axicabtagene ciloleucel product release
- Days from leukapheresis to receipt of axicabtagene ciloleucel at the study site
- Days from conditioning chemotherapy to administration of axicabtagene ciloleucel
- Duration of hospitalization for the axicabtagene ciloleucel infusion

9.7. Product Characteristics

Summary statistics and subject listings will be provided for the following:

- Total CAR T cells of the axicabtagene ciloleucel infusion
- Total T cells of the axicabtagene ciloleucel infusion
- Transduction ratio
- Percentages of CD4 and CD8 T cells
- Percentages of T cell memory phenotypes
- IFN-gamma production in co-cultures of axicabtagene ciloleucel product and $CD19^{+}$ target cells
- Vector copy number of axicabtagene ciloleucel product

9.8. Pharmacokinetics

Summary statistics for the level of CAR T cells in serum post axicabtagene ciloleucel infusion will be provided for CAR T cells measured at day 7, week 2, week 4, month 3, month 6, month 12, and month 24. The maximum CAR T cell level attained, the time at which the maximum level was attained, and the time at which there were no detectable CAR T cells in the serum will be summarized. The area under the curve (AUC) of CAR T cell levels from day 0 to day 28 and the peak value of CAR T cell levels from day 0 to day 28 will be summarized and may be used in subgroup analyses. Additional detail can be found in the translational research plan.

9.9. Pharmacodynamics

Levels of cytokines in serum in relationship with clinical outcome will be detailed in the translational research plan.

9.10. Subsequent Anti-Cancer Therapy and SCT

The incidence and type (by WHO Drug coded term and categories) of subsequent anti-lymphoma therapy and subsequent SCT (autologous, allogeneic) by treatment period will be summarized.

The subject incidence of SCT post-treatment with axicabtagene ciloleucel will be tabulated by occurrence of SCT post progression on axicabtagene ciloleucel or occurrence of SCT while in an axicabtagene ciloleucel-induced response.

10. CHANGES FROM PROTOCOL-SPECIFIED ANALYSES

There is no change from protocol-specified analyses.

11. REFERENCES

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Lee DW, Gardner R, Porter DL, Louis CU, Ahmed N, Jensen M, Grupp SA, Mackall CL. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014;124(2):188-95.

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12. APPENDICES

Appendix 1. Conventions for Clinical Data that Require Imputation for Partial or Missing Dates
Appendix 2. Derivation of Time to Event Endpoints and Last Date Known to Be Alive

Appendix 1. Conventions for Clinical Data that Require Imputation for Partial or Missing Dates

The following data will be imputed using the following algorithm:

- Adverse event start dates
- Deaths (please see exceptions below)
- Concomitant medication start dates
- Subsequent anti-cancer therapy start dates

Table 2. Imputation Rules for Partial or Missing Start Dates

Start Date		Stop Date						
		Complete: *yyyymmdd*		Partial: *yyyymm*		Partial: *yyyy*		Missing
		< Study Day 0	≥ Study Day 0	< Study Day 0 *yyyymm*	≥ Study Day 0 *yyyymm*	< Study Day 0 *yyyy*	≥ Study Day 0 *yyyy*	
Partial *yyyymm*	= Study Day 0 *yyyymm*	2	1	2	1	n/a	1	1
	≠ day 0 *yyyymm*		2		2	2	2	2
Partial *yyyy*	= Study Day 0 *yyyy*	3	1	3	1	n/a	1	1
	≠ Study Day 0 *yyyy*		3		3	3	3	3
Missing		4	1	4	1	4	1	1

1 impute the date of day 1
2 impute the first of the month
3 impute January 1 of the year
4 impute January 1 of the stop year
Note: if the start date imputation leads to a start date that is after the stop date, then do not impute the start date.

Imputation rules for partial or missing death dates:

1) If death year and month are available but day is missing:

   - If yyyymm for the last contact date yyyymm for death date, set death date to the day after the last date known to be alive.
   - If yyyymm for the last date known to be alive < yyyymm for death date, set death date to the first day of the death month.
   - If yyyymm for last date known to be alive > yyyymm for death date, data error and do not impute.

2) If both month and day are missing for death date or a death date is completely missing, do not impute and censor the subject survival time at the last date known to be alive.

Appendix 2. Derivation of Time to Event Endpoints and Last Date Known to Be Alive

Additional detail on the derivations of DOR, DORR, EFS, PFS, and OS is provided below.

Duration of response (DOR): DOR is defined only for subjects who experience an objective response (CR or PR) after axicabtagene ciloleucel infusion and is the time from the first objective response to disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression or death by the analysis data cutoff date will be censored at their last evaluable disease assessment date. The DOR for subjects who receive any subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel) in the absence of documented disease progression or death due to any cause will be censored at the last evaluable disease assessment prior to the start date of the subsequent anti-lymphoma therapy. A sensitivity analysis will be conducted in which disease assessments obtained after SCT are included in the derivation of DOR.

Primary analysis of DOR:

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Progression date
Death due to any cause without documented disease progression and without subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Death date
Remain in response without any subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment
Initiated subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel) prior to documented progression or death due to any cause	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment, whichever is earlier)
Progression or death due to any cause documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
No progression through discontinuation of study prior to the data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Sensitivity analysis of DOR (including the disease assessments after SCT):

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression after SCT, but prior to other subsequent anti-lymphoma therapy (including retreatment with axicabtagene ciloleucel)	Event	Progression date
Death due to any cause after SCT without prior documented disease progression and other subsequent anti-lymphoma therapy (including retreatment with axicabtagene ciloleucel)	Event	Death date
Remain in response after SCT without other subsequent anti-lymphoma therapy (including retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment
Remain in response after SCT prior to other subsequent anti-lymphoma therapy (including retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy or retreatment, whichever is earlier
Progression or death due to any cause documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
No progression through discontinuation of study prior to the data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Duration of response to retreatment (DORR): DORR is defined only for subjects who receive retreatment following progression of disease and then go on to experience an objective response to retreatment. It is defined as the time from the first objective response after retreatment to disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression after retreatment or death due to any cause by the analysis data cutoff date will be censored at their last evaluable disease assessment date after retreatment. The DORR for subjects who receive any subsequent anti-lymphoma therapy (including SCT) after axicabtagene ciloleucel retreatment in the absence of prior documented progression will be censored at the last evaluable disease assessment prior to subsequent anti-lymphoma therapy. Disease assessments obtained after SCT will not be used in the derivation of DORR. A sensitivity analysis may be conducted in which disease assessments obtained after the SCT are included in the derivation of DORR.

Primary analysis of DORR:

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression prior to initiation of subsequent anti-lymphoma therapy (including SCT)	Event	Progression date
Death due to any cause without documented disease progression and without subsequent anti-lymphoma therapy (including SCT)	Event	Death date
Remain in response without any subsequent anti-lymphoma therapy (including SCT)	Censored	Date of last evaluable disease assessment
Initiated subsequent anti-lymphoma therapy (including SCT) prior to documented progression or death due to any cause	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT)
Progression or death due to any cause documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
No progression through discontinuation of study prior to the data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Sensitivity analysis of DORR (including the disease assessments after SCT):

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression after SCT, but prior to other subsequent anti-lymphoma therapy	Event	Progression date
Death due to any cause after SCT without prior documented disease progression and other subsequent anti-lymphoma therapy	Event	Death date
Remain in response after SCT without other subsequent anti-lymphoma therapy	Censored	Date of last evaluable disease assessment
Remain in response after SCT prior to other subsequent anti-lymphoma therapy	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy
Progression or death due to any cause documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
No progression through discontinuation of study prior to the data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Event-free Survival (EFS): EFS is defined as the time from the axicabtagene ciloleucel infusion date to the earliest date of disease progression per the Lugano Classification (Cheson et al, 2014), commencement of subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel, or death from any cause. Subjects alive, in response, and with no new anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel will be censored at the last evaluable disease assessment.

Primary analysis of EFS:

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Progression date
Subject with CR or PR or a best response of SD and subsequently received anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment)
Subsequent anti-lymphoma therapy in the absence of any evaluable disease assessment	Event	Axicabtagene ciloleucel infusion date
Death due to any cause without documented disease progression (excluding the death after the initiation of subsequent anti-lymphoma therapy)	Event	Death date
Death due to any cause without documented disease progression and after the initiation of subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment)
Subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel) started prior to documented progression or death due to any cause	Event	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment)
Remain in response without new anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment
Progression or death documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
Remain event-free through the discontinuation of the study prior to data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
Subjects treated but no post baseline disease assessment	Censored	Axicabtagene ciloleucel infusion date

Progression-free Survival (PFS): PFS is defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression per the Lugano Classification (Cheson et al, 2014) or death due to any cause. Subjects not meeting the criteria for disease progression or death will be censored at the last evaluable disease assessment. Subjects who receive any subsequent anti-lymphoma therapy including SCT or retreatment with axicabtagene ciloleucel in the absence of documented disease progression or death due to any cause will be censored at the last evaluable disease assessment prior to the start date of the subsequent anti-lymphoma therapy.

Primary analysis of PFS:

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Progression date
Death due to any cause without documented disease progression (excluding the death after the initiation of subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Death date
Remain in response without subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment
Initiated subsequent anti-lymphoma therapy (including SCT or retreatment with axicabtagene ciloleucel) prior to documented progression or death due to any cause	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-lymphoma therapy (including SCT or retreatment)
Progression or death due to any cause documented after data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
No progression through discontinuation of study prior to the data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis
Subjects treated but no post baseline disease assessment	Censored	Axicabtagene ciloleucel infusion date

Overall Survival (OS): OS is defined as the time from the axicabtagene ciloleucel infusion to the date of death due to any cause. Subjects who have not died by the analysis data cutoff date will be censored at their last date known to be alive prior to the data cutoff date with the

exception that subjects known to be alive or determined to have died after the data cutoff date will be censored at the data cutoff date.

Circumstance	Event / Censored	Date of Event / Censoring
Death prior to data cutoff date for analysis	Event	Death date
Death after data cutoff date for analysis	Censored	Data cutoff date
Known to be alive after data cutoff date for analysis	Censored	Data cutoff date
Alive up through data cutoff date and no further information available after cutoff date	Censored	Last date known to be alive up through the data cutoff date
Alive including withdrawal of consent or lost to follow-up prior to data cutoff date	Censored	Last date known to be alive prior to withdrawal of consent or lost to follow-up

Last date known to be alive

The last date known to be alive with be derived by obtaining the maximum complete date among the following data modules:

- Start and end dates of AE (including targeted AE) and concomitant medication
- Screening dates
- Leukapheresis dates
- Conditioning chemo admin dates
- axicabtagene ciloleucel infusion dates
- CT scan dates
- PET scan dates
- Clinical symptoms of lymphoma assessment dates
- Target lesion assessment
- Non-target lesion assessment
- New lesion assessment

- Disease response assessment
- Long term follow up subject status date where status ‘alive’
- End of treatment disposition where status is not equal to death, lost to follow up
- End of post-treatment assessment period where status is not equal to death, lost to follow up
- End of study data where end of study reason is not equal to death, lost to follow up