STATISTICAL ANALYSIS PLAN

Sponsor:	Kite Pharma, Inc. 2400 Broadway Santa Monica, CA 90404 United States of America
Product Name:	Axicabtagene Ciloleucel
Protocol	A Phase 2 Multicenter Study of Axicabtagene Ciloleucel in Subjects with Relapsed/Refractory Indolent non-Hodgkin Lymphoma
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1. INTRODUCTION

This statistical analysis plan provides the pre-specification and details for the statistical analyses outlined within protocol KTE-C19-105 (ZUMA-5) entitled "A Phase 2 Multicenter Study of Axicabtagene Ciloleucel in Subjects with Relapsed/Refractory Indolent non-Hodgkin Lymphoma". The scope of this document is to provide details on the planned interim, primary, follow-up, and final analyses.

2. OBJECTIVES

The primary objective is to evaluate the efficacy of axicabtagene ciloleucel, as measured by objective response rate (ORR), in subjects with relapsed or refractory (r/r) B-cell indolent non-Hodgkin lymphoma (iNHL).

Key secondary objectives are to characterize the safety profile, complete response (CR) rate, ORR among those subjects with 3 or more lines of prior therapy, CR rate among those subjects with 3 or more lines of prior therapy, and to determine duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Additional secondary objectives will include additional safety and pharmacokinetic/pharmacodynamic endpoints and the time to next therapy endpoint.

3. STUDY OVERVIEW

3.1. Study Design

Study KTE-C19-105 is a Phase 2, multicenter, single arm, open-label study evaluating the efficacy of axicabtagene ciloleucel in subjects with r/r B-cell iNHL of FL or MZL histological subtypes.

Up to approximately 160 subjects, including up to approximately 125 subjects with FL with at least 80 subjects with FL in the inferential set, will be enrolled and treated with cyclophosphamide and fludarabine conditioning chemotherapy, followed by a target dose of 2×10^6 anti-CD19 CAR T cells per kg body weight.

Each subject will proceed through the following study periods:

- Screening
- Enrollment/Leukapheresis
- Conditioning chemotherapy
- Investigational Product (IP) treatment
- Post-treatment assessment
- Long-term follow-up (LTFU)

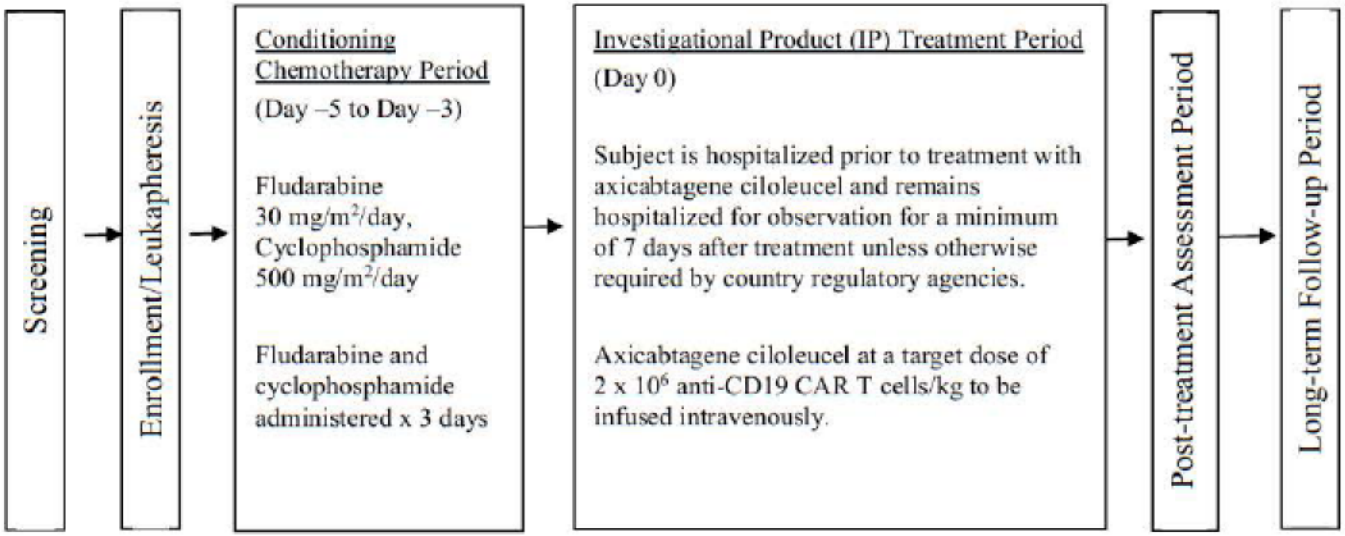
At specific time points as outlined in the schedule of assessments, subjects will undergo the following procedures: collection of informed consent, general medical history including previous treatments for iNHL, physical exam including vital signs and performance status, blood draws for complete blood count (CBC), chemistry panels, cytokines, C-reactive protein, lymphocyte subsets, anti-axicabtagene ciloleucel antibodies, and anti-CD19 CAR T cell analysis. Women of child-bearing potential will undergo a urine or serum pregnancy test.

The primary endpoint is ORR, defined as complete response (CR) + partial response (PR) per the Lugano Classification {Cheson 2014} as determined by Independent Radiology Review Committee (IRRC) review. These assessments will be referred to as "Central Read" in this document. The primary endpoint will be assessed in the set of all FL subjects treated who meet key eligibility criteria in protocol amendment #2 (please see Section 6). This set of subjects who meet these criteria are referred to throughout this SAP as the 'Inferential Analysis Set'.

Subjects will also undergo a baseline electrocardiogram (ECG), echocardiogram (ECHO), a positron emission tomography, computed tomography (PET-CT), possible bone marrow aspirate and biopsy, and leukapheresis.

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

Figure 1. Study Schema



Abbreviations: CAR, chimeric antigen receptor.

3.2. Hypothesis

Four hypotheses will be tested using a fixed sequence procedure in terms of ORR and CR rate as determined by central review to control the overall type I error at 1-sided alpha level of 0.025 with the following testing order:

- Hypothesis 1 (H_1): test for ORR as determined by central review, if significant then
- Hypothesis 2 (H_2): test for CR rate as determined by central review, if significant then
- Hypothesis 3 (H_3): test for ORR as determined by central review in the subjects who have had 3 or more lines of prior therapy, if significant then
- Hypothesis 4 (H_4): test for CR rate as determined by central review in the subjects who have had 3 or more lines of prior therapy

The hypotheses H_1 through H_4 will be assessed at the time of the interim analyses 3, 4, 5 and the primary analysis.

The H_1 is that the ORR, as determined by central review, to axicabtagene ciloleucel is significantly greater than 40% in subjects with FL in the inferential analysis set. The targeted response rate is 60%.

The H_2 is that the CR rate, as determined by central review, to axicabtagene ciloleucel is significantly greater than 15% in subjects with FL in the inferential analysis set.

The H_3 is that the ORR, as determined by central review, to axicabtagene ciloleucel is significantly greater than 40% in subjects with FL in the inferential analysis set who have had 3 or more lines of prior therapy.

The H_4 is that the CR rate, as determined by central review, to axicabtagene ciloleucel is significantly greater than 15% in subjects with FL in the inferential analysis set who have had 3 or more lines of prior therapy.

An alpha spending function will be used to allocate the alpha level between the interim analyses 3, 4, 5, and the primary analysis. Using the interpolated alpha spending functions, the nominal 1-sided alpha used to test for efficacy at interim analyses 3, 4, and 5 are 0.0003, 0.0005, and 0.0005 respectively, and the nominal 1-sided alpha used to test for efficacy at the primary analysis is 0.0237. If the criteria for early efficacy are met for H_1, the same alpha spending function will be applied to test H_2 at this interim analysis; otherwise, H_2 through H_4 will not be tested until the subsequent analysis. If the criteria for early efficacy are met for H_1 and H_2, the same alpha spending function will be applied to test H_3; otherwise, H_3 and H_4 will not be tested until the subsequent analysis. If the criteria for early efficacy are met for H_1, H_2, and H_3, the same alpha spending function will be applied to test H_4; otherwise, H_4 will not be tested until the subsequent analysis. The study will not be stopped if early efficacy is demonstrated.

No formal hypothesis testing is planned for the MZL histological subtype. The analysis will be descriptive.

3.3. Sample Size Considerations

The trial uses a single-arm design to estimate the ORR in subjects with r/r B-cell iNHL treated with axicabtagene ciloleucel. The target response rate in subjects with FL is 60%.

Up to approximately 160 subjects, including up to approximately 125 subjects with FL with at least 80 subjects with FL in the inferential analysis set, will be enrolled and treated.

The primary efficacy endpoint for this study in at least 80 subjects with FL in the inferential analysis set has 93% power to test the null hypothesis that the ORR is 40% versus the alternative hypothesis that the ORR is 60% with a 1-sided alpha level of 0.0237.

Within the inferential analysis set, interim analyses 3, 4, and 5 will be performed when 30 subjects with FL have had the opportunity to be followed for response for 6 months after the axicabtagene ciloleucel infusion, when 80 subjects with FL have had the opportunity to be followed for response for 6 months after axicabtagene ciloleucel infusion, and when 80 subjects with FL have had opportunity to be followed for response 9 months after the first disease response assessment. These interim analyses will be for safety and to assess early demonstration of efficacy. These interim analyses are based on the interpolated alpha spending function. The nominal alpha levels for the assessment of efficacy are 0.0003, 0.0005, and 0.0005. The study will not be stopped if early efficacy is demonstrated and the primary analysis will occur after at least 80 subjects with FL in the inferential analysis set have had the opportunity to be followed for 12 months after the first disease response assessment.

4. STUDY ENDPOINTS AND COVARIATES

4.1. Endpoints

4.1.1. Primary

- ORR (complete response [CR] + partial response [PR]) per the Lugano Classification {Cheson 2014} as determined by Central Read.

4.1.2. Secondary

- CR rate is defined as the incidence of CR as best overall response to treatment by the Lugano Classification {Cheson 2014} as determined by Central Read.
- ORR, defined as CR + PR per the Lugano Classification {Cheson 2014} by central read for those subjects who have had 3 or more lines of prior therapy
- CR rate, defined as CR per the Lugano Classification {Cheson 2014} by central read for those subjects who have had 3 or more lines of prior therapy
- ORR, defined as the incidence of a CR or a PR by the Lugano Classification {Cheson 2014} as determined by investigator read.
- DOR
- PFS
- OS
- Incidence of adverse events (AEs) and clinically significant changes in laboratory values
- Incidence of anti-axicabtagene ciloleucel antibodies
- Levels of anti-CD19 CAR T cells in blood
- Levels of cytokines in serum
- Time to next therapy

4.2. Subgroups and Covariates

The following baseline covariates may be used to examine ORR and other key safety and efficacy endpoints in subgroups or covariate analyses:

- Age (< 65, ≥ 65 years)
- Gender
- Race
- Ethnicity
- Histological diagnosis (eg, FL, MZL), by both local and central pathology
- Follicular Lymphoma International Prognostic Index (FLIPI) total score (0, 1, 2, 3, 4, 5, and Low risk (0-1), Intermediate risk (2), High risk (3-5))
- ECOG performance status (0, 1)
- Disease burden as defined by any of the following GELF criteria (subject meets the criteria for high tumor bulk versus subject does not meet the criteria for high tumor bulk)
  - Involvement of ≥ 3 nodal sites, each with a diameter of ≥ 3 cm
  - Any nodal or extranodal tumor mass with a diameter of ≥ 7 cm
  - B symptoms
  - Splenomegaly
  - Pleural effusions or peritoneal ascites
  - Cytopenias
  - Leukemia
- Relapsed (defined as those subjects with iNHL who progressed > 6 months from completion of the most recent prior treatment) vs. Refractory (defined as those subjects with iNHL who progressed within 6 months of completion of the most recent prior treatment) at study entry
- Time to relapse from initiation of first anti-CD20-chemotherapy combination therapy (≥ 24 months, < 24 months)
- Prior PI3K inhibitor

- Number of prior lines of therapy (excluding single agent anti-CD20 antibody as a line of therapy)
- Double refractory (subjects refractory to the first 2 lines of therapy)

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 the 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
- infections
- cytopenias, including
  - neutropenia
  - thrombocytopenia
  - anemia
- hypogammaglobulinemia

Important potential risks:

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

Neurological toxicity (Neurotoxicity): Neurological adverse events are identified with a search strategy based on known neurologic toxicities associated with anti-CD19 immunotherapy {Topp 2015}. The search strategy focuses on central nervous system toxicity, without regard to temporal relationship and concomitant conditions (eg CRS). Additionally, the 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.

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 {Lee 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).

Cytopenias: Cytopenias (neutropenia or thrombocytopenia or anemia including aplastic anemia) 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 of Infections and Infestations that occur after treatment with axicabtagene ciloleucel and in MedDRA high level groups (HLGT) that capture events of:

A) Bacterial infection, encompassing preferred terms within the MedDRA high level group terms of

   1) bacterial infectious disorders

   2) chlamydial infectious disorders

B) Viral infection, encompassing preferred terms within the MedDRA high level group term of viral infectious disorders

C) Opportunistic infections, encompassing preferred terms within the MedDRA high level group terms of

   1) fungal infectious disorders

   2) mycobacterial infectious disorders

D) Unspecified infections, encompassing preferred terms within the MedDRA high level group term of Infections – pathogen unspecified

Secondary malignancy: Secondary malignancies are identified via collection on a case report form in which the investigator classifies the event as a secondary malignancy. Additionally, 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.

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

Cardiac Failure: Cardiac failure will be identified using the SMQ of cardiac failure. The narrow version of this SMQ will be used.

Cardiac Arrhythmias: Cardiac arrhythmias will be identified using the SMQ of cardiac arrhythmias. The narrow version of this SMQ with selected broad SMQ preferred terms will be used.

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 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 antibody and have developed any AE belonging to the SMQ of anaphylactic reaction and the SMQ of hypersensitivity. The narrow version of these 2 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

ORR: ORR is defined as the incidence of a CR or a PR by the Lugano Classification {Cheson 2014}. All subjects that 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 or

the disease assessments prior to subsequent anti-cancer therapy (including stem cell transplant [SCT] or retreatment with axicabtagene ciloleucel). Response may be defined per Central Read or Investigator Read.

DOR: DOR is defined only for subjects who experience an objective response (CR or PR) and is the time from the first objective response to disease progression or death due to any cause. Response and progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for progression or death due to any cause 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-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel) in the absence of prior documented progression will be censored at the last evaluable disease assessment date prior to subsequent anti-cancer therapy. The DOR for subjects who undergo SCT while in an axicabtagene ciloleucel-induced response will be censored at the last evaluable disease assessment prior to SCT. A sensitivity analysis will be conducted in which disease assessments obtained after SCT (for subjects undergoing SCT while in an axicabtagene ciloleucel induced response) are included in the derivation of DOR. Further details on the derivation of DOR are provided in Appendix 2.

Best Overall Response (BOR) Rate: BOR is defined as the incidence of CR, PR, stable disease (SD), progressive disease (PD), or nonevaluable (NE) as best overall response to treatment by the Lugano Classification {Cheson 2014}. The derivation of this endpoint will only include response assessments obtained after the initiation of the axicabtagene ciloleucel infusion and up to PD or the disease assessments prior to any subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel). Response may be defined per Central Read or Investigator Read.

PFS: PFS is defined as the time from the axicabtagene ciloleucel infusion date for the analyses based on the inferential analysis set and the safety analysis set or the enrollment/leukapheresis date for the analysis based on the FAS to the date of disease progression per {Cheson 2014} or death due to any cause. Progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for progression by the analysis data cutoff date will be censored at their last evaluable disease assessment date. The PFS for subjects who receive any subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel) in the absence of prior documented progression will be censored at the last evaluable disease assessment prior to subsequent anti-cancer therapy. The PFS for subjects who undergo SCT while in an axicabtagene ciloleucel-induced response will be censored at the last evaluable disease assessment date prior to SCT. A sensitivity analysis will be conducted in which disease assessments obtained after SCT (for subjects undergoing SCT while in an axicabtagene ciloleucel induced response) are included in the derivation of PFS. Further details on the derivation of PFS are provided in Appendix 2.

OS: OS is defined as the time from the axicabtagene ciloleucel infusion for the analyses based on the inferential analysis set and the safety analysis set or the enrollment/leukapheresis date for the analysis based on the FAS 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. Survival for subjects known to be alive or determined to have died 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.

Time to next therapy: defined as the time from the axicabtagene ciloleucel infusion date to the start of the subsequent new lymphoma therapy or death from any cause. Subjects who have not received subsequent new therapy and are still alive will be censored at the last contact date. For subjects known to be alive without receiving any subsequent therapy after the data cutoff date the time to next therapy will be censored at the data cutoff date.

Duration of response to retreatment (DORR): DORR is defined only for subjects who receive retreatment following progression of disease per Investigator Read 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 {Cheson 2014} or death due to any cause. Response and progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for 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-cancer 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-cancer 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 SCT (for subjects undergoing SCT while in an axicabtagene ciloleucel induced response) are included in the derivation of DORR. Further details on the derivation of DORR are provided in Appendix 2.

6. ANALYSIS SUBSETS

The following analysis sets are defined.

The pivotal cohort is defined by the eligibility criteria specified in amendment #2 and subsequent amendments of the KTE-C19-105 protocol and provided below:

101. Histologically confirmed diagnosis of B-cell iNHL, with histological subtype limited to FL Grade 1, Grade 2, or Grade 3a or MZL nodal or extranodal, based on criteria established by the World Health Organization (WHO) 2016 classification

102. Relapsed or refractory disease after 2 or more prior lines of therapy. Prior therapy must have included an anti-CD20 monoclonal antibody combined with an alkylating agent. (Single agent anti-CD20 antibody will not count as a line of therapy for eligibility). Stable disease (without relapse) > 1 year from completion of last therapy is not eligible.

6.1. Safety Analysis Set

The safety analysis set is defined as all subjects treated with any dose of axicabtagene ciloleucel. The safety analysis set will be used for all safety analyses for the study, and will also be used for the sensitivity analyses of ORR, BOR rate, DOR, PFS, time to next therapy, and OS.

6.2. Inferential Analysis Set

The inferential analysis set will consist of all subjects enrolled (and who meet the eligibility criteria for the pivotal cohort) and treated with any dose of axicabtagene ciloleucel. This analysis set will be used for all analyses of objective response and endpoints based on objective response (ORR, BOR rate including CR rate, DOR, PFS), time to next therapy and OS for the study.

6.3. Full Analysis Set (FAS)

The FAS will consist of all enrolled patients and will be used for the summary of subject disposition, sensitivity analyses of ORR, BOR rate including CR rate, DOR, PFS, time to next therapy, OS, and subject listings of deaths.

6.4. Safety Re-treatment 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 baseline covariates defined in Section 4.2.

7. INTERIM ANALYSIS

7.1. Interim Analysis

The DSMB will review safety data after 10 subjects in the safety analysis set have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 4 weeks for safety. This analysis will be for safety only.

The DSMB will meet again to review safety data after 30 subjects in the safety analysis set have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 4 weeks. This analysis will be for safety only.

The DSMB will meet again to review safety and efficacy data after 30 subjects with FL in the inferential analysis set have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 6 months after axicabtagene ciloleucel infusion. This analysis will be for safety and efficacy.

The DSMB will meet again to review the safety data when 80 subjects with FL in the inferential analysis set have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 6 months after axicabtagene ciloleucel infusion.

The DSMB will meet again to review the safety data when 80 subjects with FL in the inferential analysis set have been enrolled and treated with axicabtagene ciloleucel and have had an opportunity to be followed for 9 months from the first disease assessment date.

The DSMB will also review SAE information and SUSARs on a regular basis throughout subject treatment in the study. The DSMB may request additional safety data or modifying the study conduct. The sponsor may request additional reviews by the DSMB if safety concerns are identified. Data submitted to the DSMB may be monitored or unmonitored to facilitate and ensure timely DSMB review.

At the time of expedited reporting of SUSARs to regulatory authorities Kite (or designee) will concurrently submit these reports to the DSMB chair. The DSMB chair will also review SAE narrative reports monthly. Finally, the DSMB or Kite may request additional analyses of safety data if a safety concern arises during the course of the trial.

7.2. Access to Aggregate and Subject Level Data and Individual Subject Treatment Assignments

This study is open-label. Subjects, the study sponsor, and investigators will be aware that each subject is planned to be treated with axicabtagene ciloleucel. Data handling procedures designed to maintain the trial credibility and validity in this open-label single arm study are described in the Trial Integrity Document.

An independent statistician will perform the interim safety analyses of the study and provide these reports to the DSMB. Members of the DSMB and independent statistician will not have any direct contact with study center personnel or subjects. The DSMB will communicate recommendations to Kite Pharma in accordance with the DSMB charter.

8. FOLLOW-UP ANALYSIS

After the primary analysis, additional follow-up analyses of efficacy and safety will be performed as needed to satisfy regulatory requirements and to perform long-term efficacy, safety, and OS follow-up.

- Follow-up analysis 1 will be performed when 80 subjects in the FL inferential analysis set have had the opportunity to be followed for 18 months after axicabtagene ciloleucel infusion. This analysis will be for safety and efficacy and will be descriptive.

- Follow-up analysis 2 will be performed when 80 subjects in the FL inferential analysis set have had the opportunity to be followed for 24 months after axicabtagene ciloleucel infusion. This analysis will be for safety and efficacy and will be descriptive.

9. DATA SCREENING AND ACCEPTANCE

9.1. 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 analysis 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.

9.2. Electronic Transfer and Archival of Data

The database for this study will be managed and maintained at PRA International prior to 01-Feb-2018, and then will be managed and maintained by Kite Pharma. Raw data, SDTM data, and ADaM datasets will be generated by Kite Pharma 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), the central reads for the response assessments will be generated from contract laboratories and Kite Pharma. These data will be transferred to Kite and 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. Data from the Central Read for the response assessments will be generated from the contract central imaging center (ie, Imaging Endpoints). These data will be transferred to Kite and built into the clinical trial database.

9.3. Handling of Missing and Incomplete Data

9.3.1. 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 1 will be used.

9.3.2. 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.

9.4. 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.

9.5. 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.

9.6. Distributional Characteristics

The goal of the primary statistical analysis is to compare the observed ORR among subjects with FL per Central Read to a historical control rate of 40% with an exact binomial test. This test assumes only the independence of the individual subject responses. Hypothesis testing will be one-sided, and all 95% confidence intervals will be 2-sided and calculated via the Clopper-Pearson method. At the time of the primary analysis, 95% confidence intervals for the response rate and the statistical inference on efficacy will be presented.

9.7. 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.

10. STATISTICAL METHODS OF ANALYSIS

10.1. General Principles

The goal of the primary statistical analysis is to compare the observed ORR among subjects with FL per Central Read according to {Cheson 2014} to a historical control rate of 40% with an exact binomial test. Hypothesis testing will be one-sided, and all 95% confidence intervals will be 2-sided.

At the time of the primary analysis, 95% confidence intervals for the ORR and the CR rate, and the statistical inference on efficacy will be presented.

The timing of the interim, primary, and follow-up analyses will be based on subject accrual and disease assessment milestones.

The interim analysis 5 will be performed when at least 80 subjects with FL in the inferential analysis set have had the opportunity to be followed for 9 months after the first disease response assessment. The primary efficacy analysis of response rate will be performed when approximately 80 subjects with FL in the inferential analysis set have had the opportunity to be followed for at least 12 months after the first disease response assessment. A clinical study report (CSR) will be prepared and provided to the regulatory agency(ies). The CSR will be written based on the data collected and analyzed from the primary analysis. After the primary analysis, additional follow-up analyses of efficacy and safety will be performed as needed to satisfy regulatory requirements and to perform long-term efficacy, safety, and OS follow-up.

The final analysis will occur when all subjects have completed the study.

10.2. Subject Accountability

The number of subjects screened, enrolled, leukapheresed, treated with conditioning chemotherapy, treated with axicabtagene ciloleucel, and re-treated with axicabtagene ciloleucel will be summarized. The reasons for discontinuing treatment and discontinuing study, 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.

10.3. 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.

10.4. Protocol Variations due to COVID-19

The clinical study team will collect the protocol variations due to coronavirus disease 2019 (COVID-19) and define variation categories and review all protocol variations. A listing with protocol variations will be provided, In addition, the potential impact of the COVID-19 on the safety and efficacy profiles will be evaluated and analysis maybe performed.

10.5. Demographic and Baseline Characteristics

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

- ECOG performance status at baseline
- Sex (male, female)
- Weight
- Age at baseline (< 65, ≥ 65)
- Race: white, Asian, other (categories may be collapsed or expanded based on accrual)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Number of prior lines of therapy (excluding single agent anti-CD20 antibody as a line of therapy)
- Response to last chemotherapy regimen (PD, SD)
- Prior autologous stem cell transplant (ASCT)
- Histological diagnosis (eg, FL, MZL) by both local and central pathology
- FLIPI total score (0, 1, 2, 3, 4, 5, and low risk (0-1), intermediate risk (2), high risk (3-5))
- Disease burden
- Relapsed vs Refractory disease at study entry
- Time to relapse from initiation of first anti-CD20-chemotherapy combination therapy (≥ 24 months, < 24 months)
- Prior PI3K inhibitor

- Prior anti-CD20 single agent
- Prior alkylating single agent
- Prior anti-CD20 + alkylating agent
- Prior lenalidomide
- Bone marrow involvement
- Double refractory

10.6. Efficacy Analyses

For the primary analysis, the central assessment of disease status per {Cheson 2014} will be used. The secondary analyses will be conducted to use the investigator assessment status per {Cheson 2014} for ORR, BOR rate including CR rate, DOR, and PFS. Sensitivity analyses to use the FAS and safety analysis set for ORR, BOR rate including CR rate, PFS, and OS. The investigator or central reviewer will provide the determination of disease status (CR, PR, SD, PD, NE) at each time point. SAS programs developed by Kite Pharma will derive the ORR, BOR rate, DOR and PFS based on these assessments.

The efficacy analysis will be presented in the following analysis populations:

- Inferential analysis set (primary analysis)
- FAS (sensitivity analysis)
- Safety analysis set (sensitivity analysis)

For subjects who do not meet the eligibility criteria for the pivotal cohort, a listing of the efficacy endpoints will be provided.

For subjects re-treated 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, BOR rate, DOR, and PFS, and summaries of change in tumor burden. For such re-treated 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 anti-cancer therapy (including SCT) while on study, the subject's best overall response and change in tumor burden will be derived only based on disease outcomes assessed prior to initiation of subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel). For subjects without documentation of progression prior to initiation of subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel), the DOR and PFS time will be censored at the last evaluable

disease assessment prior to the initiation of subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel). Disease assessments obtained after SCT will not be included in the derivation of DOR and PFS. A sensitivity analysis for DOR and PFS will be conducted in which disease assessments after the SCT are included Appendix 2.

Efficacy summaries will be presented by histology disease type (eg, FL and MLZ) and overall.

10.6.1. ORR and BOR rate

10.6.1.1. Primary Analyses of ORR and BOR Rate

The subject incidence of objective response will be calculated. The 2-sided 95% confidence intervals will be provided about the ORR, calculated with the Clopper-Pearson method. An exact binomial test will be used to compare the observed ORR per Central Read among the subjects with FL and among the subjects with FL who have had 3 or more lines of prior therapy to the hypothesized historical control rate of 40%.

The incidence of subjects with CR, PR, SD, PD, NE, and ND as BOR to treatment and exact 2-sided 95% confidence intervals about the incidence will be generated. An exact binomial test will be used to compare the observed CR rate per Central Read among the subjects with FL and among the subjects with FL who have had 3 or more lines of prior therapy to the hypothesized historical control rate of 15%, if hypothesis test of ORR per Central Read among the subjects with FL is statistically significant.

The primary analysis of OR and BOR will include subjects from the inferential analysis set. Sensitivity analyses of objective response and BOR rate including CR rate will be conducted in the FAS and the safety analysis set, and use the investigator assessment status per {Cheson 2014} from the inferential analysis set. The concordance of objective response and BOR per Central Read and Investigator Read will be evaluated. A summary table of concordance, concordance rate, a kappa statistic, and a 2-sided 95% confidence interval about the kappa statistic will be provided. Further analyses comparing the Investigator and Central Reads may be performed as appropriate.

10.6.1.2. Subgroup Analyses of ORR and CR rate

ORRs and CR rates, and 95% confidence intervals about ORRs and CR rates 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.

10.6.2. DOR

Kaplan-Meier plots, estimates, and 2-sided 95% confidence intervals will be generated for DOR. Kaplan-Meier estimates will be provided for the proportion of subjects who are alive and progression-free at 3-month time intervals. The number of subjects censored or having events will be summarized, as well as the reasons for censoring and the event type (PD or death). Analyses will be generated for DOR per Central Read, as well as per Investigator Read. The reverse Kaplan-Meier approach {Schemper 1996} will be used to estimate the follow up time for DOR.

A sensitivity analysis of DOR will be conducted in the FAS set and the safety analysis set. A sensitivity analysis of DOR will be conducted in which disease assessments obtained after SCT are used in the derivation of DOR. A sensitivity analysis of DOR will be conducted using the investigator assessment per {Cheson 2014}.

DOR may be summarized in subgroups defined by the BOR attained on study. The forest plots for 9-month and 12-month DOR rates by subgroups will be generated.

10.6.3. PFS

Kaplan-Meier plots, estimates and 2-sided 95% confidence intervals 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 will be summarized, as well as the reasons for censoring and type of events (PD or death) will be summarized.

The primary analysis of PFS will include subjects from the inferential analysis set.

A sensitivity analysis of PFS will be conducted in which the PFS for subjects undergoing SCT while still in response is censored at the last evaluable disease assessment after SCT.

Additional sensitivity analyses of PFS will be conducted in the FAS and the safety analysis set, and will use the investigator assessment status per {Cheson 2014} from the inferential analysis set.

Analyses of PFS in subgroups defined by covariates described in Section 4.2 may be conducted.

PFS may be summarized in subgroups defined by the BOR attained on study. The forest plots for 9-month and 12-month PFS rates by subgroups will be generated.

10.6.4. OS

The analysis of OS will use the same methods as the analysis of PFS. 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 reverse Kaplan-Meier approach {Schemper 1996} will be used to estimate the follow up time for OS.

Additional sensitivity analyses of OS will be conducted in the FAS and the safety analysis set.

Analyses of OS in subgroups defined by covariates described in Section 4.2 may be conducted.

OS may be summarized in subgroups defined by the BOR attained on study.

The forest plots for 9-month and 12-month OS rates by subgroups will be generated.

10.6.5. Time to Next Therapy

The analysis of time to next therapy will use the same methods as the analysis of OS. Kaplan-Meier plots, estimates, and 2-sided 95% confidence intervals will be generated for time to next therapy.

10.6.6. 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. Analyses will be generated for change in tumor burden per Central Read and per investigator read. Data collected after subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel) will not be included for the analyses.

10.6.7. ORR and BOR rate among Subjects Re-treated with axicabtagene ciloleucel

The subject incidence of subjects re-treated with axicabtagene ciloleucel will be tabulated. The subject incidence of objective response and BOR (CR, PR, SD, PD, NE) to the retreatment among subjects re-treated with axicabtagene ciloleucel will be calculated. Confidence intervals will be provided about the ORR and the CR rate to the retreatment. Analyses will be conducted per Central Read or Investigator Read according to {Cheson 2014}.

10.6.8. DORR

The analysis of DORR to retreatment among subjects re-treated with axicabtagene ciloleucel will use the same methods as the analysis of duration of response.

10.7. 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, AEs 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.

AEs will be coded with the Medical Dictionary for Regulatory Activities (MedDRA) at the time of each analysis. The version of the MedDRA may vary over time as the current version in use is updated. The severity of AEs will be graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 or above. CRS will be graded using a revised CRS grading scale developed by Lee et al {Lee 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 4.03 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.

Safety summaries will be presented by histology disease type (eg, FL and MLZ) and overall.

10.7.1. Adverse Events

The subject incidence of the following treatment-emergent adverse events will be tabulated:

- Summary of AEs (any, worst severity, serious, related)
- All AEs
- All serious AEs
- All axicabtagene ciloleucel-related AEs
- All axicabtagene ciloleucel-related serious AEs
- All Grade 3 or higher AEs
- All Grade 3 or higher axicabtagene ciloleucel-related AEs
- Fatal AEs (Grade 5 AEs, by PT on period [Day 0 through Day 30, Day 31 through Day 92, and ≥ Day 93])
- AEs of interest, including identified and potential risks

Summary statistics for the onset time, duration, and resolution of AEs of interest will be provided.

The subject incidence of deaths will be provided.

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

Subgroup analyses of AEs may be generated for the subgroups listed in Section 4.2.

Besides TEAEs, the subject incidence of the following AEs by PT and severity will also be tabulated:

- AEs deemed by investigator to be related to leukapheresis
- AEs deemed by investigator to be related to conditioning chemotherapy

A listing will also be provided for all AEs that occurred following leukapheresis for subjects who have been leukapheresed and not dosed with axicabtagene ciloleucel, along with subjects' conditioning chemotherapy administration information, if available.

10.7.2. Laboratory Test Results

Laboratory results will be graded according to NCI Common Toxicity Criteria (CTCAE version 4.03 or above). Laboratory data collected at baseline and throughout the axicabtagene ciloleucel Treatment Period will be summarized. The incidence of worst CTCAE grade post axicabtagene ciloleucel infusion by grade for selected analytes will be provided. Additional lab 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.

10.7.3. Anti-axicabtagene ciloleucel antibodies

The subject incidence of any anti-axicabtagene ciloleucel antibodies will be tabulated. For subjects testing positive for antibodies, the persistence of the antibody over time will be summarized.

10.7.4. 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.

10.7.5. Exposure to Study Treatment and Product Characteristics

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

- Total 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
- Total CAR T cells of the axicabtagene ciloleucel infusion
- Total T cells of the axicabtagene ciloleucel infusion

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 axicabtagene ciloleucel for subjects in the safety retreatment analysis set.

10.7.6. Exposure to Concomitant Medications and Procedures

The subject incidence of concomitant medications will be provided and summarized by medication category (general, gamma globulin, immunosuppressive, anti-infective, vaccinations, IV normal saline bolus, vasopressor, tocilizumab, and steroids) and WHO Drug coded term. The subject incidence of procedures will be tabulated. The incidences of procedure and concomitant medications overall and used to manage adverse events will be tabulated. The incidence of IVIG usage will be summarized.

10.8. Subsequent Anti-cancer Therapy and Subsequent SCT

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

10.9. Schedule of Study Treatment

Summary statistics will be provided for the following durations:

- 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
- Duration of hospitalization for the axicabtagene ciloleucel infusion

10.10. CAR T cells Measured in Peripheral Blood

Summary statistics for the level of CAR T cells in serum following 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.

11. CHANGES FROM PROTOCOL-SPECIFIED ANALYSES

There is no change from protocol-specified analyses.

12. REFERENCES

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Topp MS, Gokbuget N, Stein AS, Zugmaier G, O'Brien S, Bargou RC, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. Lancet Oncol 2015;16 (1):57-66.

13. APPENDICES

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

Table 1. 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 study day 0
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 mmyyyy for the last contact date = mmyyyy for death date, set death date to the day after the last date known to be alive.
   - If mmyyyy for the last date known to be alive < mmyyyy for death date, set death date to the first day of the death month.
   - If mmyyyy for last date known to be alive > mmyyyy 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, PFS, and OS is provided below.

Duration of response (DOR): DOR is defined only for subjects who experience an objective response (CR or PR) and is the time from the first objective response to disease progression or death due to any cause. Response and progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for progression or death due to any cause 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-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel) in the absence of prior documented progression will be censored at the last evaluable disease assessment date prior to subsequent anti-cancer therapy. The DOR for subjects who undergo SCT while in an axicabtagene ciloleucel-induced response will be censored at the last evaluable disease assessment prior to SCT. 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-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Progression date
Death due to any cause without documented disease progression and without subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel)	Event	Death date
Remain in response without any subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel)	Censored	Last evaluable disease assessment date
Initiated subsequent anti-cancer 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-cancer therapy, SCT, or retreatment, whichever the earliest
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 the withdrawal of consent or lost to follow-up prior to data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Sensitivity analysis of DOR 1 (including the disease assessments after SCT):

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression after SCT, but prior to other subsequent anti-cancer therapy (including retreatment with axicabtagene ciloleucel)	Event	Progression date
Death due to any cause after SCT without documented progression and other subsequent anti-cancer therapy (including retreatment with axicabtagene ciloleucel)	Event	Death date
Remain in response after SCT without other subsequent anti-cancer therapy (including retreatment with axicabtagene ciloleucel)	Censored	Last evaluable disease assessment date
Remain in response after SCT prior to other subsequent anti-cancer therapy (including retreatment with axicabtagene ciloleucel)	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-cancer therapy or retreatment, whichever the 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 the withdrawal of consent or lost to follow-up prior to 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 {Cheson 2014} or death due to any cause. Response and progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for 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-cancer 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-cancer 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 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-cancer therapy (including SCT)	Event	Progression date
Death due to any cause without documented disease progression and without subsequent anti-cancer therapy (including SCT)	Event	Death date
Remain in response without any subsequent anti-cancer therapy (including SCT)	Censored	Last evaluable disease assessment date
Initiated subsequent anti-cancer 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-cancer therapy, or SCT, whichever the 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 the withdrawal of consent or lost to follow-up prior to data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Sensitivity analysis of DORR 1 (including the disease assessments after SCT):

Circumstance	Event / Censored	Date of Event / Censoring
Disease progression after SCT, but prior to other subsequent anti-cancer therapy	Event	Progression date
Death due to any cause after SCT without documented progression and other subsequent anti-cancer therapy	Event	Death date
Remain in response after SCT without other subsequent anti-cancer therapy	Censored	Last evaluable disease assessment date
Remain in response after SCT prior to other subsequent anti-cancer therapy	Censored	Date of last evaluable disease assessment prior to initiation of subsequent anti-cancer 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 the withdrawal of consent or lost to follow-up prior to data cutoff for analysis	Censored	Date of last evaluable disease assessment prior to data cutoff for analysis

Progression-free Survival (PFS): PFS is defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression per {Cheson 2014} or death due to any cause. Progression may be defined per Central Read or Investigator Read. Subjects not meeting the criteria for progression by the analysis data cutoff date will be censored at their last evaluable disease assessment date. The PFS for subjects who receive any subsequent anti-cancer therapy (including SCT or retreatment with axicabtagene ciloleucel) in the absence of prior documented progression will be censored at the last evaluable disease assessment prior to subsequent anti-cancer therapy. The PFS for subjects who undergo SCT while in an axicabtagene ciloleucel-induced response will be censored at the last evaluable disease assessment date prior to SCT. A sensitivity analysis will be conducted in which disease assessments obtained after SCT are included in the derivation of PFS.

Primary analysis of PFS:

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

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

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

Overall Survival (OS): OS is defined as the time from the axicabtagene ciloleucel infusion to the date of death from 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 for each analysis will be censored at the data cutoff date.

Circumstance	Event / Censored	Date of Event / Censoring
Death before data cutoff date for analysis	Event	Date of death
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 data cutoff date	Censored	last date known to be alive date up through the data cutoff date
Withdrawal of consent or lost to follow up prior to data cutoff date	Censored	Last date known to be alive prior to consent withdrawal 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 CRS)
- Start and end dates of concomitant medications
- Start and end dates of subsequent therapy including SCT
- 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