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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Tisagenlecleucel

Trial Indication(s)

Relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

Protocol Number

CCTL019C2201

Protocol Title

A Phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019 in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: July 29, 2015 (Actual)
Primary Completion Date: December 22, 2022 (Actual)
Study Completion Date: December 22, 2022 (Actual)

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Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a single arm, open-label, multi-center, Phase II study conducted to determine the efficacy and safety of tisagenlecleucel in adult patients with r/r DLBCL. The study consisted of the following sequential periods: Screening, Pre-Treatment, Treatment and Primary follow-up, Secondary follow-up, Survival follow-up.

Patients were enrolled in 2 cohorts to receive one tisagenlecleucel infusion as follows:

- Main Cohort (patients treated with tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US, referred to as “US manufacturing facility”) and
- Cohort A (patients treated with tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany, referred to as “EU manufacturing facility”).

The Treatment and Primary follow-up was 60 months from the time of tisagenlecleucel infusion for each infused patient. After tisagenlecleucel infusion, efficacy was assessed at Day 28 and 3, 6, 9, 12, 18, 24 months and then every 12 months for 5 years until documented disease relapse or disease progression. Patients who discontinued the Treatment and Primary Follow-Up Phase before Month 60 continued to be followed in the secondary follow-up phase in order to collect health authority requested data (e.g. delayed adverse events) up to 5 years after tisagenlecleucel infusion. Safety was assessed throughout the study.

Patients who completed the Primary Follow-Up or prematurely discontinued from the primary or secondary follow-up phase were followed for survival until LPLV (22-Dec-2022), or until the patient was enrolled in the long term follow-up study to assess the lentiviral vector safety under a separate destination protocol, whichever occurred first.

Centers

26 centers in 10 countries: United States(12), Norway(1), Australia(2), Austria(1), Canada(2), Germany(2), Japan(3), Italy(1), France(1), Netherlands(1)

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Objectives:

Primary Objective:

Evaluate the efficacy of tisagenlecleucel therapy in the Main Cohort as assessed by Independent Review Committee (IRC)

Secondary Objectives:

- Evaluate safety of tisagenlecleucel
- Evaluate time to response
- Evaluate duration of overall response (DOR)
- Evaluate event free survival (EFS)
- Evaluate progression free survival (PFS)
- Evaluate overall survival (OS)
- Evaluate efficacy and safety of histological and molecular subgroups (germinal center (GC), activated B-cell (ABC), other
- Characterize the *in vivo* cellular PK profile (levels, expansion, persistence) of tisagenlecleucel transduced cells into target tissues (blood bone marrow, cerebral spinal fluid and other tissues (blood, bone marrow, cerebral spinal fluid and other tissues if available), summarized by clinical response
- Characterize immunogenicity (pre-existing (pre-dose) and post-infusion) in patient treated with tisagenlecleucel
- Describe presence of replication-competent lentivirus (RCL)
- Evaluate efficacy and safety in Cohort A
- Evaluate the ORR for all patients treated

Test Product (s), Dose(s), and Mode(s) of Administration

Tisagenlecleucel (autologous T-cells transduced with CD19 TCR-ζ/4-1BB vector) administered as a single iv infusion. Per-protocol tisagenlecleucel cell dose: 5.0×10^8 tisagenlecleucel (acceptable dose range: 1.0×10^8 to 5.0×10^8). The treatment for each patient was a single lot and had a unique cell culture identification number.

Statistical Methods

The hypothesis test for primary endpoint analysis was performed at several previous time points for this study. One pre-planned interim analysis (data cut-off date of 20-Dec-2016) was performed when first 51 patients treated with tisagenlecleucel from the Main Cohort had been followed for at least 3 months or discontinued earlier. The primary objective was met in this analysis. The primary analysis (data cut-off 08-Mar-2017) was performed when the first 81 patients treated with tisagenlecleucel from the Main Cohort had been followed for at least 3 months or discontinued earlier. The p-value was displayed as a descriptive statistic only in the primary analysis, with no inferential interpretation (since the null hypothesis of ORR <20% was already rejected with p<0.0001 at a previous interim analysis). Therefore, the hypothesis test for the primary efficacy analysis was not repeated for this final analysis. The ORR was summarized in this final CSR along with the 2-sided 95% exact Clopper-Pearson confidence intervals (CI).

Analysis of secondary or exploratory endpoints was descriptive and included summary statistics (e.g. as means, standard deviations, 95% CIs). Cumulative incidence functions, Kaplan-Meier curves, and median time to event were presented for time-to-event variables (DOR, EFS, PFS, TTR and OS), as appropriate.

Reporting of AEs (except for CRS) was based on MedDRA version 25.1. The Common Terminology Criteria for AE (CTCAE) version 4.03 was used to assess the AE severity except for CRS, which was based on a Penn grading scale. The list of AESIs and their search criteria is updated on a regular basis at program level in the electronic Case Retrieval Strategy (eCRS) form. The recent version of the eCRS form was used for the reporting activity..

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Written informed consent must be obtained prior to any screening procedures
- Histologically confirmed DLBCL at last relapse(by central pathology review before enrolment.
.- Relapsed or refractory disease after ≥2 lines of chemotherapy including rituximab and anthracycline and either having failed autologous Hematopoietic stem cell transplantation (ASCT), or being ineligible for or not consenting to ASCT
- Measurable disease at time of enrollment
- Life expectancy ≥12 weeks
- Eastern Cooperative Oncology Group (ECOG) performance status that is either 0 or 1 at screening
- Adequate organ function:

. Renal function defined as:
• A serum creatinine of ≤1.5 x Upper Limit of Normal ULN OR
• Estimated Glomerular Filtration Rate (eGFR) ≥ 60 mL/min/1.73 m^2
. Liver function defined as:
• Alanine Aminotransferase (ALT) ≤ 5 times the Upper Limit of Normal (ULN) for age
• Bilirubin ≤ 2.0 mg/dl with the exception of patients with Gilbert–Meulengracht syndrome; patients with Gilbert-Meulengracht syndrome may be included if their total bilirubin is ≤ 3.0 x ULN and direct bilirubin ≤ 1.5 x ULN
. Must have a minimum level of pulmonary reserve defined as ≤ Grade 1 dyspnea and pulse oxygenation > 91% on room air
. Hemodynamically stable and Left Ventricle Ejection Fraction (LVEF) ≥ 45% confirmed by echocardiogram or Multigated Radionuclide Angiography (MUGA)
. Adequate bone marrow reserve without transfusions defined as:
• Absolute neutrophil count (ANC) > 1.000/mm^3
• Absolute lymphocyte count (ALC) ≥ 300/mm^3 and absolute number of CD3+ T cells > 150/mm^3
• Platelets ≥ 50.000//mm^3
• Hemoglobin > 8.0 g/dl
. Must have an apheresis product of non-mobilized cells accepted for manufacturing
. Women of child-bearing potential (defined as all women physiologically capable of becoming pregnant) and all male participants must agree to use highly effective methods of contraception for at least 12 months following CTL019 infusion and until CAR T cells are no longer present by PCR on two consecutive tests

Exclusion Criteria:
- Prior treatment with any prior anti-CD19/anti-CD3 therapy, or any other anti-CD19 therapy
- Treatment with any prior gene therapy product
- Active Central Nervous System (CNS) involvement by malignancy
- Prior allogeneic HSCT
-Eligible for and consenting to HSCT
-Chemotherapy other than lymphodepleting chemotherapy within 2 weeks of infusion
-Investigational medicinal product within the last 30 days prior to screening
- The following medications are excluded:
• Steroids: Therapeutic doses of steroids must be stopped >72 hours prior to leukapheresis and >72 hours prior to CTL019 infusion. However, the following physiological replacement doses of steroids are allowed: < 12 mg/m^2/day hydrocortisone or equivalent
• Immunosuppression: Any other immunosuppressive medication must be stopped ≥2 weeks prior to leukapheresis and ≥ 2 weeks prior to CTL019 infusion. This could include check point inhibitors (monoclonal antibodies and small molecule modulators)
• Antiproliferative therapies other than lymphodepleting chemotherapy within two weeks of leukapheresis and 2 weeks prior to

infusion
-Short acting drugs used to treat leukemia or lymphoma (e.g. tyrosine kinase inhibitors, and hydroxyurea) must be stopped > 72 hour prior to leukapheresis and > 72 hours prior to CTL019 infusion
-Other cytotoxic drugs, including low dose daily or weekly maintenance chemotherapy, must not be given within 2 weeks prior to leukapheresis and within 2 weeks prior to CTL019 infusion
-Fludarabine may be associated with prolonged lymphopenia. This should be taken into consideration when evaluating the optimal timing for leukapheresis collection.
• Antibody use including anti-CD20 therapy within 4 weeks prior to infusion or 5 half-lives of the respected antibody, whichever is longer
• CNS disease prophylaxis must be stopped > 1 week prior to CTL019 infusion (e.g. intrathecal methotrexate)
- Prior radiation therapy within 2 weeks of infusion
- Active replication of or prior infection with hepatitis B or active hepatitis C(HCV RNA positive)
- HIV positive patients
- Uncontrolled acute life threatening bacterial, viral or fungal infection (e.g. blood culture positive ≤ 72 hours prior to infusion)
- Unstable angina and/or myocardial infarction within 6 months prior to screening
- Previous or concurrent malignancy with the following exceptions:
• Adequately treated basal cell or squamous cell carcinoma (adequate wound healing is required prior to study entry)
• In situ carcinoma of the cervix or breast, treated curatively and without evidence of recurrence for at least 3 years prior to the study
• A primary malignancy which has been completely resected and in complete remission for ≥ 5 years
- Pregnant or nursing (lactating) women. NOTE: female study participants of reproductive potential must have a negative serum or urine pregnancy test performed within 24 hours before lymphodepletion
- Intolerance to the excipients of the CTL019 cell product
-Cardiac arrhythmia not controlled with medical management
-Prior treatment with any adoptive T cell therapy
-Patients with T-cell rich/histiocyte rich large B-cell lymphoma (THRBCL), primary cutaneous large B-cell lymphoma, primary mediastinal B-cell lymphoma (PMBCL), EBV positive DLBCL of the elderly, Richter's transformation, and Burkitt lymphoma
-Patients with active neurological auto immune or inflammatory disorders (e.g. Guillain Barre Syndrome, Amyptrophic Lateral Sclerosis)

Participant Flow Table

Overall Study

	Tisagenlecleucel - Main cohort	Tisagenlecleucel Cohort A	Total

Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	
Started	99	16	115
Completed	26	3	29
Not Completed	73	13	86
Death	45	12	57
Progressive disease	13	1	14
Subject decision	8	0	8
Physician Decision	5	0	5
Adverse Event	1	0	1
Lost to Follow-up	1	0	1

Baseline Characteristics

	Tisagenlecleucel - Main cohort	Tisagenlecleucel Cohort A	Total
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	
Number of Participants [units: participants]	99	16	115
Baseline Analysis Population Description	Full analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.		

Age Continuous
(units: years)
Analysis Population Type: Participants
Mean ± Standard Deviation

	54.3±13.09	51.1±12.98	53.8±13.07
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	36	8	44
Male	63	8	71
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants			
White	83	15	98
Asian	10	0	10
Black	4	0	4
Other	2	1	3
Study Specific Characteristic **ECOG performance status** (units: Participants) Description: The Eastern Cooperative Oncology Group (ECOG) Performance status is a numbering scale used in Oncology w to define the population of patients to study in the trial and guide physicians who enroll patients into those studies. The lower the number the better the performance status of the patient, where 0: Fully active, able to carry on all pre-disease performance without restriction. ECOG Performance status of 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work. Analysis Population Type: Participants			
ECOG status of 0	54	11	65
ECOG status of 1	45	5	50

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Primary Outcome Result(s)

Overall Response Rate (ORR) per Independent Review Committee (IRC) in Main cohort

Description	ORR, which includes complete response (CR) and partial response (PR) in the Main cohort as determined by IRC assessment. ORR is the percentage of participants with a best overall disease response of CR or PR, where the best overall disease response is defined as the best disease response recorded from CTL019 infusion until progressive disease or start of new anticancer therapy (including ASCT), whichever comes first. Response was assessed according to Evaluation Criteria in diffuse large B cell lymphoma studies (based on Cheson Response criteria and the Lugano Classification (2014))
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised of all patients in the Main cohort who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Main cohort
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.
Number of Participants Analyzed [units: participants]	99
Overall Response Rate (ORR) per Independent Review Committee (IRC) in Main cohort (units: Percentage of participants)	**Number (95% Confidence Interval)**
	54.5 (44.2 to 64.6)

Secondary Outcome Result(s)

Overall Response Rate (ORR) per Independent Review Committee (IRC) in Cohort A & in All Patients

Description	ORR, which includes complete response (CR) and partial response (PR) in the Main cohort as determined by IRC assessment. ORR is the percentage of participants with a best overall disease response of CR or PR, where the best overall disease response is defined as the best

	disease response recorded from CTL019 infusion until progressive disease or start of new anticancer therapy (including ASCT), whichever comes first.
Time Frame	5 years
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Cohort A	Tisagenlecleucel - All Patients
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	16	115
Overall Response Rate (ORR) per Independent Review Committee (IRC) in Cohort A & in All Patients (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	43.8 (19.8 to 70.1)	53.0 (43.5 to 62.4)

Time to response (TTR) as assessed by Independent Review Committee (Main Cohort & All Patients)

Description	TTR is the time between date of CTL019 infusion until first documented response (CR or PR).
Time Frame	up to approx. 3.3 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients in the Main cohort who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Main cohort	Tisagenlecleucel - All Patients

Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	99	115
Time to response (TTR) as assessed by Independent Review Committee (Main Cohort & All Patients) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	1.0 (0.9 to 1.0)	1.0 (0.9 to 1.0)

Duration of overall response (DOR) per IRC

Description	DOR is the time from achievement of CR or PR, whichever occurs first, to relapse or death due to diffuse large B-cell lymphoma (DLBCL).
Time Frame	up to approx. 60.1 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel and who achieved a completer response (CR) or a partial response (PR).

	Tisagenlecleucel - Main cohort	Tisagenlecleucel - Cohort A	Tisagenlecleucel - All Patients
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	54	7	61

Duration of overall response (DOR) per IRC (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	N/A (10.0 to NA)[1]	NA (1.2 to NA)[1]	NA (10.0 to NA)[1]

[1] NA: The Median and the upper limit of Confidence Interval could not be reached because fewer than half of the patients experienced an event

Event free survival (EFS) per Independent Review Committee

Description	EFS is the time from date of CTL019 infusion to the date of first documented disease progression or relapse, new treatment for lymphoma or death due to any cause.
Time Frame	up to approx. 61 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Main cohort	**Tisagenlecleucel - Cohort A**	**Tisagenlecleucel - All Patients**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	99	16	115
Event free survival (EFS) per Independent Review Committee (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	2.8 (2.2 to 3.5)	2.1 (1.0 to 3.1)	2.8 (2.1 to 3.1)

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Progression free survival (PFS) per Independent Review Committee

Description	PFS is the time from date of CTL019 infusion to the date of first documented disease progression or death due to any cause.
Time Frame	up to approx. 61 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Main cohort	**Tisagenlecleucel - Cohort A**	**Tisagenlecleucel - All Patients**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at a US facility and an EU facility (Fraunhofer Institut für Zelltherapie, Leipzig, Germany).
Number of Participants Analyzed [units: participants]	99	16	115
Progression free survival (PFS) per Independent Review Committee (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	3.0 (2.4 to 6.2)	2.9 (1.0 to NA)[1]	2.9 (2.3 to 5.2)

[1] NA: The upper limit of the Confidence Interval could ne be reached because there were not enough events to estimate the time to the later events.

Overall survival (OS) per Independent Review Committee

Description	OS is the time from date of CTL019 infusion to the date of death due to any cause.
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.

	Tisagenlecleucel - Main cohort	Tisagenlecleucel - Cohort A	Tisagenlecleucel - All Patients
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	99	16	115
Overall survival (OS) per Independent Review Committee (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	12.5 (7.2 to 34.2)	5.9 (3.1 to 19.2)	11.1 (6.6 to 23.9)

Pharmacokinetics (Pk): Cmax

Description	Cmax is the maximum (peak) observed in peripheral blood or other body fluid drug concentration after single dose administration. Cmax, based on the transgene level data by qPCR, was summarized by Month 3 response, per Independent Review Committee assessment. The reported Cmax is the summary of maximum level observed based on the data from each patient and based on all the data that's been collected for up to 60 months in a patient.
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - Main cohort: CR/PR	Tisagenlecleucel - Main Cohort: SD/PD/UNK	Tisagenlecleucel - Cohort A: CR/PR	Tisagenlecleucel - Cohort A: SD/PD/UNK
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who

	received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US	received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	40	56	4	11
Pharmacokinetics (Pk): Cmax (units: copies/ug)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	5570 (271.3%)	4690 (481.1%)	14300 (67.5%)	6950 (109.3%)

Pharmacokinetics (Pk): Tmax

Description	Tmax is the time to reach maximum (peak) peripheral blood or other body fluid drug concentration after single dose administration (days). Tmax, based on the transgene level data by qPCR, was summarized by Month 3 response, per Independent Review Committee assessment. The time frame of 60 months refers to the duration for which the data were reviewed to identify the time of Cmax for this measure.
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - Main cohort: CR/PR	**Tisagenlecleucel - Main cohort: SD/PD/UNK**	**Tisagenlecleucel - Cohort A: CR/PR**	**Tisagenlecleucel - Cohort A: SD/PD/UNK**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.

Number of Participants Analyzed [units: participants]	40	56	4	11
Pharmacokinetics (Pk): Tmax (units: days)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	9.84 (5.78 to 27.7)	8.95 (0.994 to 26.7)	6.95 (5.94 to 8.96)	6.93 (6.67 to 10.9)

Pharmacokinetics (Pk): AUC0-28d and AUC0-84d

Description	The AUC from time zero to day 28 and 84 or other disease assessment days, in peripheral blood. AUC0-28d and AUC0-84d, based on the transgene level data by qPCR, were summarized by Month 3 response, per Independent Review Committee assessment.
Time Frame	0 - 28 days after infusion for AUC0-28d, 0 - 84 days after infusion for AUC0-84d
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - CR/PR	**Tisagenlecleucel - Main cohort: SD/PD/UNK**	**Tisagenlecleucel - Cohort A: CR/PR**	**Tisagenlecleucel - Cohort A: SD/PD/UNK**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	40	59	4	12
Pharmacokinetics (Pk): AUC0-28d and AUC0-84d (units: copies/ug*days)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
AUC0-28d (n= 39, 50, 4, 12)	58000 (182.1%)	49900 (388.5%)	141000 (78.2%)	63700 (134.2%)

AUC0-84d (n = 39, 24, 4, 5)	102000 (171.7%)	92900 (165.4%)	206000 (76.7%)	142000 (61.3%)

Pharmacokinetics (Pk): T1/2

Description	T1/2 is the half-life associated with the disposition phase slopes (alpha, beta, gamma etc.) of a semi logarithmic concentration-time curve in peripheral blood. T1/2, based on the transgene level data by qPCR, was summarized by Month 3 response, per Independent Review Committee assessment. This time frame of 60 months reflects the maximum duration up to which the transgene levels were collected to measure the half life.
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - Main cohort: CR/PR	**Tisagenlecleucel - Main cohort: SD/PD/UNK**	**Tisagenlecleucel - Cohort A: CR/PR**	**Tisagenlecleucel - Cohort A: SD/PD/UNK**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	28	40	3	9
Pharmacokinetics (Pk): T1/2 (units: days)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	167 (355.3%)	10.9 (205.4%)	59.4 (30402.1%)	15.6 (163.5%)

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Pharmacokinetics (Pk): Clast

Description	Clast is the last observed quantifiable concentration in peripheral blood. Clast, based on the transgene level data by qPCR, was summarized by Month 3 response, per Independent Review Committee assessment. This time frame reflects maximum duration of 60 months up to which the transgene levels were collected.
Time Frame	60 months
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - Main cohort: CR/PR	**Tisagenlecleucel - Main cohort: SD/PD/UNK**	**Tisagenlecleucel - Cohort A: CR/PR**	**Tisagenlecleucel - Cohort A: SD/PD/UNK**
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	40	55	4	12
Pharmacokinetics (Pk): Clast (units: copies/ug)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	181 (114.4%)	332 (430.9%)	272 (30.6%)	386 (540.9%)

Pharmacokinetics (Pk): Tlast

Description	Tlast is the time of last observed quantifiable concentration in peripheral blood. Tlast, based on the transgene level data by qPCR, was summarized by Month 3 response, per Independent Review Committee assessment. This time frame reflects maximum duration of 60 months up to which the transgene levels were collected.
Time Frame	60 months

Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel with valid PK assessments.

	Tisagenlecleucel - Main cohort: CR/PR	Tisagenlecleucel - Main cohort: SD/PD/UNK	Tisagenlecleucel - Cohort A: CR/PR	Tisagenlecleucel - Cohort A: SD/PD/UNK
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Number of Participants Analyzed [units: participants]	40	55	4	12
Pharmacokinetics (Pk): Tlast (units: days)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	930 (18.0 to 1830)	41.9 (0.994 to 1480)	1040 (17.1 to 1830)	59.4 (26.8 to 126)

Incidence of immunogenicity to CTL019

Description	This is defined as the percentage of participants who tested positive for anti-mCAR19 antibodies at any time post-baseline, reported by complete response (CR), partial response (PR), Stable disease (SD), progressive disease (SD), Unknown for all participants who received with tisagenlecleucel.
Time Frame	pre-infusion and at any time point post-baseline, up to duration of the study, up to 5 years
Analysis Population Description	Full Analysis Set (FAS): Comprised all patients who received infusion of tisagenlecleucel.

	Tisagenlecleucel - All Participants response
Arm/Group Description	Participants with complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD) and unknown (UNK) response post-tisagenlecleucel infusion.
Number of Participants Analyzed [units: participants]	115
Incidence of immunogenicity to CTL019 (units: participants)	**Count of Participants (Not Applicable)**
Complete response	36 (97.3%)
Partial response	6 (85.71%)
Stable disease	1 (100%)
Progressive disease	50 (92.59%)
Unknown	14 (87.5%)
All Participants	107 (93.04%)

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

All Collected Deaths

Description: On-treatment deaths, which include post-treatment survival follow-up deaths, were collected during the post-infusion period (starting at the day of first infusion) until the end of the study, approx. 61 months. All deaths refers to the sum of on-treatment deaths and post-treatment survival follow-up deaths up to approx. 61 months.

Time Frame	On-treatment deaths: Up to 61 months; Post-treatment survival follow-up deaths: Up to approx. 61 months
Analysis Population Description	Clinical Database Population: all infused participants in the Study.

	Tisagenlecleucel - Main cohort
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US.
Number of Participants Analyzed [units: participants]	115
All Collected Deaths (units: Participants)	
On-treatment deaths include post-treatment survival follow-up deaths	76
All deaths	76

Safety Results

Time Frame	Adverse Events (AEs) were collected during the post-infusion period (starting at the day of 1st infusion until the end of the study), up to maximum duration of 61 months for each patient. Deaths were collected at all points post-infusion until the patient completed the study duration (60 months) or further safety follow-up under the study protocol. Therefore on-treatment deaths include post-infusion deaths until Last patient Last Visit (LPLV).
Additional Description	AE is any sign or symptom that occurs during the post-infusion period (starting at the day of first infusion of CTL019 until the end of the study) and safety follow-up. Deaths in post treatment survival follow-up are not considered Adverse Events while still included in the All-Cause Mortality table. Adverse Adverse event data were pre-specified in the secondary objectives to be analyzed for all treated patients as one group.
Source Vocabulary for Table Default	MedDRA (25.1)

Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Tisagenlecleucel - All Patients N = 115
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Total Number Affected	76
Total Number At Risk	115

Serious Adverse Events

Time Frame	Adverse Events (AEs) were collected during the post-infusion period (starting at the day of 1st infusion until the end of the study), up to maximum duration of 61 months for each patient. Deaths were collected at all points post-infusion until the patient completed the study duration (60 months) or further safety follow-up under the study protocol. Therefore on-treatment deaths include post-infusion deaths until Last patient Last Visit (LPLV).
Additional Description	AE is any sign or symptom that occurs during the post-infusion period (starting at the day of first infusion of CTL019 until the end of the study) and safety follow-up. Deaths in post treatment survival follow-up are not considered Adverse Events while still included in the All-Cause Mortality table. Adverse Adverse event data were pre-specified in the secondary objectives to be analyzed for all treated patients as one group.
Source Vocabulary for Table Default	MedDRA (25.1)

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Collection
Approach for Table Default Systematic Assessment

	Tisagenlecleucel - All Patients N = 115
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Total # Affected by any Serious Adverse Event	84
Total # at Risk by any Serious Adverse Event	115
Blood and lymphatic system disorders	
Bone marrow failure	2 (1.74%)
Febrile neutropenia	10 (8.70%)
Lymphadenopathy	1 (0.87%)
Neutropenia	2 (1.74%)
Pancytopenia	3 (2.61%)
Cardiac disorders	
Atrial fibrillation	1 (0.87%)
Cardiac arrest	1 (0.87%)
Cardiac failure congestive	1 (0.87%)
Cardiopulmonary failure	1 (0.87%)
Cardio-respiratory arrest	1 (0.87%)

Ear and labyrinth disorders	
Vertigo	1 (0.87%)
Gastrointestinal disorders	
Abdominal pain	1 (0.87%)
Anal fissure	1 (0.87%)
Duodenal ulcer haemorrhage	1 (0.87%)
Gastrointestinal haemorrhage	2 (1.74%)
Haematemesis	1 (0.87%)
Large intestinal obstruction	1 (0.87%)
Melaena	1 (0.87%)
Pancreatitis acute	1 (0.87%)
Vomiting	1 (0.87%)
General disorders and administration site conditions	
Face oedema	1 (0.87%)
Fatigue	4 (3.48%)
Influenza like illness	1 (0.87%)
Multiple organ dysfunction syndrome	3 (2.61%)
Pyrexia	9 (7.83%)
Hepatobiliary disorders	
Cholecystitis acute	1 (0.87%)
Hepatic failure	1 (0.87%)
Immune system disorders	
Cytokine release syndrome	31 (26.96%)

Haemophagocytic lymphohistiocytosis	1 (0.87%)
Infections and infestations	
Atypical pneumonia	1 (0.87%)
Bronchitis	1 (0.87%)
Bronchopulmonary aspergillosis	1 (0.87%)
Candida infection	1 (0.87%)
Cerebral toxoplasmosis	1 (0.87%)
Clostridium difficile infection	3 (2.61%)
Corynebacterium infection	1 (0.87%)
Escherichia infection	1 (0.87%)
Infection	2 (1.74%)
Influenza	2 (1.74%)
Lower respiratory tract infection	1 (0.87%)
Pneumocystis jirovecii pneumonia	2 (1.74%)
Pneumonia	9 (7.83%)
Pneumonia aspiration	1 (0.87%)
Pseudomonas infection	1 (0.87%)
Respiratory tract infection	2 (1.74%)
Sepsis	3 (2.61%)
Sinusitis	1 (0.87%)
Staphylococcal infection	2 (1.74%)
Systemic infection	1 (0.87%)
Urinary tract infection	1 (0.87%)
Urosepsis	1 (0.87%)
Vaginal infection	1 (0.87%)

Injury, poisoning and procedural complications	
Infusion related reaction	1 (0.87%)
Upper limb fracture	1 (0.87%)
Investigations	
Blood bilirubin increased	1 (0.87%)
C-reactive protein increased	1 (0.87%)
Liver function test increased	1 (0.87%)
Neutrophil count decreased	3 (2.61%)
Platelet count decreased	2 (1.74%)
White blood cell count decreased	1 (0.87%)
Metabolism and nutrition disorders	
Decreased appetite	1 (0.87%)
Dehydration	2 (1.74%)
Hypercalcaemia	1 (0.87%)
Tumour lysis syndrome	1 (0.87%)
Musculoskeletal and connective tissue disorders	
Back pain	1 (0.87%)
Myopathy	1 (0.87%)
Pain in extremity	1 (0.87%)
Polyarthritis	1 (0.87%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Acute myeloid leukaemia	1 (0.87%)
Invasive ductal breast carcinoma	1 (0.87%)

Malignant melanoma	1 (0.87%)
Myelodysplastic syndrome	4 (3.48%)
Neuroendocrine carcinoma	1 (0.87%)
Prostate cancer	3 (2.61%)
Refractory cytopenia with multilineage dysplasia	1 (0.87%)
Tumour associated fever	1 (0.87%)
Tumour haemorrhage	1 (0.87%)
Nervous system disorders	
Acute polyneuropathy	1 (0.87%)
Cerebral haemorrhage	1 (0.87%)
Demyelinating polyneuropathy	1 (0.87%)
Encephalopathy	4 (3.48%)
Ischaemic cerebral infarction	1 (0.87%)
Metabolic encephalopathy	1 (0.87%)
Somnolence	1 (0.87%)
Status epilepticus	1 (0.87%)
Syncope	1 (0.87%)
Psychiatric disorders	
Anxiety	1 (0.87%)
Confusional state	3 (2.61%)
Mental status changes	1 (0.87%)
Renal and urinary disorders	
Acute kidney injury	4 (3.48%)
Chronic kidney disease	1 (0.87%)

Cystitis haemorrhagic	1 (0.87%)
Urinary tract obstruction	1 (0.87%)
Respiratory, thoracic and mediastinal disorders	
Allergic bronchitis	1 (0.87%)
Asphyxia	1 (0.87%)
Cough	1 (0.87%)
Dyspnoea	3 (2.61%)
Hypoxia	1 (0.87%)
Oropharyngeal pain	1 (0.87%)
Pharyngeal haemorrhage	1 (0.87%)
Pneumonitis	1 (0.87%)
Pulmonary embolism	2 (1.74%)
Pulmonary haemorrhage	1 (0.87%)
Respiratory failure	2 (1.74%)
Vascular disorders	
Deep vein thrombosis	1 (0.87%)
Hypotension	2 (1.74%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse Events (AEs) were collected during the post-infusion period (starting at the day of 1st infusion until the end of the study), up to maximum duration of 61 months for each patient. Deaths were collected at all points post-infusion until the patient completed the study duration (60 months) or further safety follow-up under the study protocol. Therefore on-treatment deaths include post-infusion deaths until Last patient Last Visit (LPLV).

Additional Description	AE is any sign or symptom that occurs during the post-infusion period (starting at the day of first infusion of CTL019 until the end of the study) and safety follow-up. Deaths in post treatment survival follow-up are not considered Adverse Events while still included in the All-Cause Mortality table. Adverse Adverse event data were pre-specified in the secondary objectives to be analyzed for all treated patients as one group.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Tisagenlecleucel - All Patients N = 115
Arm/Group Description	Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who received tisagenlecleucel manufactured at the Novartis manufacturing facility in Morris Plains, US and at the Fraunhofer Institut für Zelltherapie, Leipzig, Germany.
Total # Affected by any Other Adverse Event	113
Total # at Risk by any Other Adverse Event	115
Blood and lymphatic system disorders	
Anaemia	55 (47.83%)
Febrile neutropenia	11 (9.57%)
Neutropenia	21 (18.26%)
Thrombocytopenia	15 (13.04%)

Cardiac disorders	
Tachycardia	12 (10.43%)
Gastrointestinal disorders	
Abdominal pain	9 (7.83%)
Constipation	19 (16.52%)
Diarrhoea	36 (31.30%)
Dry mouth	6 (5.22%)
Nausea	33 (28.70%)
Stomatitis	7 (6.09%)
Vomiting	9 (7.83%)
General disorders and administration site conditions	
Asthenia	8 (6.96%)
Chills	14 (12.17%)
Fatigue	28 (24.35%)
Influenza like illness	9 (7.83%)
Oedema peripheral	17 (14.78%)
Pain	6 (5.22%)
Pyrexia	35 (30.43%)
Immune system disorders	
Cytokine release syndrome	47 (40.87%)
Hypogammaglobulinaemia	10 (8.70%)
Infections and infestations	
Influenza	7 (6.09%)

Nasopharyngitis	9 (7.83%)
Pneumonia	8 (6.96%)
Sinusitis	8 (6.96%)
Upper respiratory tract infection	15 (13.04%)
Urinary tract infection	10 (8.70%)
Investigations	
Blood creatinine increased	12 (10.43%)
Blood immunoglobulin G decreased	7 (6.09%)
Lymphocyte count decreased	7 (6.09%)
Neutrophil count decreased	40 (34.78%)
Platelet count decreased	38 (33.04%)
Weight decreased	14 (12.17%)
White blood cell count decreased	41 (35.65%)
Metabolism and nutrition disorders	
Decreased appetite	15 (13.04%)
Hypocalcaemia	6 (5.22%)
Hypokalaemia	26 (22.61%)
Hypomagnesaemia	19 (16.52%)
Hyponatraemia	9 (7.83%)
Hypophosphataemia	19 (16.52%)
Musculoskeletal and connective tissue disorders	
Arthralgia	16 (13.91%)
Back pain	7 (6.09%)
Myalgia	7 (6.09%)

Pain in extremity	10 (8.70%)
Nervous system disorders	
Dizziness	14 (12.17%)
Headache	24 (20.87%)
Psychiatric disorders	
Anxiety	11 (9.57%)
Confusional state	8 (6.96%)
Insomnia	8 (6.96%)
Renal and urinary disorders	
Acute kidney injury	6 (5.22%)
Respiratory, thoracic and mediastinal disorders	
Cough	19 (16.52%)
Dyspnoea	16 (13.91%)
Hypoxia	8 (6.96%)
Oropharyngeal pain	6 (5.22%)
Pleural effusion	6 (5.22%)
Skin and subcutaneous tissue disorders	
Night sweats	6 (5.22%)
Rash	6 (5.22%)
Vascular disorders	
Hypotension	28 (24.35%)

Other Relevant Findings

None

Conclusion:

Overall, longer-term follow-up data for this study further supports the conclusions previously made, demonstrating compelling efficacy of tisagenlecleucel therapy with high tumor response rates and sustained duration of response.

The safety profile of tisagenlecleucel remained acceptable up to 60 months post infusion in adult patients with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL) disease after at least 2 lines of therapy and either having failed HSCT, or being ineligible for, or not consenting to autologous Hematopoietic stem cell transplantation (HSC)T. No new safety signals emerged with longer follow-up.

Date of Clinical Trial Report

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