Clinical trial results:
A Phase 1 Multicenter Study Evaluating the Safety and Tolerability of KTE-X19 in Adult Subjects with Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

Summary

EudraCT number	2018-001923-38
Trial protocol	DE ES GB IT
Global end of trial date	18 November 2022

Results information

Result version number	v1 (current)
This version publication date	16 November 2023
First version publication date	16 November 2023

Trial information

Trial identification

Sponsor protocol code	KTE-C19-108

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03624036
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	18 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2021
Global end of trial reached?	Yes
Global end of trial date	18 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety and tolerability of brexucabtagene autoleucel (KTE-X19) in adults with relapsed/refractory chronic lymphocytic leukemia (r/r CLL) and small lymphocytic lymphoma (r/r SLL) who had received at least 2 prior lines of treatment, one of which must include a Bruton's tyrosine kinase (BTK) inhibitor.

After the end of KTE-C19-108, participants who received an infusion of brexucabtagene autoleucel will complete the remainder of the 15-year follow-up assessments in a separate Long-term Follow-up study, KT-US-982-5968 (2020-005843-21).

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	15 November 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	15 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	16
EEA total number of subjects	1

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)	9
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Italy. The study was terminated before enrolling participants in the Cohort 4B.

Pre-assignment

Screening details:

17 participants were screened.

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	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Arm description:

Participants with relapsed/refractory (r/r) chronic lymphocytic leukemia (CLL) received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered intravenously (IV) on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-cluster of differentiate 19 (CD19) chimeric antigen receptor (CAR) T cells/kg administered IV on Day 0.

Arm type	Experimental
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:

30 mg/m^2/day administered over 30 minutes on days -5 to -3.

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 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:

500 mg/m^2/day administered over 30-60 minutes on days -5 to -3.

Arm title	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r CLL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 2 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

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 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:

30 mg/m^2/day administered over 30 minutes on days -5 to -3.

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:

500 mg/m^2/day administered over 30-60 minutes on days -5 to -3.

Arm title	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r CLL and small lymphocytic lymphoma (SLL) with ≤1% malignant cells in peripheral blood or absolute lymphocyte count (ALC) < 5,000 cells/µL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

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 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:

30 mg/m^2/day administered over 30 minutes on days -5 to -3.

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:

500 mg/m^2/day administered over 30-60 minutes on days -5 to -3.

Arm title	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Arm description:

Participants with r/r CLL who previously received two lines of therapy along with ibrutinib with or without anti CD20 antibodies, B-cell lymphoma 2 (BCL-2) and Phosphoinositide 3-kinase (PI3k) inhibitors received ibrutinib up to 30 hours prior to leukapheresis along with conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

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 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:

30 mg/m^2/day administered over 30 minutes on days -5 to -3.

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:

500 mg/m^2/day administered over 30-60 minutes on days -5 to -3.

Number of subjects in period 1	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Started	7	3	3
Completed	0	0	0
Not completed	7	3	3
Death	2	3	-
Withdrawal by Subject	1	-	1
Reason not Specified	3	-	2
Enrolled but Never Treated	1	-	-

Number of subjects in period 1	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Started	3
Completed	0
Not completed	3
Death	1

Withdrawal by Subject	-
Reason not Specified	2
Enrolled but Never Treated	-

Baseline characteristics

Reporting groups	
Reporting group title	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with relapsed/refractory (r/r) chronic lymphocytic leukemia (CLL) received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered intravenously (IV) on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-cluster of differentiate 19 (CD19) chimeric antigen receptor (CAR) T cells/kg administered IV on Day 0.	
Reporting group title	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r CLL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 2 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.	
Reporting group title	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r CLL and small lymphocytic lymphoma (SLL) with ≤1% malignant cells in peripheral blood or absolute lymphocyte count (ALC) < 5,000 cells/µL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.	
Reporting group title	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Reporting group description:	
Participants with r/r CLL who previously received two lines of therapy along with ibrutinib with or without anti CD20 antibodies, B-cell lymphoma 2 (BCL-2) and Phosphoinositide 3-kinase (PI3k) inhibitors received ibrutinib up to 30 hours prior to leukapheresis along with conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.	

Reporting group values	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Number of subjects	7	3	3
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60.8	58.7	68.0
standard deviation	± 5.8	± 5.9	± 11.5
Gender categorical Units: Subjects			
Female	3	1	0
Male	4	2	3
Race Units: Subjects			
Black or African American	1	0	0
White	6	3	3
Ethnicity Units: Subjects			

Not Hispanic or Latino	7	3	3

Reporting group values	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Total	
Number of subjects	3	16	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.3		
standard deviation	± 9.1	-	
Gender categorical Units: Subjects			
Female	1	5	
Male	2	11	
Race Units: Subjects			
Black or African American	1	2	
White	2	14	
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	16	

End points

End points reporting groups

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

Reporting group description:

Participants with relapsed/refractory (r/r) chronic lymphocytic leukemia (CLL) received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered intravenously (IV) on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-cluster of differentiate 19 (CD19) chimeric antigen receptor (CAR) T cells/kg administered IV on Day 0.

Reporting group title	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 2 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Reporting group title	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL and small lymphocytic lymphoma (SLL) with ≤1% malignant cells in peripheral blood or absolute lymphocyte count (ALC) < 5,000 cells/µL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Reporting group title	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL who previously received two lines of therapy along with ibrutinib with or without anti CD20 antibodies, B-cell lymphoma 2 (BCL-2) and Phosphoinositide 3-kinase (PI3k) inhibitors received ibrutinib up to 30 hours prior to leukapheresis along with conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Primary: Number of Participants Experiencing Dose Limiting Toxicities (DLTs)

End point title	Number of Participants Experiencing Dose Limiting Toxicities (DLTs)[1]

End point description:

DLTs refer to toxicities with onset experienced during the first 28 days of study treatment that have been judged to be clinically significant and related to study treatment. DLTs evaluated may include with some exceptions: All brexucabtagene autoleucel related Grade 3 non-hematologic toxicities lasting for more than 7 days, Grade 4 non-hematologic toxicities regardless of duration, and Grade 4 hematologic toxicity lasting more than 30 days if not attributable to underlying disease. DLT Evaluable Set included all participants treated with the target brexucabtagene autoleucel dose and followed for at least 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 Grade 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.

End point values	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: participants	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) Per Investigator Review Assessed by International Workshop on CLL (IWCLL) 2018 Criteria

End point title	Objective Response Rate (ORR) Per Investigator Review Assessed by International Workshop on CLL (IWCLL) 2018 Criteria

End point description:

ORR: percentage of participants achieving either complete response (CR), CR with incomplete hematopoetic recovery (CRi)/partial response (PR). CR criteria: no lymphadenopathy >1.5 cm/hepatomegaly/splenomegaly, lymphocytes <4000/microliters (µL), bone marrow sample is normocellular with 30% lymphocytes&no B-lymphoid nodules, platelets ≥100,000/µL, hemoglobin ≥11 grams per deciliter (g/dL). CRi: All CR criteria were met except with platelet count <100,000/µL, hemoglobin <11 g/dL or neutrophil count <500/µL.PR: ≥1 of these:≥50% decrease in lymphocytes, lymphadenopathy, size of liver&spleen, 50% decrease in bone marrow infiltrates;&≥1 of these:platelets ≥100,000/µL or ≥50% increase from Baseline, hemoglobin ≥11 g/dL or ≥50% increase from Baseline. Participants who did not meet criteria were considered nonresponders. 95% confidence interval (CI) was calculated by Clopper-Pearson method. All Treated Subjects Set=all participants who were treated with any dose of brexucabtagene autoleucel.

End point type	Secondary

End point timeframe:

First infusion date up to last follow up visit (maximum duration: 42 months)

End point values	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: percentage of participants				
number (confidence interval 95%)	50 (11.8 to 88.2)	33 (0.8 to 90.6)	100 (29.2 to 100.0)	0 (0.0 to 70.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Treatment Emergent Adverse

Events (TEAEs)

End point title	Percentage of Participants Experiencing Treatment Emergent Adverse Events (TEAEs)

End point description:

An AE is defined as any untoward medical occurrence in a clinical trial participant that does not necessarily have a relationship with study treatment or worsening of a pre-existing medical condition. TEAEs were defined as AEs with onset on or after the initiation of brexucabtagene autoleucel infusion. Safety Analysis Set included all participants who were treated with any dose of brexucabtagene autoleucel.

End point type	Secondary

End point timeframe:

First infusion date up to last follow up visit (maximum duration: 42 months)

End point values	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: percentage of participants				
number (not applicable)	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Level of Anti-CD19 CAR T-Cells in Blood

End point title	Peak Level of Anti-CD19 CAR T-Cells in Blood

End point description:

Peak was defined as the maximum number of CAR T cells measured post-infusion. Participants in the safety analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

First infusion date up to 3 months post-infusion (approximately 3 months)

End point values	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	2	3	3
Units: cells/µL				
median (inter-quartile range (Q1-Q3))	1.46 (0.58 to 2.35)	1.08 (0.00 to 2.15)	42.18 (27.52 to 679.38)	1.00 (0.00 to 1.27)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Enrollment up to last follow up visit (maximum: 43 months); Adverse Events: First infusion date up to last follow up visit (maximum: 42 months)

Adverse event reporting additional description:

All-Cause Mortality: All Enrolled Analysis Set included all the enrolled participants.
Adverse Events: Safety Analysis Set included all participants who were treated with any dose of brexucabtagene autoleucel.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

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

Reporting group description:

Participants with r/r CLL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Reporting group title	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL who previously received two lines of therapy along with ibrutinib with or without anti CD20 antibodies, BCL-2 and PI3k inhibitors received ibrutinib up to 30 hours prior to leukapheresis along with conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Reporting group title	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL and SLL with ≤1% malignant cells in peripheral blood or ALC < 5,000 cells/µL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 1 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Reporting group title	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg

Reporting group description:

Participants with r/r CLL received conditioning chemotherapy (fludarabine 30 mg/m^2/day over 30 minutes and cyclophosphamide 500 mg/m^2/day over 30-60 minutes) administered IV on Days -5 to -3 with 2 rest days, followed by single infusion of brexucabtagene autoleucel 2 x 10^6 anti-CD19 CAR T cells/kg administered IV on Day 0.

Serious adverse events	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	3 / 3 (100.00%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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			
Aphasia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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			
Systemic candida			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Serious adverse events	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 3 (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	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Systemic candida			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhinovirus infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 3 (33.33%)		
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	First Stage Cohort 1: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 4A: 1 x 10^6 Anti-CD19 CAR T Cells/kg	Second Stage Cohort 3: 1 x 10^6 Anti-CD19 CAR T Cells/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	2	1
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
Pyrexia			
subjects affected / exposed	4 / 6 (66.67%)	2 / 3 (66.67%)	3 / 3 (100.00%)
occurrences (all)	5	3	3
Pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Chills			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Pruritus genital			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Hallucination			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Frustration tolerance decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Delirium			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	2	1	4
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	5	2
White blood cell count decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	2
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood bicarbonate decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lymphocyte count increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	2
Nervous system disorders			

Encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	5 / 6 (83.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	8	4	1
Dizziness			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	2
Tremor			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	2
Aphasia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Cognitive disorder			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Amnesia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysgraphia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nystagmus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	3	5	1
Neutropenia			
subjects affected / exposed	4 / 6 (66.67%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	9	4	0
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Retinal tear			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vitreous floaters			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	2
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Petechiae			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rash maculo-papular			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Candida infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Covid-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	3
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperglycaemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypervolaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Non-serious adverse events	First Stage Cohort 2: 2 x 10^6 Anti-CD19 CAR T Cells/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Pyrexia			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Pruritus genital			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Cough			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Tachypnoea			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Frustration tolerance decreased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Platelet count decreased			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
White blood cell count decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Alanine aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood bicarbonate decreased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Blood bilirubin increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
C-reactive protein increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lymphocyte count increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Aphasia			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysgraphia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nystagmus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	5		

Neutropenia			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	7		
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	4		
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Retinal tear			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vitreous floaters			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Urinary incontinence subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Pollakiuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Acute kidney injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Bone pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Infections and infestations			
Candida infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Covid-19 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Cytomegalovirus viraemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Folliculitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Oral candidiasis			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rhinovirus infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypervolaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Hyponatraemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2019	• Moved "Levels of anti-CD19 CAR T-cells in blood" to secondary endpoints, removing it from exploratory endpoints • Updated 'bridging therapy' text to clarify language • Added pharmacokinetics to secondary objectives and removed from exploratory objectives • Updated 'study rationale' text to clarify language • Updated the number of participating sites from "30" to "35" • Updated inclusion criteria: to expand participant population and add washout period that was not previously specified • Updated exclusion criteria: removed 'prior' in regard to no prior allo-stem cell transplant (SCT) versus no prior allo-SCT within 6 months, separated criteria into multiple criteria, included participants who may not receive KTE-X19 infusion • Added "The investigational medicinal product (KTE-X19) must be available before initiation of conditioning chemotherapy" • Added "The safety review team (SRT) safety review outcome was communicated to the active clinical study sites after the SRT safety review meeting. • Removed "during the time between the planned interim analysis and primary analysis" • Updated sample size considerations as "The primary analysis occurred when 60 participants in the modified intent to treat (mITT) set have had the opportunity to complete the month 6 disease assessment." • Updated serious adverse event (SAE) reporting requirements as "reported in accordance with the European Union (EU) guidelines, or if applicable, per local reporting guidelines." • Added "Post-infusion monitoring of participants must be for a minimum of 7 days unless otherwise required by country regulatory agencies." • Added language to align with Yescarta label "Participants should be advised to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, for at least 8 weeks following KTE-X19 infusion."
27 May 2020	• Title was updated to "A Phase 1 Multicenter Study Evaluating the Safety and Tolerability of KTE-X19 in Adult Subjects with Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma" • Updated primary, secondary, and exploratory objectives • To account for the addition of SLL, background and updated publication data were added • Updated study design based on suboptimal CAR T expansion seen in Phase 1 Cohort 1 and Cohort 2 • Added rationale for Cohorts 3 and 4 • Updated to reflect that due to the smaller enrollment of the study, limited to activated sites • Updated to reflect enrollment in Phase 1 study to assess expansion of CAR T cell. Clarification throughout protocol that participants enrolled are enrolled and dosed with KTE-X19 • Inclusion criteria updated to include SLL and classified by cohort, imaging to confirm structural defects • Removed sections: Patient Reported Outcomes, Central Review of Response, Data Safety Monitoring Board • Updated to remove Phase 2 data safety monitoring board (DSMB) review criteria as no longer applicable • Revised endpoints with removal of Phase 2: ORR remained as the secondary endpoint for Phase 1, revised secondary endpoints in response to removal of Phase 2 of study, patient reported outcomes no longer a component of the study; ORR secondary endpoint in selected Safe Dose Cohort • Removal of Phase 2 references and planned interim analysis for futility and primary analysis due to the removal of Phase 2; updated sample size considerations to reflect revised study endpoints.

01 September 2021	• Added footnote in study schema to account for rollover to the long-term follow-up study • Added "Upon completion of Cohort 4A SRT, it was determined not to enroll participants in Cohort 4B." • Added Long-term follow-up (LTFU). After the end of KTE-C19-108, participants who received an infusion of KTE-X19 will complete the remainder of the 15-year follow-up assessments in a separate LTFU study, KT-US-982-5968 • Updated study duration 'The duration of the study for individual participants vary depending on a participant`s screening requirements, response to treatment, and survival, and if applicable, timing of transition to the separate LTFU study, KT-US-982-5968 • Updated LTFU details: All participants who received an infusion of KTE-X19 were provided the opportunity to transition to a separate LTFU study, KT-US-982-5968, where they were monitored for occurrence of late-onset targeted AEs/SAEs suspected to be possibly related to KTE-X19, presence of replication-competent retrovirus (RCR), and/or insertional mutagenesis for up to 15 years from the time of KTE-X19 infusion; In KT-US-982-5968, participants will continue assessments at timepoints contiguous with the LTFU timepoints in this study • Removed section KTE-X19 Retreatment • Updated SAEs reporting as 'Following completion of KTE-C19-108, any relevant information regarding ongoing SAEs must be submitted to Kite Pharma within 24 hours of the investigator's knowledge of the event using the hardcopy format SAE Report Form and sent via e-mail to the SAE Reporting mailbox: safety_FC@gilead.com.'

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 November 2022	Development program terminated.	-

Notes:

Limitations and caveats

None reported