STUDY SYNOPSIS

STUDY KTE-C19-106
Kite Pharma, Inc.
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USA

Title of Study: A Phase 1-2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-C19 in Combination with Atezolizumab in Subjects with Refractory Diffuse Large B Cell Lymphoma (DLBCL)
Investigators: Multicenter study.
Study Centers: This study was conducted at a total of 5 study centers in the US.
Publications: Citations for meeting presentations based upon this study are provided below. Jacobson CA, Locke FL, Miklos DB, Herrera AF, Westin JR, Lee J, et al. End of Phase 1 results for ZUMA-6: Axicabtagene ciloleucel (axi-cel) in combination with atezolizumab for the treatment of patients with refractory diffuse large B cell lymphoma. Presented at ASH, 2018. Locke FL, Westin JR, Miklos DB, Herrera AF, Jacobson CA, Lee J, et al. Phase 1 results from ZUMA-6: Axicabtagene ciloleucel (axi-cel; KTE-C19) in combination with atezolizumab for the treatment of patients with refractory diffuse large B cell lymphoma. Presented at ASH, 2018, presentation #2628.
Study Period: 29 September 2016 (First Subject Enrolled in Phase 1) 21 February 2019 (Last Subject Last Observation for this Report)
Phase of Development: Phase 1/2

Objectives:

Rationale: The addition of a PD-L1 inhibitor (atezolizumab) to the axicabtagene ciloleucel regimen may improve clinical outcomes seen with axicabtagene ciloleucel alone.

The primary objectives of this study were as follows:

- The primary objective of Phase 1 was to evaluate the safety of axicabtagene ciloleucel and atezolizumab treatment regimens.
- The primary objective of Phase 2 was to evaluate the efficacy of axicabtagene ciloleucel and atezolizumab, as measured by the CR rate in subjects with refractory DLBCL.

The secondary objectives of this study were as follows:

- The secondary objectives included assessing the safety and tolerability of axicabtagene ciloleucel and atezolizumab and additional efficacy, biomarker, pharmacokinetic (PK), and immunogenicity endpoints.

Methodology:

ZUMA-6 is an ongoing Phase 1/2, open-label multicenter study evaluating the safety and efficacy of axicabtagene ciloleucel and atezolizumab in subjects with refractory diffuse large B cell lymphoma (DLBCL). The study comprises Phase 1 and Phase 2 portions. Phase 1 and Phase 2 enrollment and study treatment dosing have been completed (last subject dosed with axicabtagene ciloleucel on 08 August 2018) and follow-up is continuing for all subjects who remain alive. The total duration of the study for individual subjects will vary depending on a subject's screening requirements, response to treatment, and survival. For a subject who completes the entire protocol from the date of informed consent through the completion of the long-term follow-up period, the duration of the study will take approximately 5 years to complete (samples for replication competent retrovirus [RCR] will be collected and held for up to 15 years).

Completion of the study is defined as the time at which the last subject completes the long-term follow-up period visit, is considered lost to follow-up, withdraws consent, or dies. The primary analysis was conducted when all subjects for the overall study population have had the opportunity to complete the 6 month disease response assessment, were lost to follow-up, withdrew from the study, or died, whichever occurred first.

Phase 1 was planned to enroll approximately 3 to 9 subjects in up to 3 cohorts. Subjects were to receive conditioning chemotherapy consisting of 30 mg/m^2 fludarabine and 500 mg/m^2 cyclophosphamide per day for 3 days followed by axicabtagene ciloleucel at a target dose of 2×10^6 anti-CD19 CAR T cells/kg followed by 4 doses of atezolizumab (1200 mg/dose). Atezolizumab was to be given every 21 days as follows: Cohort 1, beginning 21 days following axicabtagene ciloleucel infusion; Cohort 2, beginning 14 days following axicabtagene ciloleucel infusion; and Cohort 3, beginning 1 day following axicabtagene ciloleucel infusion. An internal safety review team (SRT) was to comprise at least one investigator from the Phase 1 portion of the study, the Kite medical monitor, project statistician, and other experts with significant experience with the CAR T-cell therapy, as needed. The SRT was to review safety data after all subjects in each Phase 1 cohort had been

followed for dose limiting toxicities (DLTs) for 21 days after the first infusion of atezolizumab. When the SRT deemed the dosing regimen of Cohort 1 safe for further study, then Phase 1 proceeded with subsequent enrollment of Cohort 2. Likewise, if Cohort 2 was deemed safe by the SRT, then Cohort 3 would begin enrollment. If the SRT deemed the dosing regimen of Cohort 3 to be safe for further study, then enrollment in Phase 2 would proceed with the Cohort 3 dosing regimen.

In Phase 2, approximately 22 subjects were to be enrolled to receive treatment with axicabtagene ciloleucel and atezolizumab based on the dose and schedule selected to move forward from the Phase 1 portion of the study as recommended by the SRT.

To ensure subject safety, all subjects were hospitalized during and for a minimum of 7 days following the axicabtagene ciloleucel infusion (Day 0). Subsequently, subjects returned to the clinic at Day 14 (± 2 days), Day 22 (± 3 days), Day 28 (± 2 days) for Phase 2 or Day 35 (± 2 days) for Phase 1, Day 43 (± 2 days), Day 49 (± 2 days) optional, Day 64 (± 2 days), Day 69 (± 2 days) and Day 94 (± 1 week). Safety assessment were performed at each of these visits. Disease response was assessed starting at Month 6. Long-term follow-up for disease status (among subjects remaining in response) and survival continued every 3 months through Month 18, then every 6 months through 5 years, and then annually for a maximum of 15 years.

The following assessments/procedures/data collection were conducted: informed consent (baseline visit only); general medical history including previous treatments for DLBCL (baseline visit only); physical examination, including vital signs and performance status; neurological assessments; blood draws for complete blood count (CBC) and lymphocyte subsets, chemistry panels; antibodies to FMC63 (the parental murine antibody used for development of the anti-CD19 variable regions of the CAR construct); antibodies to atezolizumab; and the presence of replication competent retrovirus (RCR).

Subjects who achieved a PR or CR had an option to receive a second course of conditioning chemotherapy, axicabtagene ciloleucel and treatment course of atezolizumab if their disease subsequently progresses greater than 3 months following the axicabtagene ciloleucel infusion, provided CD19 expression on tumor cells was confirmed locally by biopsy after disease progression and prior to re-treatment, and after consultation and agreement of the study sponsor.

Number of Subjects (Planned and Analyzed):
Phase 1

Planned enrollment: 3 to 9 subjects in up to 3 cohorts.

Enrolled/leukapheresed: 3 subjects in Cohort 1, 4 subjects in Cohort 2, and 7 subjects in Cohort 3.

Phase 2

Planned enrollment: 22 subjects.

Enrolled/leukapheresed: 23 subjects

Diagnosis and Main Criteria for Inclusion:

1) Histologically proven DLBCL
2) Chemotherapy-refractory disease, defined as:
   - No response to first-line therapy (primary refractory disease); subjects who are intolerant to first-line therapy chemotherapy are excluded, OR
   - No response to second or greater lines of therapy, OR
   - Refractory after ASCT
3) Subjects must have received adequate prior therapy, including at a minimum:
   - Anti-CD20 monoclonal antibody unless investigator determines that tumor is CD20 negative, and
   - An anthracycline containing chemotherapy regimen;
4) At least 1 measurable lesion according to the revised International Working Group (IWG) Response Criteria for Malignant Lymphoma. Lesions that had been previously irradiated were considered measurable only if progression had been documented following completion of radiation therapy
5) Magnetic resonance imaging (MRI) of the brain showing no evidence of central nervous system (CNS) lymphoma
6) At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed since any prior systemic therapy at the time the subject was planned for leukapheresis
7) Age 18 years or older at the time of informed consent
8) Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
9) Adequate bone marrow, renal, hepatic, pulmonary and cardiac function

Duration of Treatment:

Following leukapheresis, subjects received a 3-day-cycle of conditioning chemotherapy followed by a single infusion of axicabtagene ciloleucel followed by 4 doses of atezolizumab. Atezolizumab was to be given every 21 days as follows: Cohort 1, beginning 21 days following axicabtagene ciloleucel infusion; Cohort 2, beginning 14 days following axicabtagene ciloleucel infusion; and Cohort 3, beginning 1 day following axicabtagene ciloleucel infusion. Subjects were followed through Day 94 for safety observations. Long-term follow-up for disease progression and survival continue for subjects who responded to the treatment through a maximum of 15 years.

Test Product, Dose, and Volume of Infusion:

Investigational Product:

Axicabtagene ciloleucel is supplied cryopreserved in cryostorage bags. The product in the bag is slightly cloudy and cream to yellow. The cryostorage bags containing axicabtagene ciloleucel arrive frozen in a liquid nitrogen dry shipper. The bags must be stored in vapor phase of liquid nitrogen and the product is to remain frozen until the subject is ready for treatment to assure viable live autologous cells are administered to the subject. Several inactive ingredients are added to the product to assure viability and stability of the live cells through the freezing, thawing, and infusion process. Axicabtagene ciloleucel is a subject-specific product and the intended subject was identified by a unique subject ID number. Axicabtagene ciloleucel is administered after a conditioning chemotherapy regimen consisting of fludarabine 30 mg/m^2/day and cyclophosphamide 500 mg/m^2/day, administered x 3 days.

Subjects received a single infusion of axicabtagene ciloleucel at a target dose of 2 x 10^6 anti CD19 CAR T cells/kg.

Test Product, Dose, and Volume of Infusion:

Atezolizumab:

Atezolizumab treatment consisted of an intravenous infusion of 1200 mg (as a prepared dilution in a 250 mL of 0.9% NaCl) given every 21 days for 4 doses. During Phase 1, the first dose of atezolizumab was administered in 3 cohorts:

- Cohort 1: Beginning on Day 21 following axicabtagene ciloleucel infusion
- Cohort 2: Beginning on Day 14 following axicabtagene ciloleucel infusion
- Cohort 3: Beginning on Day 1 following axicabtagene ciloleucel infusion

The initial dose of atezolizumab was delivered over 60 (± 15) minutes. If the first infusion was tolerated without infusion-associated AEs, the second infusion may have been delivered over 30 (± 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions may have been delivered over 30 (± 10) minutes.

Phase 2 followed the dosing paradigm of Phase 1 Cohort 3.

Reference Therapy, Dose, Mode of Administration, and Batch No.:

None

Criteria for Evaluation:

Primary Endpoints

- Phase 1: Incidence of DLTs
- Phase 2: Complete response rate (CR per the revised IWG Response Criteria for Malignant Lymphoma) as determined by study investigators.

Secondary Endpoints

Phase 1 and Phase 2:

- Objective response rate (CR + PR) per the revised IWG Response Criteria for Malignant Lymphoma
- Duration of response
- Progression free survival
- Overall survival
- Incidence of AEs and clinically significant changes in safety laboratory values
- Levels of axicabtagene ciloleucel in blood
- Incidence of antibodies to FMC63 (parent antibody for the scFv used for production of the anti CD19 CAR in axicabtagene ciloleucel)
- Atezolizumab PK
- Incidence of anti-atezolizumab antibodies in serum
- Levels of cytokines and other markers in serum

Exploratory Endpoints

Phase 1 and Phase 2:

- Objective response rate based on PD-L1 expression on tumor cells or infiltrating immune cells
- Investigation of potential biomarker development based on assessment of product cells, blood cells, tumor tissue at baseline and post-treatment, and the proposed actions of the IP (ie, PD-L1 expression on tumor and immune infiltrating cells)
- Frequency of atezolizumab dose delays for ongoing acute toxicities following axicabtagene ciloleucel

Pharmacokinetics/Pharmacodynamics:

PK/PD evaluation criteria are described in m5.4.3.2.

Statistical Methods:

Efficacy:

Efficacy analyses were conducted on the mITT analysis set and used the investigator's assessment of disease status per Cheson 2007.

Complete Response and Objective Response

The subject incidence of CR and objective response (CR + PR) was calculated. Two-sided 95% CIs were generated using the Clopper-Pearson (an exact interval) method. The number and percentage of subjects who initially did not attain CR and who subsequently attained a CR was summarized.

The response rates and exact 2-sided 95% CIs were generated for subgroups of the mITT analysis set based on, but not limited to, the covariates defined in Section 7.7.3.2.

Duration of Response

The Kaplan-Meier approach was used to estimate DOR. The number of subjects censored and the reasons for censoring are summarized. The reverse Kaplan-Meier approach was used to estimate the follow-up time for DOR.

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

DOR was to be summarized in subgroups defined by the best response attained on study.

Progression-free Survival

Kaplan-Meier plots, estimates, and 2-sided 95% CIs were generated for PFS. Estimates of the proportion of subjects alive and progression-free at 3-month intervals were to be provided. The number of subjects censored or having events, and the reasons for censoring or type of events (PD or death), were to be summarized. The reverse Kaplan-Meier approach was to be used to estimate the follow up time for PFS.

A sensitivity analysis of PFS was to be conducted in which the disease assessments obtained after ASCT was to be included in the derivation of disease assessment. Subgroup analyses of the PFS rate at 6 months may have been generated in subgroups defined by the covariates in Section 7.7.3.2.

PFS may have been summarized in subgroups defined by the best response attained on study.

Overall Survival

The analysis of OS used the same methods as the analysis of PFS. The reverse Kaplan-Meier approach was used to estimate the follow-up time for overall survival. The OS may have been summarized in subgroups defined by the best response attained on study.

Tumor Burden

The change in tumor burden, as measured by the sum of the product of the diameters of the selected lesions, from baseline to post-baseline nadir was to be summarized in absolute numbers (mm^2) and percentages. Summary statistics was to be provided for this change. Data collected after new anti-cancer therapy or SCT was not to be included for the analyses.

Safety:

Safety analyses were conducted on the SAS. The primary analysis of safety data was to summarize all TEAEs and laboratory values.

Exposure to Study Treatment and Product Characteristics

Summary statistics and subject listings were 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
- Total CAR T cells of the axicabtagene ciloleucel infusion
- Total T cells of the axicabtagene ciloleucel infusion
- Transduction percentage
- Ratio of CD4 and CD8 T cells
- Percentages of T-cell memory phenotypes
- IFN-γ production in cocultures of axicabtagene ciloleucel product
- Summary of atezolizumab infusion

Adverse Events

AEs were coded with the version 21.1 of MedDRA. The severity of AEs were graded using the NCI CTCAE v4.03. The incidence and severity of CRS were graded using a revised CRS grading scale developed by Lee and colleagues. Individual symptoms associated with CRS were graded per CTCAE v4.03.

The subject incidence of the AEs were tabulated by SOC and PT. Summary statistics for the study day of onset, the study day of resolution, and the duration of AEs of interest were provided. A subject listing of deaths and SAEs (including narratives) were provided by overall and by treatment period. Subgroup analyses of AEs may have been generated using the covariates listed in Section 7.7.3.2, if applicable.

Subjects enrolled, but not dosed with the study combination treatment, were followed for AEs for 30 days after the last study procedure. AEs reported in these subjects were to be archived in the study database and available in study data tabulation model and analysis data model (ADaM) datasets, but were not tabulated in AE summaries.

Laboratory Test Results

Laboratory results were graded according CTCAE (v4.03). Laboratory data collected at baseline and through the treatment and follow-up periods were summarized. Shifts from baseline to minimum postbaseline and/or maximum postbaseline values were presented for selected analytes. The incidence of worst grade CTCAE shift for selected analytes were provided.

Anti-axicabtagene Ciloleucel Antibodies

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

Anti-therapeutic Antibodies to Atezolizumab

A central laboratory used validated immunoassays to assay serum samples for the presence of ATAs to atezolizumab and atezolizumab concentrations. Atezolizumab PK and incidence of ATA in serum were tabulated. For subjects testing positive for antibodies, the persistence of the antibody over time was to be summarized.

Replication-competent Retrovirus

The subject incidence of RCR detected in blood samples was tabulated overall and by assessment time. The persistence of RCR over time was summarized.

Exposure to Concomitant Medications and Procedures

The subject incidence of concomitant medications was provided and summarized by medication category (general, immunosuppressive, anti-infective, vasopressor, corticosteroid, and tocilizumab) and WHO-Drug Global coded term. The subject incidence of procedures were tabulated.

Duration of Study Treatment

Summary statistics are provided for the following durations:

- Days from screening to commencement of leukapheresis and administration of axicabtagene ciloleucel.
- Days from leukapheresis to commencement of conditioning chemotherapy, receipt of axicabtagene ciloleucel at the study site, and administration of axicabtagene ciloleucel.
- Days from conditioning chemotherapy to administration of axicabtagene ciloleucel.
- Duration of hospitalization for the axicabtagene ciloleucel infusion.

Subsequent Anticancer Therapy

The incidence and type (by WHODrug Global coded term and categories) of subsequent anti-cancer therapy and SCT (autologous, allogeneic) were summarized.

Pharmacokinetics/Pharmacodynamics:

PK/pharmacodynamics analysis methods are described in m5.3.4.2.

SUMMARY OF RESULTS:

Subject Disposition and Demographics:

Phase 1 Cohort 1

Three subjects were enrolled (defined as having leukapheresis initiated), and all had conditioning chemotherapy, completed treatment with axicabtagene ciloleucel, and completed treatment with atezolizumab (defined as receiving all 4 doses).

Phase 1 Cohort 2

Four subjects were enrolled; 3 subjects (75%) received conditioning chemotherapy and completed treatment with both axicabtagene ciloleucel and atezolizumab. One subject did not receive treatment due to having low platelets.

Phase 1 Cohort 3

Four subjects were treated, and 1 of these subjects (Subject 106 003-002) experienced DLTs of Grade 4 neutropenia (Day 13 to Day 54) and Grade 4 thrombocytopenia (Day 25 to Day 189). As a result of this DLT, the SRT recommended to enroll an additional 3 subjects in Cohort 3, allowing further evaluation of safety prior to deciding on the atezolizumab dosing schedule for Phase 2. No DLTs occurred in the Cohort 3 expansion phase. Thus, 7 subjects were enrolled in Phase 1 Cohort 3. Of these, six subjects (86%) received conditioning chemotherapy and completed treatment with axicabtagene ciloleucel, and 4 subjects (57%) received conditioning chemotherapy, completed treatment with axicabtagene ciloleucel, and completed treatment with atezolizumab.

Phase 2

All 23 enrolled subjects (100%) were treated with conditioning chemotherapy and 22 subjects (96%) received axicabtagene ciloleucel; one subject (Subject 106-003-009) had AEs of Grade 3 bacteremia, Grade 4 septic shock, and Grade 3/Grade 4 cytopenias, which precluded treatment with axicabtagene ciloleucel. All 22 subjects who received axicabtagene ciloleucel were treated with atezolizumab and 14 subjects (61%) completed atezolizumab treatment. Of those who did not complete atezolizumab treatment, 5 subjects (22%) had an AE, 1 subject (4%) died, and 2 subjects (8%) had disease progression.

In the mITT analysis set, the median age was 58 years (range: 42 to 71 years). Men comprised 57% (16 of 28 subjects) of the mITT analysis set and most subjects were white (82%, 23 of 28 subjects).

Efficacy Results:

1) Phase 1 findings supported proceeding to Phase 2 using the Phase 1 Cohort 3 atezolizumab dosing schedule. All 3 dosing schedules tested in Phase 1 were deemed safe by the SRT. Phase 2 proceeded with the Cohort 3 dosing regimen (infusion of axicabtagene ciloleucel at 2 x 106 anti-CD19 CAR T cells/kg on Day 0 followed by first infusion of 1200 mg atezolizumab on Day 1) based on the observation of 1 of 12 evaluable subjects having a DLT.

   The mITT analysis set comprised the 6 subjects treated in Phase 1 Cohort 3 combined with the 22 subjects treated in Phase 2. Four of 6 subjects in Phase 1 Cohort 3 and 14 of 22 subjects (61%) in Phase 2 received all 4 doses of atezolizumab.

2) Efficacy Results for the mITT Set

   a) Primary Efficacy Endpoint

      i) The CR rate was 46% (13 of 28 subjects, 95% CI: 28%, 66%).

   b) Secondary Efficacy Endpoints

      i) The ORR was 75% (21 of 28 subjects, 95% CI: 55%, 89%), with a PR rate of 29%.

      ii) With a median (95% CI) follow-up time for DOR of 5.1 months (95% CI: 4.6, 10.6 months), the median DOR among subjects with an objective response was not reached. KM estimates of the proportion of subjects in response at 6, 9, and 12 months from first response were 61.9%.

      iii) PFS rate estimates at 6, 9, and 12 months all were 50.0%. The median duration of PFS was not reached.

      iv) OS rates at 6, 9, and 12 months all were 71.4%. At the median study follow-up time of 9.0 months, the median OS duration was not reached.

Safety Results:

1) Treatment with a single infusion of axicabtagene ciloleucel followed by 1 to 4 doses of atezolizumab had a manageable safety profile. Data presented below are for the mITT set unless otherwise noted.

   a) Nine of 22 subjects (41%) in Phase 2 and 2 of 6 subjects in Phase 1 Cohort 3 had Grade 3 or higher axicabtagene ciloleucel related AEs.

   b) Ten of 22 subjects (45%) in Phase 2 and 2 of 6 subjects in Phase 1 Cohort 3 experienced at least 1 axicabtagene ciloleucel related SAE.

   c) Three of 22 subjects (14%) in Phase 2 and 1 of 6 subjects in Phase 1 Cohort 3 had Grade 3 or higher atezolizumab related AEs.

   d) Four of 22 subjects (18%) in Phase 2 and 1 of 6 subjects in Phase 1 Cohort 3 experienced at least 1 atezolizumab related SAE.

e) In Phase 2 (N 22), one subject (5%) had Grade 3 CRS. The Grade 3 individual CRS events per CTCAE v4.03 were hypoxia (10%), pyrexia (5%), diarrhea (5%) and fatigue (5%). In Phase 1 Cohort 3 (N 6), no subjects had Grade 3 or higher CRS. The Grade 3 individual CRS events per CTCAE v4.03 were pyrexia (n 1) and diarrhea (n 1).

i) The median time to onset of first CRS symptoms of any grade after axicabtagene ciloleucel infusion was 2 days (range: 2 to 13 days) in Phase 2 and 3 days (range: 1 to 7 days) in Phase 1 Cohort 3.

ii) CRS events resolved in all 33 subjects who had CRS. The median duration of CRS symptoms was 6 days (range: 1 to 92 days) for Phase 2 and 9.5 days (range: 6 to 16 days) for Phase 1 Cohort 3.

f) Six of 22 subjects (27%) in Phase 2 and 2 of 6 subjects in Phase 1 Cohort 3 had Grade 3 or higher neurologic events.

i) The median time to onset of the first neurologic event of any grade after axicabtagene ciloleucel infusion was 6 days (range: 2 to 23 days) for Phase 2 and 5 days (range: 1 to 10 days) for Phase 1 Cohort 3.

ii) Neurologic events resolved in 13 of 15 subjects (87%) in Phase 2 and all subjects with neurologic events in Phase 1 Cohort 3. The median duration of neurologic events was 9.0 days (range: 2 to 60 days) for Phase 2 and 14.0 days (range: 6 to 24 days) for Phase 1 Cohort 3.

g) Eight of 22 subjects (36%) in Phase 2 and 1 of 6 subjects in Phase 1 Cohort 3 had Grade 3 or higher cytopenias (thrombocytopenia, neutropenia, or anemia) present on or after Day 30.

h) Eleven of 22 subjects (50%) in Phase 2 and 2 of 6 subjects in Phase 2 Cohort 3 had infections, and the majority were Grade 1 or Grade 2.

i) Across all cohorts and both phases, no subjects had Grade 3 or higher hypogammaglobulinemia.

j) One of 22 subjects in Phase 2 and 1 of 3 subjects in Phase 1 Cohort 1 had a secondary malignancy.

k) Across both phases and all cohorts, no subjects had TLS, SIA, a positive test for postbaseline antibodies to axicabtagene ciloleucel or atezolizumab, or a positive postbaseline test for presence of RCR.

Other:

One subject was retreated with axicabtagene ciloleucel. The best response to initial treatment was PR. The best response to retreatment was PD.

CONCLUSIONS:

Subjects with refractory DLBCL treated with axicabtagene ciloleucel followed by up to 4 doses of atezolizumab given every 21 days beginning on Day 1 had an ORR of 75%, with a CR rate of 46% and a PR rate of 29%. At a minimum follow-up of 6 months, more than half of all responding subjects remained in response, and 46% of all subjects remained in response. At a median follow-up of 9 months for OS, median overall survival has not been reached. The results from this study demonstrated that axicabtagene ciloleucel infusion followed by PD-L1 blockade with atezolizumab appeared to have a manageable safety profile consistent with that observed in ZUMA-1, a large study of axicabtagene ciloleucel alone in a population with similar eligible criteria as ZUMA-6. Overall, CRS and neurologic events did not recur or worsen following atezolizumab administration, and no new safety signals were observed for atezolizumab. In the Phase 2 portion of ZUMA-1, with a minimum follow-up of 6 months, 44% of subjects remained in ongoing response. In conclusion, axicabtagene ciloleucel in combination with atezolizumab demonstrated a manageable safety profile. These data suggest that the efficacy of axicabtagene ciloleucel in combo with atezolizumab, as measured by complete response rate, objective response rate, duration of response, and the proportion of subjects in ongoing response is not improved relative to the efficacy outcomes in subjects treated with axicabtagene ciloleucel alone.