Clinical trial results:
A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-X19 in Adult Subjects with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (r/r ALL) (ZUMA-3)

Summary

EudraCT number	2015-005009-35
Trial protocol	DE NL FR
Global end of trial date	03 November 2023

Results information

Result version number	v1 (current)
This version publication date	15 November 2024
First version publication date	15 November 2024

Trial information

Trial identification

Sponsor protocol code	KTE-C19-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02614066
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 July 2022
Global end of trial reached?	Yes
Global end of trial date	03 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to determine the safety and efficacy of brexucabtagene autoleucel (KTE-X19) in adult participants with relapsed/refractory (r/r) B-precursor acute lymphoblastic leukemia (ALL).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	United States: 106
Worldwide total number of subjects	125
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	105
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Canada, France, Germany, the Netherlands, and the United States.

Pre-assignment

Screening details:

173 participants were screened. Bridging therapy was recommended for all participants particularly those participants with high disease burden at baseline (M3 marrow [> 25% leukemic blasts] or ≥ 1,000 blasts/mm^3 in the peripheral circulation) to control participant's disease post apheresis/enrollment and prior to conditioning chemotherapy.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg

Arm description:

Participants with relapsed or refractory B-precursor acute lymphoblastic leukemia (r/r B-ALL) received conditioning chemotherapy (fludarabine 25 mg/m^2 intravenously [IV] over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel (KTE-X19) chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Arm type	Experimental
Investigational medicinal product name	Brexucabtagene autoleucel
Investigational medicinal product code	
Other name	KTE-X19
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single infusion of 2 x 10^6 anti-CD19 CAR T cells/kg administered on Day 0.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

900 mg/m^2 administered over 60 minutes on Day -2

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m^2 administered over 30 minutes on Day -4, Day -3, and Day -2

Arm title	Phase 1: 1 x 10^6 anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Arm type	Experimental
Investigational medicinal product name	Brexucabtagene autoleucel
Investigational medicinal product code	
Other name	KTE-X19
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single infusion of 1 x 10^6 anti-CD19 CAR T cells/kg administered on Day 0.

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m^2 administered over 30 minutes on Day -4, Day -3, and Day -2

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

900 mg/m^2 administered over 60 minutes on Day -2

Arm title	Phase 1: 0.5 x 10^6 anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 0.5 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 0.5 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Arm type	Experimental
Investigational medicinal product name	Brexucabtagene autoleucel
Investigational medicinal product code	
Other name	KTE-X19
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single infusion of 0.5 x 10^6 anti-CD19 CAR T cells/kg administered on Day 0.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

900 mg/m^2 administered over 60 minutes on Day -2

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m^2 administered over 30 minutes on Day -4, Day -3, and Day -2

Arm title	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Arm type	Experimental
Investigational medicinal product name	Brexucabtagene autoleucel
Investigational medicinal product code	
Other name	KTE-X19
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single infusion of 1 x 10^6 anti-CD19 CAR T cells/kg administered on Day 0.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

900 mg/m^2 administered over 60 minutes on Day -2

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m^2 administered over 30 minutes on Day -4, Day -3, and Day -2

Number of subjects in period 1	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg	Phase 1: 1 x 10^6 anti-CD19 CAR T Cells/kg	Phase 1: 0.5 x 10^6 anti-CD19 CAR T Cells/kg
Started	6	28	20
Completed	0	0	0
Not completed	6	28	20
Full consent withdrawn	-	1	-
Enrolled but did not Initiate KTE-X19	-	5	4
Death	6	14	11
Rolled over or consented to a long term follow-up	-	4	2

Lost to follow-up	-	2	2
Reason not specified	-	2	1

Number of subjects in period 1	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg
Started	71
Completed	0
Not completed	71
Full consent withdrawn	8
Enrolled but did not Initiate KTE-X19	16
Death	29
Rolled over or consented to a long term follow-up	15
Lost to follow-up	2
Reason not specified	1

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with relapsed or refractory B-precursor acute lymphoblastic leukemia (r/r B-ALL) received conditioning chemotherapy (fludarabine 25 mg/m^2 intravenously [IV] over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel (KTE-X19) chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.	
Reporting group title	Phase 1: 1 x 10^6 anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.	
Reporting group title	Phase 1: 0.5 x 10^6 anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 0.5 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 0.5 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.	
Reporting group title	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.	

Reporting group values	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg	Phase 1: 1 x 10^6 anti-CD19 CAR T Cells/kg	Phase 1: 0.5 x 10^6 anti-CD19 CAR T Cells/kg
Number of subjects	6	28	20
Age categorical Units: Subjects			
18 – 64 Years	6	22	17
65 – 84 Years	0	6	3
Age continuous Units: years			
arithmetic mean	38	46	44
standard deviation	± 13.8	± 18.2	± 16.1
Gender categorical Units: Subjects			
Female	1	16	10
Male	5	12	10

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	3	2
Black or African American	0	0	1
White	4	23	16
Native Hawaiian or Other Pacific Islander	0	1	0
Not Collected	0	0	0
Other or More Than One Race	1	1	1
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	16	16
Hispanic or Latino	3	12	4
Not Collected	0	0	0

Reporting group values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg	Total	
Number of subjects	71	125	
Age categorical Units: Subjects			
18 – 64 Years	60	105	
65 – 84 Years	11	20	
Age continuous Units: years			
arithmetic mean	44		
standard deviation	± 16.2	-	
Gender categorical Units: Subjects			
Female	30	57	
Male	41	68	
Race Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	4	10	
Black or African American	2	3	
White	51	94	
Native Hawaiian or Other Pacific Islander	0	1	
Not Collected	4	4	
Other or More Than One Race	9	12	
Ethnicity Units: Subjects			
Not Hispanic or Latino	57	92	
Hispanic or Latino	12	31	
Not Collected	2	2	

End points

End points reporting groups

Reporting group title	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with relapsed or refractory B-precursor acute lymphoblastic leukemia (r/r B-ALL) received conditioning chemotherapy (fludarabine 25 mg/m^2 intravenously [IV] over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel (KTE-X19) chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 1: 1 x 10^6 anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 1: 0.5 x 10^6 anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 0.5 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 0.5 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Primary: Phase 1: Percentage of Participants Experiencing Dose Limiting Toxicities (DLTs)

End point title	Phase 1: Percentage of Participants Experiencing Dose Limiting Toxicities (DLTs)[1][2]

End point description:

DLT is drug-related events within first 28 days post infusion:Grade(GR)4 hematologic toxicity lasting more than 30 days (except lymphopenia) if not attributed to underlying disease and related GR 3 lasting for >7 days or 4 non-hematologic toxicities regardless of duration (except: aphasia/dysphasia or confusion/cognitive disturbance which resolves to at least GR 1/baseline within 2 weeks or baseline within 4 weeks, fever GR 3/ 4, immediate hypersensitivity reactions(2 hours of infusion) that are reversible ≤ GR 2 within 24 hours, renal toxicity(dialysis for ≤ 7 days), intubation for airway protection if ≤ 7 days, tumor lysis syndrome, GR 3 liver function test elevation (if resolution to ≤ GR 2 in 14 days), GR 4 transient serum hepatic enzyme abnormalities (if resolution to ≤ GR 3 within < 72 hours),hypogammaglobulinemia GR 3/ 4 and GR 3 nausea and/or anorexia).DLT-Evaluable Analysis Set included first 3 participants in Phase 1 treated with target dose and followed for 28 days.

End point type	Primary

End point timeframe:

First infusion date of brexucabtagene autoleucel up to 28 days. Participants were evaluated in specified period but GR 4 hematologic toxicity (specified in description) having onset in this period were further observed for 30 days for confirmation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, only participants from Phase 1: 2 X 10^6 Anti-CD19 CAR T Cells/kg were pre-specified to be assessed for this Outcome Measure.

End point values	Phase 1: 2 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall complete remission (OCR) Rate (Complete remission [CR]+ complete remission with incomplete hematologic recovery [CRi]) as Assessed per Independent Review

End point title	Phase 2: Overall complete remission (OCR) Rate (Complete remission [CR]+ complete remission with incomplete hematologic recovery [CRi]) as Assessed per Independent Review[3][4]

End point description:

OCR rate:percentage of participants achieving CR+CRi.CR: ≤5% blasts by morphology in bone marrow(BM);ANC≥1000/µL and platelets(Plt) ≥100000/µL in peripheral blood(PB);CNS extramedullary disease(CNS EMD) of CNS-1(no detectable leukemia in CSF);Non-CNS baselineEMD:if present(images shows CR),if no(images not needed),if performed shows negative PET baseline,baseline lesions shows CR as disappearance of measurable and nonmeasurable nodal lesions(Nodal masses >1.5 cm in greatest transverse diameter[GTD] at baseline have regressed to ≤l.5 cm GTD,nodes that were 1.1 to 1.5 cm[long axis] and >1.0 cm[short axis] have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size) and no new lesions.CRi:all CR criteria except in PB ANC≥1000/µL and Plt<100000/µL or ANC<1000/µL and Plt ≥100000/µL.95% CI was calculated by Clopper-Pearson method.The modified Intent-to-Treat (mITT) Analysis Set included all enrolled participants treated with brexucabtagene autoleucel in Phase 2.

End point type	Primary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	70.9 (57 to 82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Minimum Residual Disease (MRD) Negative Remission Rate

End point title	Phase 2: Minimum Residual Disease (MRD) Negative Remission Rate[5]

End point description:

MRD was assessed utilizing multicolor flow cytometry to detect residual cancerous cells with a sensitivity of 10^-4. MRD negative remission was defined as MRD < 10^-4 threshold. Percentage of participants with MRD negative remission was reported. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	76 (63 to 87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Complete Remission (CR) Rate per Independent Review

End point title	Phase 2: Complete Remission (CR) Rate per Independent Review[6]

End point description:

CR: ≤ 5% blasts by morphology in BM; ANC ≥ 1000/µL and Plt ≥ 100000/µL in PB; CNS EMD of CNS-1 (no detectable leukemia in CSF); Non-CNS EMD: if baseline EMD present (images must show CR), if no baseline EMD (then images not required), but if performed should show negative PET baseline, baseline lesions must show CR as disappearance of measurable and nonmeasurable nodal lesions (Nodal masses > 1.5 cm in GTD at baseline must have regressed to ≤ l.5 cm GTD, nodes that were 1.1 to 1.5 cm [long

axis] and > 1.0 cm [short axis] must have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size) and no new lesions. Percentage of participants with CR was reported. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	56.4 (42 to 70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Percentage of Participants With Allogeneic stem cell transplant (allo-SCT)

End point title	Phase 2: Percentage of Participants With Allogeneic stem cell transplant (allo-SCT)[7]

End point description:

Participants in mITT Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 5 years

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Complete Remission With Incomplete Hematologic Recovery (CRi) Rate per Independent Review

End point title	Phase 2: Complete Remission With Incomplete Hematologic Recovery (CRi) Rate per Independent Review[8]

End point description:

CRi: ≤ 5% blasts by morphology in BM; ANC ≥ 1000/µL and Plt < 100000/µL or ANC < 1000/µL and Plt ≥ 100000/µL in PB; CNS EMD of CNS-1 (no detectable leukemia in CSF); Non-CNS EMD: if baseline EMD present (images must show CR), if no baseline EMD (then images not required), but if performed should show negative PET baseline, baseline lesions must show CR as disappearance of measurable and nonmeasurable nodal lesions (Nodal masses > 1.5 cm in GTD at baseline must have regressed to ≤ l.5 cm GTD, nodes that were 1.1 to 1.5 cm [long axis] and > 1.0 cm [short axis] must have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size, if tested) and no new lesions. Percentage of participants with CRi was reported. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	14.5 (6 to 27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Remission (DOR) per Independent Review

End point title	Phase 2: Duration of Remission (DOR) per Independent

End point description:

DOR is the time from first CR or CRi to relapse or any death in the absence of documented relapse. Relapse: ≤ 5% blasts by morphology in BM; or circulating leukemia present in PB; or CNS EMD of CNS-2 (detectable CSF blast cells in a sample of CSF with < 5 white blood cells [WBCs] per mm^3 with neurological changes) or CNS-3 (detectable CSF blast cells in a sample of CSF with ≥ 5 WBCs per mm^3 with or without neurological changes); or PD: at least one of the following (≥ 50% increase from nadir in the sum of at least two lymph nodes, or if a single node is involved at least a 50% increase in the product of the diameters of this one node; at least a 50% increase in the longest diameter of any single previously identified node more than 1 cm in its short axis; ≥ 50% increase in size of splenic, hepatic or any other non-nodal lesion). Kaplan-Meier (KM) estimates was used for analyses. Participants in the mITT Analysis Set with overall complete remission (CR or CRi) were analyzed.

End point type	Secondary

End point timeframe:

From first CR or CRi (Phase 2) up to 3.7 years

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: months				
median (confidence interval 95%)	14.6 (9.4 to 24.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: MRD Negative Remission Rate Among Complete Remission (CR) Participants

End point title	Phase 2: MRD Negative Remission Rate Among Complete Remission (CR) Participants[10]

End point description:

Percentage of participants with MRD negative remission among CR participants was reported. MRD was assessed by multicolor flow cytometry to detect residual cancerous cells with a sensitivity of 10^-4. Remission was defined as MRD < 10^-4 threshold. CR: ≤5% blasts by morphology in BM; ANC ≥ 1000/µL and Plt ≥ 100000/µL in PB; CNS EMD of CNS-1 (no detectable leukemia in CSF); Non-CNS EMD: if baseline EMD present (images must show CR), if no baseline EMD (images not required), but if performed should show negative PET baseline, baseline lesions must show CR as disappearance of measurable and nonmeasurable nodal lesions (Nodal masses > 1.5 cm in GTD at baseline must have regressed to ≤ l.5 cm GTD, nodes that were 1.1 to 1.5 cm [long axis] and > 1.0 cm [short axis] must have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size) and no new lesions. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set with CR were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 95%)	97 (83 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: OCR Rate (CR + CRi) Per Investigator Review

End point title	Phase 2: OCR Rate (CR + CRi) Per Investigator Review[11]

End point description:

OCR rate: percentage of participants achieving CR+CRi. CR: ≤ 5% blasts by morphology in BM; ANC ≥1000/µL and Plt ≥ 100000/µL in PB; CNS EMD of CNS-1 (no detectable leukemia in CSF); Non-CNS EMD: if baseline EMD present (images must show CR), if no baseline EMD (then images not required), but if performed should show negative PET baseline, baseline lesions must show CR as disappearance of measurable and nonmeasurable nodal lesions (Nodal masses >1.5 cm in GTD at baseline must have regressed to ≤l.5 cm GTD, nodes that were 1.1 to 1.5 cm [long axis] and >1.0 cm [short axis] must have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size, if tested) and no new lesions. CRi: all CR criteria except in PB ANC ≥1000/µL and Plt <100000/µL or ANC <1000/µL and Plt ≥100000/µL. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 5 years

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (confidence interval 95%)	72.7 (59 to 84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Relapse-free survival (RFS)

End point title	Phase 2: Relapse-free survival (RFS)[12]

End point description:

RFS: time from brexucabtagene autoleucel infusion to date of disease relapse or death from any cause. Participants not meeting criteria for relapse by the analysis data cutoff date were censored at their last evaluable disease assessment date. Participants who had not achieved a CR or CRi at analysis data cutoff were evaluated as an RFS event at Day 0. CR and CRi are defined in Outcome Measures 4 and 5. Relapse is defined in Outcome Measure 6. KM estimates was used for analyses. Participants in mITT

Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: months				
median (confidence interval 95%)	11.6 (2.7 to 20.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall survival (OS)

End point title	Phase 2: Overall survival (OS)[13]

End point description:

OS was defined as the time from brexucabtagene autoleucel infusion to the date of death from any cause. Participants who had not died by the analysis data cutoff date were censored at their last contact date. KM estimates was used for analyses. Participants in mITT Analysis Set were analyzed. 9999 indicates that the upper limit of confidence interval was not estimable due to insufficient number of events.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 5 years

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: months				
median (confidence interval 95%)	26.0 (16.2 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: MRD Negative Remission Rate Among Complete Remission With Incomplete Hematologic Recovery (CRi) Participants

End point title	Phase 2: MRD Negative Remission Rate Among Complete Remission With Incomplete Hematologic Recovery (CRi) Participants[14]

End point description:

Percentage of participants with MRD negative remission among CRi participants was reported. MRD by multicolor flow cytometry to detect residual cancerous cells(sensitivity of 10^-4).Remission was defined as MRD < 10^-4 threshold. CRi: ≤ 5% blasts by morphology in BM; ANC ≥ 1000/µL and Plt < 100000/µL or ANC < 1000/µL and Plt ≥ 100000/µL in PB; CNS EMD of CNS-1(no detectable leukemia in CSF); Non-CNS EMD: if baseline EMD(images must show CR), if no baseline EMD (then images not required), if performed should show negative PET baseline, baseline lesions must show CR as disappearance of measurable and nonmeasurable nodal lesions (Nodal masses >1.5 cm in GTD at baseline must have regressed to ≤l.5 cm GTD, nodes that were 1.1 to 1.5 cm [long axis] and >1.0 cm [short axis] must have decreased to 1.0 cm in their short axis, spleen and/or liver must be normal size) and no new lesions. 95% CI was calculated by Clopper-Pearson method. Participants in mITT Analysis Set with CRi were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 3.7 years

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (confidence interval 95%)	100 (63 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Percentage of Participants Experiencing Treatment Emergent Adverse Events (TEAEs)

End point title	Phase 2: Percentage of Participants Experiencing Treatment Emergent Adverse Events (TEAEs)[15]

End point description:

An AE was any untoward medical occurrence in a participant after brexucabtagene autoleucel infusion, which did not necessarily have a causal relationship with the treatment. An AE could therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. TEAEs included all AEs with onset on or after initiation of the brexucabtagene autoleucel infusion. The Safety Analysis Set included all participants treated with any dose of brexucabtagene autoleucel.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants Experiencing Laboratory Toxicity Grade 3 or Higher TEAEs Resulting From Increased Parameter Value

End point title	Phase 2: Number of Participants Experiencing Laboratory Toxicity Grade 3 or Higher TEAEs Resulting From Increased Parameter Value[16]

End point description:

Grading categories are determined by Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Grade 1: mild, Grade 2: moderate, Grade 3: severe or medically significant, Grade 4: life-threatening. Participants in Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: participants				
Hematology: Lymphocytes	1			
Hematology: Leukocytes	4			
Hematology: Hemoglobin	0			
Hematology: Neutrophils	0			
Hematology: Platelets	0			
Chemistry: Creatinine	4			
Chemistry: Glucose	13			
Chemistry: Aspartate Aminotransferase	14			
Chemistry: Alanine Aminotransferase	17			
Chemistry: Bilirubin	5			
Chemistry: Alkaline Phosphatase	3			
Chemistry: Direct Bilirubin	8			
Chemistry: Urate	12			
Chemistry: Sodium	1			
Chemistry: Potassium	2			
Chemistry: Magnesium	3			
Chemistry: Calcium	0			
Chemistry: Albumin	0			
Chemistry: Phosphate	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants Experiencing Laboratory Toxicity Grade 3 or Higher TEAEs Resulting From Decreased Parameter Value

End point title	Phase 2: Number of Participants Experiencing Laboratory Toxicity Grade 3 or Higher TEAEs Resulting From Decreased Parameter Value[17]

End point description:

Grading categories are determined by CTCAE version 4.03. Grade 1: mild, Grade 2: moderate, Grade 3: severe or medically significant, Grade 4: life-threatening. Participants in Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: participants				
Hematology: Hemoglobin	42			
Hematology: Leukocytes	54			
Hematology: Platelets	46			
Hematology: Lymphocytes	52			
Hematology: Neutrophils	53			
Chemistry: Calcium	9			
Chemistry: Albumin	5			
Chemistry: Phosphate	27			
Chemistry: Magnesium	0			
Chemistry: Sodium	11			
Chemistry: Potassium	7			
Chemistry: Glucose	0			
Chemistry: Alanine Aminotransferase	0			
Chemistry: Alkaline Phosphatase	0			
Chemistry: Aspartate Aminotransferase	0			
Chemistry: Bilirubin	0			
Chemistry: Creatinine	0			
Chemistry: Direct Bilirubin	0			
Chemistry: Urate	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Percentage of Participants With Anti-KTE-X19 Antibodies

End point title	Phase 2: Percentage of Participants With Anti-KTE-X19 Antibodies[18]

End point description:

Participants in Safety Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First infusion date of brexucabtagene autoleucel (Phase 2) up to 2.7 years

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percentage of participants				
number (not applicable)	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With 5-Level European Quality of Life-5 Dimensions (EQ-5D-5L): Health Utility Index scale

End point title	Phase 2: Number of Participants With 5-Level European Quality of Life-5 Dimensions (EQ-5D-5L): Health Utility Index scale[19]

End point description:

The EQ-5D-5 levels (EQ-5D-5L) is a standardized measure of health status of the participant that provides a simple, generic measure of health for clinical and economic appraisal. It is a self-reported questionnaire used for assessing the overall health status of a participant scoring 5 dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. EQ-5D health states, defined by the EQ-5D descriptive system, are converted into a single summary index by applying a formula that attaches values (also called QOL utilities) to each of the levels in each dimension. EQ-5D Summary Index values range from -0.11 (worst health) to 1.00 (perfect health).This results in a 1-digit number. The digits for 5 dimensions can be combined into a 5-digit number. Higher scores=better health. Participants in Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Day 28, Month 3, Month 6, Month 9, Month 12, Month 15, Month 18, and Month 24

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint. .

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: participants				
Baseline: Mobility (No problem)	39			
Baseline: Mobility (Slight problem)	7			
Baseline: Mobility (Moderate problem)	4			
Baseline: Mobility (Severe problem)	1			
Baseline: Mobility (Unable to walk)	0			
D 28: Mobility (No problem) N=42	19			
D 28: Mobility (Slight problem) N=42	10			
D 28: Mobility (Moderate problem) N=42	9			
D 28: Mobility (Severe problem) N=42	1			

D 28: Mobility (Unable to walk) N=42	3			
Month 3: Mobility (No problem) N=26	19			
Month 3: Mobility (Slight problem) N=26	5			
Month 3: Mobility (Moderate problem) N=26	1			
Month 3: Mobility (Severe problem) N=26	0			
Month 3: Mobility (Unable to walk) N=26	1			
Month 6: Mobility (No problem) N=25	16			
Month 6: Mobility (Slight problem) N=25	6			
Month 6: Mobility (Moderate problem) N=25	2			
Month 6: Mobility (Severe problem) N=25	0			
Month 6: Mobility (Unable to walk) N=25	1			
Month 9: Mobility (No problem) N=10	8			
Month 9: Mobility (Slight problem) N=10	1			
Month 9: Mobility (Moderate problem) N=10	0			
Month 9: Mobility (Severe problem) N=10	0			
Month 9: Mobility (Unable to walk) N=10	1			
Month 12: Mobility (No problem) N=14	11			
Month 12: Mobility (Slight problem) N=14	3			
Month 12: Mobility (Moderate problem) N=14	0			
Month 12: Mobility (Severe problem) N=14	0			
Month 12: Mobility (Unable to walk) N=14	0			
Month 15: Mobility (No problem) N=10	7			
Month 15: Mobility (Slight problem) N=10	2			
Month 15: Mobility (Moderate problem) N=10	1			
Month 15: Mobility (Severity problem) N=10	0			
Month 15: Mobility (Unable to walk) N=10	0			
Month 18: Mobility (No problem) N=4	3			
Month 18: Mobility (Slight problem) N=4	1			
Month 18: Mobility (Moderate problem) N=4	0			
Month 18: Mobility (Severe problem) N=4	0			
Month 18: Mobility (Unable to walk) N=4	0			
Month 24: Mobility (No problem) N=4	3			
Month 24: Mobility (Slight problem) N=4	1			
Month 24: Mobility (Moderate problem) N=4	0			

Month 24: Mobility (Severe problem) N=4	0			
Month 24: Mobility (Unable to Walk) N=4	0			
Baseline: Self-care (No problem)	44			
Baseline: Self-care (Slight problem)	5			
Baseline: Self-care (Moderate problem)	1			
Baseline: Self-care (Severe problem)	1			
Baseline: Self-care (Unable to wash or dress)	0			
D 28: Self-care (No problem) N=42	31			
D 28: Self-care (Slight problem) N=42	6			
D 28: Self-care (Moderate problem) N=42	1			
D 28: Self-care (Severe problem) N=42	2			
D 28: Self-care (Unable to wash or dress) N=42	2			
Month 3: Self-care (No problem) N=25	23			
Month 3: Self-care (Slight problem) N=25	1			
Month 3: Self-care (Moderate problem) N=25	1			
Month 3: Self-care (Severe problem) N=25	0			
Month 3: Self-care (Unable to wash or dress) N=25	0			
Month 6: Self-care (No problem) N=25	23			
Month 6: Self-care (Slight problem)	0			
Month 6: Self-care (Moderate problem)	1			
Month 6: Self-care (Severe problem)	1			
Month 6: Self-care (Unable to wash or dress) N=10	0			
Month 9: Self-care (No problem) N=10	9			
Month 9: Self-care (Slight problem) N=10	0			
Month 9: Self-care (Moderate problem) N=10	0			
Month 9: Self-care (Severe problem) N=10	1			
Month 9: Self-care (Unable to wash or dress)	0			
Month 12: Self-care (No problem) N=14	14			
Month 12: Self-care (Slight problem) N=14	0			
Month 12: Self-care (Moderate problem) N=14	0			
Month 12: Self-care (Severe problem) N=14	0			
Mon 12: Self-care (Unable to wash or dress) N=14	0			
Month 15: Self-care (No problem) N=10	10			
Month 15: Self-care (Slight problem) N=10	0			
Month 15: Self-care (Moderate problem) N=10	0			
Month 15: Self-care (Severe problem) N=10	0			
Mon 15: Self-care (Unable to wash or dress) N=10	0			

Month 18: Self-care (No problem) N=4	4			
Month 18: Self-care (Slight problem) N=4	0			
Month 18: Self-care (Moderate problem) N=4	0			
Month 18: Self-care (Severe problem) N=4	0			
Month 18: Self-care (Unable to wash or dress) N=4	0			
Month 24: Self-care (No problem) N=4	4			
Month 24: Self-care (Slight problem) N=4	0			
Month 24: Self-care (Moderate problem) N=4	0			
Month 24: Self-care (Severe problem) N=4	0			
Month 24: Self-care (Unable to wash or dress) N=4	0			
Baseline: Usual activities (No problem)	24			
Baseline: Usual activities (Slight problem)	14			
Baseline: Usual activities (Moderate problem)	9			
Baseline: Usual activities (Severe problem)	3			
Bas Usu activities (Unable to do usual activities)	1			
D 28: Usual activities (No problem) N=42	17			
D 28: Usual activities (Slight problem) N=42	13			
D 28: Usual activities (Moderate problem) N=42	8			
D 28: Usual activities (Severe problem) N=42	3			
D 28: Usu act (Unable to do usual activities) N=42	1			
Month 3: Usual activities (No problem) N=25	14			
Month 3: Usual activities (Slight problem) N=25	9			
Month 3: Usual activities (Moderate problem) N=25	1			
Month 3: Usual activities (Severe problem) N=25	1			
Mon 3: Usu act (Un to do usual activities) N=25	0			
Month 6: Usual activities (No problem) N=25	17			
Month 6: Usual activities (Slight problem) N=25	4			
Month 6: Usual activities (Moderate problem) N=25	2			
Month 6: Usual activities (Severe problem) N=25	2			
Mon 6: Usu act (Un to do usual activities) N=25	0			
Month 9: Usual activities (No problem) N=10	9			
Month 9: Usual activities (Slight problem) N=10	0			

Month 9: Usual activities (Moderate problem) N=10	0			
Month 9: Usual activities (Severe problem) N=10	0			
Mon 9: Usu act (Un to do usual activities) N=10	1			
Month 12: Usual activities (No problem) N=14	11			
Month 12: Usual activities (Slight problem) N=14	3			
Month 12: Usual activities (Moderate problem) N=14	0			
Month 12: Usual activities (Severe problem) N=14	0			
Mon 12: Usu act (Un to do usual activities) N=14	0			
Month 15: Usual activities (No problem) N=10	8			
Month 15: Usual activities (Slight problem) N=10	2			
Month 15: Usual activities (Moderate problem) N=10	0			
Month 15: Usual activities (Severe problem) N=10	0			
Mon 15: Usu act (Un to do usual activities) N=10	0			
Month 18: Usual activities (No problem) N=4	1			
Month 18: Usual activities (Slight problem) N=4	3			
Month 18: Usual activities (Moderate problem) N=4	0			
Month 18: Usual activities (Severe problem) N=4	0			
Mon 18: Usu act (Un to do usual activities) N=4	0			
Month 24: Usual activities (No problem) N=4	4			
Month 24: Usual activities (Slight problem) N=4	0			
Month 24: Usual activities (Moderate problem) N=4	0			
Month 24: Usual activities (Severe problem) N=4	0			
Mon 24: Usu act (Un to do usual activities) N=4	0			
Baseline: Pain/Discomfort (No Problem)	23			
Baseline: Pain/Discomfort (Slight Problem)	16			
Baseline: Pain/Discomfort (Moderate Problem)	12			
Baseline: Pain/Discomfort (Severe Problem)	0			
Bas Pain/Discomfort (Extreme Pain or discomfort)	0			
D 28: Pain/Discomfort (No Problem) N=42	19			
D 28: Pain/Discomfort (Slight Problem) N=42	14			
D 28: Pain/Discomfort (Moderate Problem) N=42	9			

D 28: Pain/Discomfort (Severe Problem) N=42	0			
D 28: Pai (Extreme Pain or discomfort) N=42	0			
Month 3: Pain/Discomfort (No Problem) N=26	11			
Month 3: Pain/Discomfort (Slight Problem) N=26	9			
Month 3: Pain/Discomfort (Moderate Problem) N=26	6			
Month 3: Pain/Discomfort (Severe Problem) N=26	0			
Mon 3: Pai (Extreme Pain or discomfort) N=26	0			
Month 6: Pain/Discomfort (No Problem) N=25	11			
Month 6: Pain/Discomfort (Slight Problem) N=25	5			
Month 6: Pain/Discomfort (Moderate Problem) N=25	7			
Month 6: Pain/Discomfort (Severe Problem) N=25	2			
Mon 6: Pai (Extreme Pain or discomfort) N=25	0			
Month 9: Pain/Discomfort (No Problem) N=10	7			
Month 9: Pain/Discomfort (Slight Problem) N=10	1			
Month 9: Pain/Discomfort (Moderate Problem) N=10	2			
Month 9: Pain/Discomfort (Severe Problem) N=10	0			
Mon 9: Pai (Extreme Pain or discomfort) N=10	0			
Month 12: Pain/Discomfort (No Problem) N=14	7			
Month 12: Pain/Discomfort (Slight Problem) N=14	6			
Month 12: Pain/Discomfort (Moderate Problem) N=14	1			
Month 12: Pain/Discomfort (Severe Problem) N=14	0			
Mon 12: Pai (Extreme Pain or discomfort) N=14	0			
Month 15: Pain/Discomfort (No Problem) N=10	6			
Month 15: Pain/Discomfort (Slight Problem) N=10	4			
Month 15: Pain/Discomfort (Moderate Problem) N=10	0			
Month 15: Pain/Discomfort (Severe Problem) N=10	0			
Mon 15: Pai (Extreme Pain or discomfort) N=10	0			
Month 18: Pain/Discomfort (No Problem) N=4	1			
Month 18: Pain/Discomfort (Slight Problem) N=4	3			
Month 18: Pain/Discomfort (Moderate Problem) N=4	0			
Month 18: Pain/Discomfort (Severe Problem) N=4	0			

Mon 18: Pai (Extreme Pain or discomfort) N=4	0			
Month 24: Pain/Discomfort (No Problem) N=4	3			
Month 24: Pain/Discomfort (Slight Problem) N=4	1			
Month 24: Pain/Discomfort (Moderate Problem) N=4	0			
Month 24: Pain/Discomfort (Severe Problem) N=4	0			
Mon 24: Pai (Extreme Pain or discomfort) N=4	0			
Baseline: Anxiety/Depression (No problem)	30			
Baseline: Anxiety/Depression (Slight problem)	12			
Baseline: Anxiety/Depression (Moderate problem)	7			
Baseline: Anxiety/Depression (Severe problem)	2			
Bas Anx (Extreme Anxious or Depressed)	0			
D 28: Anxiety/Depression (No problem) N=42	28			
D 28: Anxiety/Depression (Slight problem) N=42	11			
D 28: Anxiety/Depression (Moderate problem) N=42	3			
D 28: Anxiety/Depression (Severe problem) N=42	0			
D 28: Anx (Extreme Anxious or Depressed) N=42	0			
Month 3: Anxiety/Depression (No problem) N=26	17			
Month 3: Anxiety/Depression (Slight problem) N=26	6			
Mon 3: Anxiety/Depression (Moderate problem) N=26	3			
Month 3: Anxiety/Depression (Severe problem) N=26	0			
Mon 3: Anx (Extreme Anxious or Depressed) N=26	0			
Month 6: Anxiety/Depression (No problem) N=25	18			
Month 6: Anxiety/Depression (Slight problem) N=25	4			
Mon 6: Anxiety/Depression (Moderate problem) N=25	3			
Month 6: Anxiety/Depression (Severe problem) N=25	0			
Mon 6: Anx (Extreme Anxious or Depressed) N=25	0			
Month 9: Anxiety/Depression (No problem) N=10	9			
Month 9: Anxiety/Depression (Slight problem) N=10	0			
Mon 9: Anxiety/Depression (Moderate problem) N=10	1			
Month 9: Anxiety/Depression (Severe problem) N=10	0			
Mon 9: Anx (Extreme Anxious or Depressed) N=10	0			

Month 12: Anxiety/Depression (No problem) N=14	10			
Month 12: Anxiety/Depression (Slight problem) N=14	2			
Mon 12: Anxiety/Depression (Moderate problem) N=14	2			
Month 12: Anxiety/Depression (Severe problem) N=14	0			
Mon 12: Anx (Extreme Anxious or Depressed) N=14	0			
Month 15: Anxiety/Depression (No problem) N=10	7			
Month 15: Anxiety/Depression (Slight problem) N=10	2			
Mon 15: Anxiety/Depression (Moderate problem) N=10	1			
Month 15: Anxiety/Depression (Severe problem) N=10	0			
Mon 15: Anx (Extreme Anxious or Depressed) N=10	0			
Month 18: Anxiety/Depression (No problem) N=4	3			
Month 18: Anxiety/Depression (Slight problem) N=4	1			
Mon 18: Anxiety/Depression (Moderate problem) N=4	0			
Month 18: Anxiety/Depression (Severe problem) N=4	0			
Mon 18: Anx (Extreme Anxious or Depressed) N=4	0			
Month 24: Anxiety/Depression (No problem) N=4	4			
Month 24: Anxiety/Depression (Slight problem) N=4	0			
Mon 24: Anxiety/Depression (Moderate problem) N=4	0			
Month 24: Anxiety/Depression (Severe problem) N=4	0			
Mon 24: Anx (Extreme Anxious or Depressed) N=4	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: EQ-5D Visual Analogue Scale (VAS) Score

End point title	Phase 2: EQ-5D Visual Analogue Scale (VAS) Score[20]

End point description:

EQ-5D is a self-reported questionnaire used for assessing the overall health status of a participant. The EQ-5D is a participant rated questionnaire to assess health-related quality of life in terms of a single index value. The EQ-5D-VAS records the participant's self-rated health on a 20-cm vertical visual analogue scale and is asked to make a global assessment of their current state of health with 0 indicating the worst health they can imagine and 100 indicating the best health they can imagine. Higher scores indicate a better health state. Participants in Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Day 28, Month 3, Month 6, Month 9, Month 12, Month 15, Month 18, and Month 24

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per prespecified analysis, the data for this endpoint was collected only for Phase 2 of the study. Hence the data for Phase 1 arms is not reported for this endpoint.

End point values	Phase 2: 1 x 10^6 anti-CD19 CAR T Cells/kg			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	68.2 (± 21.8)			
Day 28 N=41	74.7 (± 17.9)			
Month 3 N=26	79.7 (± 12.2)			
Month 6 N=25	81.0 (± 17.6)			
Month 9 N=10	81.7 (± 23.1)			
Month 12 N=14	86.9 (± 10.0)			
Month 15 N=10	87.8 (± 11.6)			
Month 18 N=4	93.3 (± 5.9)			
Month 24 N=4	97.5 (± 2.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Event: Up to 5 years; All-Cause mortality: Up to 7.1 years

Adverse event reporting additional description:

Adverse Events: The Safety Analysis Set included all participants treated with any dose of brexucabtagene autoleucel.
All-cause mortality: All Enrolled Analysis Set included all enrolled participants in the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Phase 1: 2 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 2: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 1: 0.5 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 0.5 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 0.5 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Reporting group title	Phase 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r B-ALL received conditioning chemotherapy (fludarabine 25 mg/m^2 IV over 30 minutes on Day -4, Day -3, and Day -2 and cyclophosphamide 900 mg/m^2 IV over 60 minutes on Day -2) followed by a single infusion of brexucabtagene autoleucel CAR transduced autologous T cells administered IV at a target dose of 1 x 10^6 anti-CD19 CAR T cells/kg of body weight on Day 0. For participants weighing > 100 kg, a maximum flat dose of 1 x 10^8 anti-CD19 CAR T cells/kg of body weight was administered.

Serious adverse events	Phase 1: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Phase 2: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Phase 1: 0.5 x 10^6 Anti-CD19 CAR T Cells/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	41 / 55 (74.55%)	12 / 16 (75.00%)
number of deaths (all causes)	6	39	15
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoma in situ			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 55 (7.27%)	4 / 16 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 4
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 6 (50.00%)	16 / 55 (29.09%)	3 / 16 (18.75%)
occurrences causally related to treatment / all	2 / 3	16 / 16	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 6 (0.00%)	15 / 55 (27.27%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	16 / 17	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			

Acute respiratory distress syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	7 / 55 (12.73%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 1	7 / 7	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restlessness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Brain herniation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	2 / 6 (33.33%)	4 / 55 (7.27%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	2 / 2	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoplegia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune effector cell-associated ~ neurotoxicity syndrome			

subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cauda equina syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			

subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	4 / 16 (25.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular ~ coagulation			

subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Tongue oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	2 / 6 (33.33%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Enterococcal bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	3 / 16 (18.75%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

Herpes simplex viraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis fungal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related bacteraemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia respiratory syncytial ~ viral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 23 (91.30%)		
number of deaths (all causes)	17		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carcinoma in situ			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypotension			
subjects affected / exposed	9 / 23 (39.13%)		
occurrences causally related to treatment / all	8 / 11		
deaths causally related to treatment / all	0 / 0		
Hypertension			

subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Shock				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 23 (17.39%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Face oedema				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypogammaglobulinaemia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Drug hypersensitivity				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemophagocytic lymphohistiocytosis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Graft versus host disease				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	3 / 23 (13.04%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachypnoea				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Acute respiratory failure				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary alveolar haemorrhage				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Restlessness				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pulseless electrical activity			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Encephalopathy			
subjects affected / exposed	8 / 23 (34.78%)		
occurrences causally related to treatment / all	10 / 12		
deaths causally related to treatment / all	0 / 0		
Monoplegia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune effector cell-associated ~ neurotoxicity syndrome			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Facial paralysis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cauda equina syndrome			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Brain oedema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraparesis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cerebrovascular accident				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	3 / 23 (13.04%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytopenia				

subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular ~ coagulation				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Tongue oedema				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia oral				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Enterococcal bacteraemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	4 / 23 (17.39%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Herpes simplex viraemia				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Escherichia sepsis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis fungal				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related bacteraemia				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia fungal				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial ~ viral				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypervolaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Phase 1: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Phase 2: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Phase 1: 0.5 x 10^6 Anti-CD19 CAR T Cells/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	55 / 55 (100.00%)	16 / 16 (100.00%)
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	5 / 6 (83.33%)	27 / 55 (49.09%)	7 / 16 (43.75%)
occurrences (all)	6	41	12
Hypertension			

subjects affected / exposed	0 / 6 (0.00%)	7 / 55 (12.73%)	2 / 16 (12.50%)
occurrences (all)	0	10	2
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Distributive shock			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Pyrexia			
subjects affected / exposed	6 / 6 (100.00%)	49 / 55 (89.09%)	11 / 16 (68.75%)
occurrences (all)	7	66	13
Chills			
subjects affected / exposed	3 / 6 (50.00%)	18 / 55 (32.73%)	3 / 16 (18.75%)
occurrences (all)	5	21	4
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	13 / 55 (23.64%)	6 / 16 (37.50%)
occurrences (all)	2	14	6
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	10 / 55 (18.18%)	4 / 16 (25.00%)
occurrences (all)	1	13	4
Pain			
subjects affected / exposed	0 / 6 (0.00%)	7 / 55 (12.73%)	0 / 16 (0.00%)
occurrences (all)	0	9	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	4	1
Malaise			

subjects affected / exposed	0 / 6 (0.00%)	5 / 55 (9.09%)	1 / 16 (6.25%)
occurrences (all)	0	5	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Catheter site pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gravitational oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypothermia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Drug hypersensitivity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pelvic pain			

subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	2 / 6 (33.33%)	12 / 55 (21.82%)	5 / 16 (31.25%)
occurrences (all)	2	17	7
Pulmonary oedema			
subjects affected / exposed	1 / 6 (16.67%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	4 / 55 (7.27%)	3 / 16 (18.75%)
occurrences (all)	1	4	3
Cough			
subjects affected / exposed	1 / 6 (16.67%)	7 / 55 (12.73%)	2 / 16 (12.50%)
occurrences (all)	1	7	2
Pneumonitis			
subjects affected / exposed	1 / 6 (16.67%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Paranasal sinus discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rales			

subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinus pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	2
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Delirium			
subjects affected / exposed	2 / 6 (33.33%)	1 / 55 (1.82%)	2 / 16 (12.50%)
occurrences (all)	2	1	2
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	7 / 55 (12.73%)	0 / 16 (0.00%)
occurrences (all)	1	10	0

Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	4 / 55 (7.27%)	2 / 16 (12.50%)
occurrences (all)	1	5	2
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	7 / 55 (12.73%)	2 / 16 (12.50%)
occurrences (all)	0	7	2
Confusional state			
subjects affected / exposed	2 / 6 (33.33%)	11 / 55 (20.00%)	6 / 16 (37.50%)
occurrences (all)	2	14	6
Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 6 (33.33%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	3	4	0
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	18 / 55 (32.73%)	5 / 16 (31.25%)
occurrences (all)	1	61	18
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	15 / 55 (27.27%)	4 / 16 (25.00%)
occurrences (all)	0	67	6
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	12 / 55 (21.82%)	0 / 16 (0.00%)
occurrences (all)	1	16	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	10 / 55 (18.18%)	0 / 16 (0.00%)
occurrences (all)	1	18	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	14 / 55 (25.45%)	4 / 16 (25.00%)
occurrences (all)	0	24	5
Weight decreased			
subjects affected / exposed	3 / 6 (50.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	6	1	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 6 (0.00%)	4 / 55 (7.27%)	0 / 16 (0.00%)
occurrences (all)	0	6	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	4 / 55 (7.27%)	1 / 16 (6.25%)
occurrences (all)	0	8	1
Weight increased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	4	0	1
Blood creatinine increased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	2	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Procedural pain			
subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 6 (33.33%)	19 / 55 (34.55%)	2 / 16 (12.50%)
occurrences (all)	4	21	2
Tachycardia			
subjects affected / exposed	2 / 6 (33.33%)	13 / 55 (23.64%)	6 / 16 (37.50%)
occurrences (all)	2	15	7
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 55 (9.09%)	2 / 16 (12.50%)
occurrences (all)	0	5	2
Sinus bradycardia			

subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Angina pectoris			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	3
Ventricular tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	8 / 55 (14.55%)	2 / 16 (12.50%)
occurrences (all)	1	11	2
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	6 / 55 (10.91%)	3 / 16 (18.75%)
occurrences (all)	0	6	3
Encephalopathy			
subjects affected / exposed	4 / 6 (66.67%)	9 / 55 (16.36%)	1 / 16 (6.25%)
occurrences (all)	5	11	1
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	15 / 55 (27.27%)	4 / 16 (25.00%)
occurrences (all)	2	17	4
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0

Headache			
subjects affected / exposed	1 / 6 (16.67%)	20 / 55 (36.36%)	8 / 16 (50.00%)
occurrences (all)	2	24	12
Neuropathy peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cerebral ischaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Brain fog			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Seizure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 6 (50.00%)	29 / 55 (52.73%)	4 / 16 (25.00%)
occurrences (all)	4	67	9
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	8 / 55 (14.55%)	1 / 16 (6.25%)
occurrences (all)	1	13	1
Thrombocytopenia			

subjects affected / exposed	1 / 6 (16.67%)	9 / 55 (16.36%)	1 / 16 (6.25%)
occurrences (all)	1	13	3
Febrile neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	5 / 55 (9.09%)	2 / 16 (12.50%)
occurrences (all)	1	8	2
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Bone marrow failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Bone marrow reticulin fibrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Splenic infarction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypofibrinogenaemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vitreous floaters			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	4 / 55 (7.27%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Photophobia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	21 / 55 (38.18%)	3 / 16 (18.75%)
occurrences (all)	1	24	4
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)	11 / 55 (20.00%)	6 / 16 (37.50%)
occurrences (all)	6	15	7
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	8 / 55 (14.55%)	2 / 16 (12.50%)
occurrences (all)	1	8	2
Abdominal pain			
subjects affected / exposed	3 / 6 (50.00%)	10 / 55 (18.18%)	2 / 16 (12.50%)
occurrences (all)	6	13	4
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	9 / 55 (16.36%)	2 / 16 (12.50%)
occurrences (all)	1	10	2
Abdominal distension			
subjects affected / exposed	1 / 6 (16.67%)	4 / 55 (7.27%)	1 / 16 (6.25%)
occurrences (all)	1	5	2

Dry mouth			
subjects affected / exposed	2 / 6 (33.33%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	2	3	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mucous stools			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Anal incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	3 / 16 (18.75%)
occurrences (all)	1	1	4
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 6 (0.00%)	5 / 55 (9.09%)	2 / 16 (12.50%)
occurrences (all)	0	5	4
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Drug eruption			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Urinary retention			
subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	3 / 55 (5.45%)	2 / 16 (12.50%)
occurrences (all)	2	3	2
Back pain			

subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	1	4	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	6 / 55 (10.91%)	1 / 16 (6.25%)
occurrences (all)	0	8	1
Muscular weakness			
subjects affected / exposed	2 / 6 (33.33%)	6 / 55 (10.91%)	0 / 16 (0.00%)
occurrences (all)	4	6	0
Coccydynia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Bone lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	3	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 55 (5.45%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	0 / 16 (0.00%)
occurrences (all)	1	2	0

Clostridium difficile infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	2 / 6 (33.33%)	15 / 55 (27.27%)	3 / 16 (18.75%)
occurrences (all)	5	18	5
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	15 / 55 (27.27%)	2 / 16 (12.50%)
occurrences (all)	1	24	2
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	8 / 55 (14.55%)	5 / 16 (31.25%)
occurrences (all)	1	9	5
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	12 / 55 (21.82%)	1 / 16 (6.25%)
occurrences (all)	1	15	1
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	8 / 55 (14.55%)	4 / 16 (25.00%)
occurrences (all)	0	8	4
Hypocalcaemia			

subjects affected / exposed	2 / 6 (33.33%)	9 / 55 (16.36%)	1 / 16 (6.25%)
occurrences (all)	3	13	1
Hyponatraemia			
subjects affected / exposed	3 / 6 (50.00%)	4 / 55 (7.27%)	2 / 16 (12.50%)
occurrences (all)	4	4	4
Hypoalbuminaemia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	7	3	0
Hypermagnesaemia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	5	2	0
Dehydration			
subjects affected / exposed	2 / 6 (33.33%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolic alkalosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Iron overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Acidosis hyperchloraemic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 55 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypervolaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Hyperkalaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 55 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 55 (1.82%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			

subjects affected / exposed	1 / 6 (16.67%)	2 / 55 (3.64%)	1 / 16 (6.25%)
occurrences (all)	1	3	1

Non-serious adverse events	Phase 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)		
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	13 / 23 (56.52%)		
occurrences (all)	16		
Hypertension			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	6		
Flushing			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Distributive shock			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	21 / 23 (91.30%)		
occurrences (all)	26		
Chills			
subjects affected / exposed	12 / 23 (52.17%)		
occurrences (all)	14		
Fatigue			

subjects affected / exposed	7 / 23 (30.43%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	7 / 23 (30.43%)		
occurrences (all)	8		
Pain			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Catheter site pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gravitational oedema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypothermia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		

Drug hypersensitivity			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	6		
Pulmonary oedema			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	3		
Pneumonitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Atelectasis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Paranasal sinus discomfort			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Sinus pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Pleural effusion			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Tachypnoea			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Epistaxis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Mental status changes subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Delirium subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 3		
Anxiety subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 5		
Agitation subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 5		
Confusional state subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 9		
Investigations Blood bilirubin increased subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 4		
Platelet count decreased subjects affected / exposed occurrences (all)	10 / 23 (43.48%) 22		
Neutrophil count decreased subjects affected / exposed occurrences (all)	8 / 23 (34.78%) 12		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	8 / 23 (34.78%) 10		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	9 / 23 (39.13%) 12		
White blood cell count decreased			

subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	6		
Weight decreased			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	6		
Blood fibrinogen decreased			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Lymphocyte count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Procedural pain			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Cardiac disorders			

Sinus tachycardia subjects affected / exposed occurrences (all)	8 / 23 (34.78%) 12		
Tachycardia subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 6		
Bradycardia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Sinus bradycardia subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 5		
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Angina pectoris subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Ventricular tachycardia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Nervous system disorders Lethargy subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 3		
Somnolence subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Dizziness subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Aphasia			

subjects affected / exposed	8 / 23 (34.78%)			
occurrences (all)	9			
Encephalopathy				
subjects affected / exposed	6 / 23 (26.09%)			
occurrences (all)	9			
Tremor				
subjects affected / exposed	8 / 23 (34.78%)			
occurrences (all)	9			
Cognitive disorder				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	10 / 23 (43.48%)			
occurrences (all)	19			
Neuropathy peripheral				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Dysgeusia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Cerebral ischaemia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Brain fog				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Peripheral sensory neuropathy				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Memory impairment				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Seizure				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	4			
Ataxia				

subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 23 (60.87%)		
occurrences (all)	32		
Neutropenia			
subjects affected / exposed	7 / 23 (30.43%)		
occurrences (all)	15		
Thrombocytopenia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Febrile neutropenia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	6		
Disseminated intravascular coagulation			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Bone marrow failure			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Bone marrow reticulin fibrosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Splenic infarction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypofibrinogenaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	3		
Eye disorders			
Vitreous floaters			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Photophobia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	11 / 23 (47.83%)		
occurrences (all)	16		
Diarrhoea			
subjects affected / exposed	11 / 23 (47.83%)		
occurrences (all)	15		
Constipation			

subjects affected / exposed	11 / 23 (47.83%)			
occurrences (all)	15			
Abdominal pain				
subjects affected / exposed	5 / 23 (21.74%)			
occurrences (all)	6			
Vomiting				
subjects affected / exposed	7 / 23 (30.43%)			
occurrences (all)	11			
Abdominal distension				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	2			
Dry mouth				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	3			
Dyspepsia				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	2			
Haemorrhoids				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Dysphagia				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	3			
Stomatitis				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Abdominal pain upper				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Ileus				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Haematochezia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Lower gastrointestinal haemorrhage				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Mucous stools			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Anal incontinence			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Night sweats			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Rash maculo-papular			

subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Decubitus ulcer			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Rash macular			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Drug eruption			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Acute kidney injury			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		

Pollakiuria			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	6		
Myalgia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	8		
Coccydynia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Bone lesion			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Flank pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Arthralgia			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Bacteraemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Clostridium difficile infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rhinovirus infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Staphylococcal infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	13 / 23 (56.52%)		
occurrences (all)	24		
Hypokalaemia			

subjects affected / exposed	11 / 23 (47.83%)			
occurrences (all)	14			
Hyperglycaemia				
subjects affected / exposed	8 / 23 (34.78%)			
occurrences (all)	9			
Hypomagnesaemia				
subjects affected / exposed	8 / 23 (34.78%)			
occurrences (all)	9			
Decreased appetite				
subjects affected / exposed	9 / 23 (39.13%)			
occurrences (all)	9			
Hypocalcaemia				
subjects affected / exposed	8 / 23 (34.78%)			
occurrences (all)	12			
Hyponatraemia				
subjects affected / exposed	7 / 23 (30.43%)			
occurrences (all)	8			
Hypoalbuminaemia				
subjects affected / exposed	5 / 23 (21.74%)			
occurrences (all)	8			
Hypermagnesaemia				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	3			
Dehydration				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Vitamin D deficiency				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Metabolic alkalosis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Iron overload				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Acidosis hyperchloraemic				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypervolaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Hypernatraemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2015	• Modified study design in Phase 1 from a 6+6 to a 3+3 • Updated secondary and exploratory endpoints • Updated eligibility criteria • Added medical assessments and monitoring requirements prior to the initiation of • leukapheresis, lymphodepleting chemotherapy, and KTE-C19 • Aligned enrollment into the study with initiation of leukapheresis to ensure that subjects were • not prematurely enrolled into the study prior to meeting all eligibility criteria • Clarified expectations for bone marrow and extramedullary disease assessments • Updated toxicity management guidelines, including addition of more detailed guidance for the management of neurotoxicity
09 November 2015	• Clarified response criteria and definitions for CR, CRh, CRi, and CRp • Introduced criteria to pause enrollment to be assessed at regular intervals during the study • Refined eligibility criteria • Clarified timing and requirements for disease assessments
28 November 2016	• Updated eligibility criteria, including allowance for prior blinatumomab treatment and exclusion of subjects with a history of autoimmune disease • Provided additional toxicity management guidance related to CRS, neurotoxicity, cardiac function, and hemophagocytic lymphohistiocytosis (HLH) • Added laboratory assessments: CD3 count at enrollment, CD19 expression, MRD analysis at Month 3 (central analysis), and collection of a PBMC sample at time of progression (for central analysis) • Updated targeted AE, SAE, and concomitant medication reporting requirements • Clarified possible SRT recommendations based on the incidence of DLTs among subjects treated in Phase 1 • Updated primary, secondary, and exploratory endpoints to clarify definitions for CR, CRh, CRi, BFBM, and RFS • Provided further guidance regarding the administration of CSF prophylaxis • Updated statistical considerations: the timing of the 2 interim analyses in Phase 2 were revised to occur after 20 and 35 subjects in the mITT analysis set had had the opportunity to complete the Month 3 disease assessment. A review of efficacy data by the DSMB was added after 7 subjects previously treated with blinatumomab in the mITT analysis set had had the opportunity to complete the Day 28 disease assessment. • Added additional requirements and conditions for retreatment

10 March 2017	• Based on the outcome of SRT review: • Updated sample size in Phase 1 to allow additional subjects to be enrolled at the 1 x 106 anti-CD19 CAR T cells/kg dose level and added a new lower dose of 0.5 x 106 anti-CD19 CAR T cells/kg • Added a mandatory dose of tocilizumab at 36 hours (± 2 hours) after KTE-C19 infusion • Added new exclusion criteria related to severe hypersensitivity to aminoglycosides or any agent used in the study • Added requirement for subjects to be closely monitored and aggressively treated for possible infection • Added requirement to complete a lumbar puncture for subjects with a first onset of Grade 2 or higher neurological symptoms • Added option for redose for subjects who were MRD+ (≤ 5% lymphoblasts in bone marrow) ≥ 2 weeks after the initial KTE-C19 infusion; following this change, subjects could receive up to 3 doses of KTE-C19 (ie, original infusion, redose for MRD+ disease, and retreatment following PD with > 5% bone marrow lymphoblasts) • Updated toxicity management guidance related to HLH, neurologic events, and cerebral edema • Updated laboratory assessments: updated and clarified bone marrow sample collection requirements, added mandatory bone marrow biopsy at Day −4, and added PBMC sample at Week 8 • Updated AE, SAE, and concomitant medication reporting requirements • Updated timing of the 2 interim safety analyses in Phase 2 to occur after 20 and 35 subjects in the mITT analysis set had had the opportunity to be followed for 30 days after the KTE-C19 infusion • Updated timing of the first interim efficacy analysis in Phase 2 to occur after 20 subjects in the mITT analysis set had had the opportunity to be followed for 30 days after the KTE-C19 infusion; removed the second planned interim efficacy analysis of 35 subjects • Added MRD− rate per central assessment as a secondary endpoint

25 October 2017	• Updated the definition of OCR rate in the primary objective from CR + CRh to CR + CRi • Added requirement for EQ-5D for subjects in Phase 2 and added secondary objective of changes in EQ-5D scores • Updated sample size in Phase 1 from 30 to 40 subjects and total sample size from 90 to 100 subjects • Refined eligibility criteria, including the definition of r/r disease • Updated timing of completion of bridging chemotherapy: bridging therapy was to be completed at least 7 days or 5 half-lives, whichever is shorter, prior to initiating lymphodepleting chemotherapy • Removed requirement for MMSE • Updated timing of Day 28 lumbar puncture: for subjects with CNS-2 at baseline, a CSF sample was required at the time of first presumed response (ie, bone marrow blasts < 5%) • Updated imaging requirements for subjects with known non-CNS extramedullary disease at baseline: the first on-study images were to occur at the time of first presumed response (ie, bone marrow blasts ≤ 5%), rather than at the first occurrence of PR or better based on the bone marrow evaluation • Clarified time points for RCR testing • Updated requirements to be met at the time of leukapheresis regarding the need to meet all eligibility criteria and avoiding corticosteroid therapy for 7 days prior to leukapheresis • Added requirement to assess peripheral blast counts prior to lymphodepleting chemotherapy (ie, Day −4) for subjects who did not have a Day −4 bone marrow evaluation • Eliminated the requirement to administer tocilizumab at 36 hours after the KTE-C19 infusion • Changed analysis of applicable endpoints from local review to independent review per the updated overall disease response classification appendix • Updated definitions of OCR, DOR, and RFS used for study endpoints
31 October 2018	• Updated number of participating sites to 35 • Added rationale for the recommended Phase 2 dose of 1 x 106 anti-CD19 CAR T cells/kg • Added lumbar punctures for subjects with CNS-2 disease at screening and described that for subjects with new onset of a Grade 2 or higher neurologic event after KTE-X19 infusion, a lumbar puncture may be performed as applicable • Added a requirement for the IP to be available before initiation of lymphodepletingchemotherapy • Added language for safety criteria to be met prior to initiation of lymphodepleting chemotherapy, including timing of fever prior to lymphodepleting chemotherapy, infection/inflammation assessment, treatment with antimicrobials, and anti-infective workup • Added section to include safety criteria to be met prior to KTE-X19 infusion, including timing of fever and high C-reactive protein (CRP) prior to infusion, WBC counts, infection/inflammation assessment, treatment with antimicrobials, and anti-infective workup • Clarified the required length of hospitalization to be aligned with country-specific Requirements • Added EQ-5D time points during the long-term follow-up period • Updated AE and SAE reporting requirements • Updated guidelines for use of contraception during the course of the study • Added appendix for monitoring of subjects after IP administration per German country requirements

14 December 2021	• A Long-term Follow-up (LTFU) protocol, KT-US-982-5968 has been developed to allow for rollover of subjects to complete the 15-year follow-up after infusion of KTE-X19 on the KTE-C19-103 study. Subjects were provided the opportunity to rollover to the LTFU protocol for safety followup and reduced burden of study-specific assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34097852

http://www.ncbi.nlm.nih.gov/pubmed/33827116