



Clinical trial results:

A PHASE 2, SINGLE-ARM, MULTI-COHORT, MULTICENTER TRIAL TO DETERMINE THE EFFICACY AND SAFETY OF JCAR017 IN ADULT SUBJECTS WITH AGGRESSIVE B-CELL NON-HODGKIN LYMPHOMA (TRANSCEND WORLD).

Summary

EudraCT number	2017-000106-38
Trial protocol	BE FR FI ES DE AT NL GB IT
Global end of trial date	15 December 2023

Results information

Result version number	v1 (current)
This version publication date	07 December 2024
First version publication date	07 December 2024

Trial information

Trial identification

Sponsor protocol code	JCAR017-BCM-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03484702
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International, Bristol-Myers Squibb, clinical.trials@bms.com
Scientific contact	EU Study Start-Up Unit, Bristol-Myers Squibb International, Bristol-Myers Squibb, clinical.trials@bms.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	23 February 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cohorts 1, 2, 3, 4, and 5

- To determine the efficacy, defined as overall response rate (ORR) of JCAR017 in subjects with aggressive B-cell non-Hodgkin lymphoma

Cohort 7

- To evaluate the safety of JCAR017 treatment in subjects intended to be treated as outpatients

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2018
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	Austria: 10
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	113
EEA total number of subjects	88

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)	54
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

116 participants underwent leukapheresis, 98 participants started treatment with lymphodepleting chemotherapy. Cohort 6 was planned but subsequently removed from the study. No participants were enrolled into Cohort 6.

Period 1

Period 1 title	Pre-Treatment Period - Leukapheresis
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy

Arm description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100×10^6 JCAR017-positive transfected viable T cells

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

Dosage and administration details:

300 mg/m² /day for 3 days

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

Dosage and administration details:

30 mg/m² /day for 3 days

Arm title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
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Arm description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
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Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
100 x 10 ⁶ JCAR017-positive transfected viable T cells	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
300 mg/m ² /day for 3 days	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Arm title	Cohort 3: Japan Specific
Arm description:	
JCAR017 was infused at a dose of 100 x 10 ⁶ JCAR017-positive transfected viable T cells (50 x 10 ⁶ CD8+ CAR+ T cells and 50 x 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
100 x 10 ⁶ JCAR017-positive transfected viable T cells	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
300 mg/m ² /day for 3 days	
Arm title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Arm description:	
JCAR017 was infused at a dose of 100 x 10 ⁶ JCAR017-positive transfected viable T cells (50 x 10 ⁶ CD8+ CAR+ T cells and 50 x 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of	

Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 x 10⁶ JCAR017-positive transfected viable T cells

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

Dosage and administration details:

300 mg/m² /day for 3 days

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

Dosage and administration details:

30 mg/m² /day for 3 days

Arm title	Cohort 5: Primary Central Nervous System Lymphoma
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Arm description:

JCAR017 was infused at a dose of 100 x 10⁶ JCAR017-positive transfected viable T cells (50 x 10⁶ CD8+ CAR+ T cells and 50 x 10⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 x 10⁶ JCAR017-positive transfected viable T cells

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

Dosage and administration details:

300 mg/m² /day for 3 days

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

Dosage and administration details:

30 mg/m² /day for 3 days

Arm title	Cohort 7: Outpatient Treatment
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Arm description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100×10^6 JCAR017-positive transduced viable T cells

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

Dosage and administration details:

300 mg/m² /day for 3 days

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

Dosage and administration details:

30 mg/m² /day for 3 days

Number of subjects in period 1	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific
Started	45	32	14
Completed	43	27	12
Not completed	2	5	2
Other reasons	2	5	2

Number of subjects in period 1	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment
Started	4	7	11
Completed	1	5	10
Not completed	3	2	1
Other reasons	3	2	1

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy
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Arm description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100×10^6 JCAR017-positive transfected viable T cells

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

Dosage and administration details:

300 mg/m² /day for 3 days

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

Dosage and administration details:

30 mg/m² /day for 3 days

Arm title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
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Arm description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100×10^6 JCAR017-positive transfected viable T cells

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

Dosage and administration details: 300 mg/m ² /day for 3 days	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Arm title	Cohort 3: Japan Specific
Arm description: JCAR017 was infused at a dose of 100 x 10 ⁶ JCAR017-positive transfected viable T cells (50 x 10 ⁶ CD8+ CAR+ T cells and 50 x 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 x 10 ⁶ JCAR017-positive transfected viable T cells	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 300 mg/m ² /day for 3 days	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Arm title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Arm description: JCAR017 was infused at a dose of 100 x 10 ⁶ JCAR017-positive transfected viable T cells (50 x 10 ⁶ CD8+ CAR+ T cells and 50 x 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 x 10 ⁶ JCAR017-positive transfected viable T cells	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
300 mg/m ² /day for 3 days	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Arm title	Cohort 5: Primary Central Nervous System Lymphoma
Arm description:	
JCAR017 was infused at a dose of 100 × 10 ⁶ JCAR017-positive transfected viable T cells (50 × 10 ⁶ CD8+ CAR+ T cells and 50 × 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
100 × 10 ⁶ JCAR017-positive transfected viable T cells	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
300 mg/m ² /day for 3 days	
Investigational medicinal product name	Fludarabine IV
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 for 3 days	
Arm title	Cohort 7: Outpatient Treatment
Arm description:	
JCAR017 was infused at a dose of 100 × 10 ⁶ JCAR017-positive transfected viable T cells (50 × 10 ⁶ CD8+ CAR+ T cells and 50 × 10 ⁶ CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Arm type	Experimental
Investigational medicinal product name	JCAR017
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
100 × 10 ⁶ JCAR017-positive transfected viable T cells	

Investigational medicinal product name	Fludarabine IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 30 mg/m2 /day for 3 days	
Investigational medicinal product name	Cyclophosphamide IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 300 mg/m2 /day for 3 days	

Number of subjects in period 2	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific
Started	43	27	12
JCAR017 Treated Set	36 ^[1]	27	10 ^[2]
Completed	39	24	12
Not completed	4	3	0
Adverse event, serious fatal	3	1	-
Participant Withdrew from Study	-	1	-
Physician decision	-	1	-
Adverse event, non-fatal	1	-	-

Number of subjects in period 2	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment
Started	1	5	10
JCAR017 Treated Set	1	5	9
Completed	1	5	9
Not completed	0	0	1
Adverse event, serious fatal	-	-	-
Participant Withdrew from Study	-	-	-
Physician decision	-	-	1
Adverse event, non-fatal	-	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all LDC treated participants received JCAR017

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the

arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all LDC treated participants received JCAR017

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 3: Japan Specific
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 5: Primary Central Nervous System Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 7: Outpatient Treatment
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	

Reporting group values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific
Number of subjects	45	32	14
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	26	1	11
From 65-84 years	19	31	3
85 years and over	0	0	0

Age Continuous Units: Years arithmetic mean standard deviation	60.2 ± 10.60	73.3 ± 5.50	57.6 ± 10.08
Sex: Female, Male Units: Participants			
Female	15	13	6
Male	30	19	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	1	0
Not Hispanic or Latino	29	22	14
Unknown or Not Reported	9	9	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	3	14
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	37	19	0
More than one race	0	0	0
Unknown or Not Reported	8	10	0

Reporting group values	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment
Number of subjects	4	7	11
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	7	8
From 65-84 years	3	0	3
85 years and over	0	0	0
Age Continuous Units: Years arithmetic mean standard deviation	63.5 ± 21.11	57.0 ± 5.74	58.1 ± 12.47
Sex: Female, Male Units: Participants			
Female	1	3	4
Male	3	4	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1

Not Hispanic or Latino	2	5	7
Unknown or Not Reported	1	2	3
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	5	7
More than one race	0	0	0
Unknown or Not Reported	1	2	4

Reporting group values	Total		
Number of subjects	113		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	54		
From 65-84 years	59		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	42		
Male	71		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	10		
Not Hispanic or Latino	79		
Unknown or Not Reported	24		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	17		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	71		
More than one race	0		
Unknown or Not Reported	25		

End points

End points reporting groups

Reporting group title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 3: Japan Specific
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 5: Primary Central Nervous System Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 7: Outpatient Treatment
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 3: Japan Specific
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	
Reporting group title	Cohort 5: Primary Central Nervous System Lymphoma
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	

Lymphodepleting chemotherapy).

Reporting group title	Cohort 7: Outpatient Treatment
Reporting group description: JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transfected viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).	

Primary: Overall Response Rate (ORR) in Cohorts 1, 2, 3, 4

End point title	Overall Response Rate (ORR) in Cohorts 1, 2, 3, 4 ^{[1][2]}
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End point description:

ORR by Independent Review Committee (Cohorts 1, 2, 3) or Investigator (Cohort 4). ORR is the percent of participants with best overall response of complete response (CR) or partial response (PR).

Complete response via PET-CT:

- Lymph nodes/extralymphatic: Score 1, 2, 3a with/w-out residual mass on 5-point scale
- New lesions: No
- Bone marrow: No FDG-avid disease

Complete response via CT scan:

- Lymph nodes/extralymphatic: Target nodes/nodal masses ≤ 1.5 cm longest transverse diameter.
- Nonmeasured lesion: None
- New lesions: No
- Bone marrow: Normal

Partial response via PET-CT:

- Lymph nodes/extralymphatic: Score 4, 5b, reduced uptake from baseline
- New lesions: No
- Bone marrow: Residual uptake higher than normal, reduced from baseline

Partial response via CT scan:

- Lymph nodes/extralymphatic: 50% decrease in sum of diameters of ≤ 6 target measurable nodes/extranodal sites
- Nonmeasured lesion: No
- Organ enlargement: Spleen length decreased $> 50\%$
- New lesions: No

End point type	Primary
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End point timeframe:

From JCAR017 infusion until disease progression, end of study, the start of another anticancer therapy, or hemopoietic stem cell transplant (HSCT) (up to approximately 24 months)

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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohorts 1, 2, 3, 4 only.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Percent of Participants				
number (confidence interval 95%)	61.1 (43.5 to 76.9)	63.0 (42.4 to 80.6)	70.0 (34.8 to 93.3)	100 (100 to 100)

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in Cohort 5

End point title	Overall Response Rate (ORR) in Cohort 5 ^{[3][4]}
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End point description:

ORR determined by Investigator assessment after JCAR017 infusion. The ORR is the percent of participants with best overall response (BOR) of either complete response (CR), complete response unconfirmed (CRu) or partial response (PR).

Complete response (CR):

- Brain imaging: No contrast enhancement
- Corticosteroid dose: None
- Eye examination: Normal
- Cerebrospinal fluid cytology: Negative

Complete response unconfirmed (CRu):

- Brain imaging: No contrast enhancement, Minimal abnormality
- Corticosteroid dose: Any
- Eye examination: Normal, minor RPE abnormality
- Cerebrospinal fluid cytology: Negative

Partial response (PR):

- Brain imaging: 50% decrease in enhancing tumor, no contrast enhancement.
- Corticosteroid dose: Irrelevant
- Eye examination: Minor RPE abnormality, decrease in vitreous cells or retinal infiltrate.
- Cerebrospinal fluid cytology: Negative, persistent or suspicious

End point type	Primary
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End point timeframe:

From JCAR017 infusion until disease progression, end of study, the start of another anticancer therapy, or hemopoietic stem cell transplant (HSCT) (up to approximately 24 months)

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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohort 5 only.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed \geq 2 Lines of Therapy			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Percent of Participants				
number (confidence interval 95%)	80.0 (28.4 to 99.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events in Cohort 7

End point title	Number of Participants with Adverse Events in Cohort 7 ^{[5][6]}
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End point description:

An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or

worsen in a participant during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the participant's health, including laboratory test values, regardless of etiology. Any worsening (i.e., any clinically significant adverse change in the frequency or intensity of a preexisting condition) should be considered an AE. Graded according to NCI CTCAE (Version 4.03) guidelines where grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life threatening, grade 5 = death.

End point type	Primary
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End point timeframe:

From leukapheresis to end of study (up to approximately 24 months)

Notes:

[5] - 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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohort 7 only.

End point values	Cohort 7: Outpatient Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
AEs between leukapheresis and LDC	0			
AEs occurring LDC and JCAR017 infusion	2			
AEs between JCAR017 infusion and Day 30	9			
AEs between Day 31 and Day 90	7			
AEs between Day 91 and end of study	7			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events (SAEs) in Cohort 7

End point title	Number of Participants with Serious Adverse Events (SAEs) in Cohort 7 ^{[7][8]}
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End point description:

A serious adverse event (SAE) is defined as any adverse event (AE) occurring at any dose that:

- Results in death;
- Is life-threatening (ie, in the opinion of the Investigator, the participant is at immediate risk of death from the AE);
- Requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay).
- Results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions);
- Is a congenital anomaly/birth defect;
- Constitutes an important medical event.

Graded according to NCI CTCAE (Version 4.03) guidelines where grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life threatening, grade 5 = death.

End point type	Primary
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End point timeframe:

From leukapheresis to end of study (up to approximately 24 months)

Notes:

[7] - 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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohort 7 only.

End point values	Cohort 7: Outpatient Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
SAEs between leukapheresis and LDC	0			
SAEs between LDC and JCAR017 infusion	0			
SAEs between JCAR017 infusion and Day 30	1			
SAEs between Day 31 and Day 90	0			
SAEs between Day 91 and end of study	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Increase from Baseline in Select Hematology Parameters - Cohort 7

End point title	Number of Participants with Increase from Baseline in Select Hematology Parameters - Cohort 7 ^[9] ^[10]
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End point description:

JCAR017 treatment-emergent laboratory abnormalities are defined as an abnormality that, compared to baseline, worsens by at least one grade after JCAR017 infusion. The baseline value is defined as the last available recorded value on or prior to the date of JCAR017 infusion.

End point type	Primary
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End point timeframe:

At Baseline and Day 29 after JCAR017 infusion

Notes:

[9] - 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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohort 7 only.

End point values	Cohort 7: Outpatient Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Leukocytes (10 ⁹ /L) - Day 29	0			

Neutrophils, Segmented (10 ⁹ /L) - Day 29	2			
Platelets (10 ⁹ /L) - Day 29	5			
Activated Partial Thromboplastin Time (sec) Day 29	0			
Prothrombin Intl. Normalized Ratio - Day 29	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Increase from Baseline in Select Serum Chemistry Parameters - Cohort 7

End point title	Number of Participants with Increase from Baseline in Select Serum Chemistry Parameters - Cohort 7 ^{[11][12]}
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End point description:

JCAR017 treatment-emergent laboratory abnormalities are defined as an abnormality that, compared to baseline, worsens by at least one grade after JCAR017 infusion. The baseline value is defined as the last available recorded value on or prior to the date of JCAR017 infusion.

End point type	Primary
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End point timeframe:

At Baseline and Day 29 after JCAR017 infusion

Notes:

[11] - 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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be reported for Cohort 7 only.

End point values	Cohort 7: Outpatient Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Albumin (g/L) - Day 29	0			
Phosphate (mmol/L) - Day 29	0			
Alkaline Phosphatase (U/L) - Day 29	0			
Alanine Aminotransferase (U/L) - Day 29	0			
Aspartate Aminotransferase (U/L) - Day 29	1			
Bilirubin (umol/L) - Day 29	0			
Creatinine (umol/L) - Day 29	7			
Triglycerides (mmol/L) - Day 29	3			
Urate (umol/L) - Day 29	0			

Statistical analyses

Secondary: Number of Participants with Adverse Events in Cohorts 1, 2, 3, 4, and 5

End point title	Number of Participants with Adverse Events in Cohorts 1, 2, 3, 4, and 5 ^[13]
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End point description:

An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the participant's health, including laboratory test values, regardless of etiology. Any worsening (i.e., any clinically significant adverse change in the frequency or intensity of a preexisting condition) should be considered an AE. Graded according to NCI CTCAE (Version 4.03) guidelines where grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life threatening, grade 5 = death.

End point type	Secondary
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End point timeframe:

From leukapheresis to end of study (up to approximately 24 months)

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: Only descriptive statistics were planned for this endpoint.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Participants				
AEs between leukapheresis and LDC	5	5	0	0
AEs between LDC and JCAR017 infusion	29	23	8	0
AEs between JCAR017 infusion and Day 30	36	26	10	1
AEs between Day 31 and Day 90	25	10	8	1
AEs between Day 91 and end of study	10	9	7	0

End point values	Cohort 5: Primary Central Nervous System Lymphoma			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
AEs between leukapheresis and LDC	0			
AEs between LDC and JCAR017 infusion	4			
AEs between JCAR017 infusion and Day 30	5			
AEs between Day 31 and Day 90	3			
AEs between Day 91 and end of study	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serious Adverse Events (SAEs) in Cohorts 1, 2, 3, 4, and 5

End point title	Number of Participants with Serious Adverse Events (SAEs) in Cohorts 1, 2, 3, 4, and 5 ^[14]
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End point description:

A serious adverse event (SAE) is defined as any adverse event (AE) occurring at any dose that:

- Results in death;
- Is life-threatening (ie, in the opinion of the Investigator, the participant is at immediate risk of death from the AE);
- Requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay).
- Results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions);
- Is a congenital anomaly/birth defect;
- Constitutes an important medical event.

Graded according to NCI CTCAE (Version 4) guidelines where grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life threatening, grade 5 = death.

End point type	Secondary
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End point timeframe:

From leukapheresis to end of study (up to approximately 24 months)

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: Prespecified to be reported for Cohorts 1, 2, 3, 4, and 5 only.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Participants				
SAEs between leukapheresis and LDC	0	1	0	0
SAEs between LDC and JCAR017 infusion	1	0	0	0
SAEs between JCAR017 infusion and Day 30	16	7	0	0
SAEs between Day 31 and Day 90	7	3	2	0
SAEs between Day 91 and end of study	5	3	1	0

End point values	Cohort 5: Primary Central			
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	Nervous System Lymphoma			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
SAEs between leukapheresis and LDC	0			
SAEs between LDC and JCAR017 infusion	0			
SAEs between JCAR017 infusion and Day 30	1			
SAEs between Day 31 and Day 90	1			
SAEs between Day 91 and end of study	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Increase from Baseline in Select Hematology Parameters - Cohorts 1, 2, 3, 4, and 5

End point title	Number of Participants with Increase from Baseline in Select Hematology Parameters - Cohorts 1, 2, 3, 4, and 5 ^[15]
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End point description:

JCAR017 treatment-emergent laboratory abnormalities are defined as an abnormality that, compared to baseline, worsens by at least one grade after JCAR017 infusion. The baseline value is defined as the last available recorded value on or prior to the date of JCAR017 infusion.

End point type	Secondary
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End point timeframe:

At Baseline and Day 29 after JCAR017 infusion

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: Prespecified to be reported for Cohorts 1, 2, 3, 4, and 5 only.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	21	10	1
Units: Participants				
Leukocytes (10 ⁹ /L) - Day 29	4	2	1	0
Neutrophils, Segmented (10 ⁹ /L) - Day 29	11	6	3	0
Platelets (10 ⁹ /L) - Day 29	13	8	9	1
Activated Partial Thromboplastin Time (sec) Day 29	0	1	1	0
Prothrombin Intl. Normalized Ratio - Day 29	1	0	0	0

End point values	Cohort 5: Primary Central Nervous System Lymphoma			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
Leukocytes (10 ⁹ /L) - Day 29	1			
Neutrophils, Segmented (10 ⁹ /L) - Day 29	1			
Platelets (10 ⁹ /L) - Day 29	3			
Activated Partial Thromboplastin Time (sec) Day 29	1			
Prothrombin Intl. Normalized Ratio - Day 29	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Increase from Baseline in Select Serum Chemistry Parameters - Cohorts 1, 2, 3, 4, and 5

End point title	Number of Participants with Increase from Baseline in Select Serum Chemistry Parameters - Cohorts 1, 2, 3, 4, and 5 ^[16]
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End point description:

JCAR017 treatment-emergent laboratory abnormalities are defined as an abnormality that, compared to baseline, worsens by at least one grade after JCAR017 infusion. The baseline value is defined as the last available recorded value on or prior to the date of JCAR017 infusion.

End point type	Secondary
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End point timeframe:

At Baseline and Day 29 after JCAR017 infusion

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: Prespecified to be reported for Cohorts 1, 2, 3, 4, and 5 only.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	24	10	1
Units: Participants				
Albumin (g/L) - Day 29	0	0	0	0
Phosphate (mmol/L) - Day 29	0	1	0	0
Alkaline Phosphatase (U/L) - Day 29	2	1	0	0

Alanine Aminotransferase (U/L) - Day 29	10	3	1	0
Aspartate Aminotransferase (U/L) - Day 29	6	3	1	0
Bilirubin (umol/L) - Day 29	2	0	0	0
Creatinine (umol/L) - Day 29	23	20	6	1
Triglycerides (mmol/L) - Day 29	10	6	2	0
Urate (umol/L) - Day 29	1	0	0	0

End point values	Cohort 5: Primary Central Nervous System Lymphoma			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Participants				
Albumin (g/L) - Day 29	0			
Phosphate (mmol/L) - Day 29	0			
Alkaline Phosphatase (U/L) - Day 29	1			
Alanine Aminotransferase (U/L) - Day 29	2			
Aspartate Aminotransferase (U/L) - Day 29	3			
Bilirubin (umol/L) - Day 29	0			
Creatinine (umol/L) - Day 29	3			
Triglycerides (mmol/L) - Day 29	2			
Urate (umol/L) - Day 29	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) in Cohort 7

End point title	Overall Response Rate (ORR) in Cohort 7 ^[17]
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End point description:

ORR by Independent Review Committee. ORR is the percent of participants with best overall response of complete response (CR) or partial response (PR).

Complete response via PET-CT:

- Lymph nodes/extralympathic: Score 1, 2, 3a with/without residual mass on 5-point scale
- New lesions: No
- Bone marrow: No FDG-avid disease

Complete response via CT scan:

- Lymph nodes/extralympathic: Target nodes/nodal masses ≤ 1.5 cm longest transverse diameter.
- Nonmeasured lesion: None
- New lesions: No
- Bone marrow: Normal

Partial response via PET-CT:

- Lymph nodes/extralympathic: Score 4, 5b, reduced uptake from baseline
- New lesions: None
- Bone marrow: Residual uptake higher than normal, reduced from baseline

Partial response via CT scan:

- Lymph nodes/extralympathic: 50% decrease in sum of diameters of ≤ 6 target measurable nodes/extranodal sites

- Nonmeasured lesion: None/normal
- Organ enlargement: Spleen length decreased > 50%
- New lesions: No

End point type	Secondary
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End point timeframe:

From JCAR017 infusion until disease progression, end of study, the start of another anticancer therapy, or hemopoietic stem cell transplant (HSCT) (up to approximately 24 months)

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: Prespecified to be reported for Cohort 7 only.

End point values	Cohort 7: Outpatient Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percent of Participants				
number (confidence interval 95%)	88.9 (51.8 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)
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End point description:

Complete response rate is defined as percentage of participants achieving a best overall response of complete response.

Complete response via PET-CT:

- Lymph nodes/extralymphatic: Score 1, 2, 3a with/without residual mass on 5-point scale
- New lesions: No
- Bone marrow: No FDG-avid disease

Complete response via CT scan:

- Lymph nodes/extralymphatic: Target nodes/nodal masses ≤ 1.5 cm longest transverse diameter.
- Nonmeasured lesion: None
- New lesions: No
- Bone marrow: Normal

Complete response (CR) (Cohort 5):

- Brain imaging: No contrast enhancement
- Corticosteroid dose: None
- Eye examination: Normal

Cerebrospinal fluid cytology: Negative

Complete response unconfirmed (CRu) (Cohort 5):

- Brain imaging: No contrast enhancement, Minimal abnormality
- Corticosteroid dose: Any
- Eye examination: Normal, minor RPE abnormality
- Cerebrospinal fluid cytology: Negative

End point type	Secondary
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End point timeframe:

From JCAR017 infusion until disease progression, end of study, the start of another anticancer therapy, or hemopoietic stem cell transplant (HSCT) (up to approximately 24 months)

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Percent of Participants				
number (confidence interval 95%)	33.3 (18.6 to 51.0)	48.1 (28.7 to 68.1)	50.0 (18.7 to 81.3)	0 (0 to 0)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Percent of Participants				
number (confidence interval 95%)	0 (0 to 0)	88.9 (51.8 to 99.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Event Free Survival (EFS)

End point title	Event Free Survival (EFS)
End point description:	
Event-free survival is defined as the interval from the date of JCAR017 infusion to the earliest of the following events: death from any cause, progressive disease, or starting a new anticancer therapy. If a participant did not have an EFS event prior to data cutoff date, EFS was censored at the date of the last adequate disease assessment.	
Estimated using Kaplan-Meier product-limit estimates. "99999" = N/A	
End point type	Secondary
End point timeframe:	
From JCAR017 infusion to death due to any reason, progressive disease, or starting a new anticancer therapy (up to approximately 24 months).	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Months				
median (confidence interval 95%)	2.99 (2.60 to	3.12 (1.97 to	6.33 (0.56 to	23.95 (23.95

5.22)	7.36)	99999)	to 23.95)
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End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Months				
median (confidence interval 95%)	14.23 (0.76 to 24.02)	99999 (5.65 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) using European Medicines Agency (EMA) Criteria

End point title	Progression Free Survival (PFS) using European Medicines Agency (EMA) Criteria
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End point description:

Progression-free survival is defined as the interval from the date of JCAR017 infusion to progressive disease or death due to any cause, whichever occurred first. Participants who did not experience progressive disease and who did not die before the data cutoff date were censored at the time of the last visit with adequate response assessment when the participants were known not to have progressed. Estimated using Kaplan-Meier product-limit estimates. "99999" = N/A

End point type	Secondary
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End point timeframe:

From JCAR017 infusion to progressive disease or death due to any reason, whichever occurred first (up to approximately 24 months)

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Months				
median (confidence interval 95%)	2.99 (2.76 to 5.22)	3.12 (1.97 to 7.36)	6.33 (0.56 to 99999)	14.23 (0.76 to 24.02)

End point values	Cohort 5: Primary Central Nervous	Cohort 7: Outpatient Treatment		
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	System Lymphoma			
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Months				
median (confidence interval 95%)	23.95 (23.95 to 23.95)	99999 (5.65 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

Overall survival is defined as the interval from the date of JCAR017 infusion to the date of death due to any reason. Data from surviving participants was censored at the last time that the participant was known to be alive.

Estimated using Kaplan-Meier product-limit estimates. "99999" = N/A

End point type	Secondary
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End point timeframe:

From the date of JCAR017 infusion to the date of death due to any reason (up to approximately 24 months).

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	27	10	1
Units: Months				
arithmetic mean (confidence interval 95%)	15.84 (5.82 to 23.95)	16.82 (4.27 to 99999)	14.72 (1.71 to 99999)	31.74 (31.74 to 31.74)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Months				
arithmetic mean (confidence interval 95%)	14.23 (4.30 to 99999)	99999 (11.60 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
End point description:	
DoR is the time from first response to progressive disease or death due to any reason. Estimated using Kaplan-Meier estimates. Those without progressive disease/did not die were censored at last response assessment visit.	
Complete response - PET-CT:	
<ul style="list-style-type: none">• Lymph nodes/extralymphatic: Score 1/2/3a w/w-out residual mass on 5-point scale• New lesions: No• Bone marrow: No FDG-avid disease	
Complete response - CT scan:	
<ul style="list-style-type: none">• Lymph nodes/extralymphatic: Target nodes/nodal masses ≤ 1.5 cm longest transverse diameter.• Nonmeasured lesion: No• New lesions: No• Bone marrow: Normal	
Partial response - PET-CT:	
<ul style="list-style-type: none">• Lymph nodes/extralymphatic: Score 4/5b, reduced uptake from baseline• New lesions: No• Bone marrow: Residual uptake higher than normal, reduced from baseline	
Partial response - CT scan:	
<ul style="list-style-type: none">• Lymph nodes/extralymphatic: 50% decrease in sum of diameters of ≤ 6 target measurable nodes/extranodal• Nonmeasured lesion: No• Organ enlargement: Spleen decreased $> 50\%$• New lesions: No	
"99999" = N/A	
End point type	Secondary
End point timeframe:	
From JCAR017 infusion until disease progression, death due to any reason, end of study, the start of another anticancer therapy, or hemopoietic stem cell transplant (HSCT) (up to approximately 24 months)	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	20	7	1
Units: Months				
median (confidence interval 95%)	3.83 (2.07 to 17.05)	3.91 (1.87 to 99999)	9.07 (2.04 to 99999)	17.97 (17.97 to 17.97)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	8		
Units: Months				
median (confidence interval 95%)	17.63 (2.46 to 23.10)	99999 (2.69 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of JCAR017 by qPCR

End point title	Maximum Concentration (Cmax) of JCAR017 by qPCR
End point description:	
Cmax is the maximum or peak concentration of drug reached in the plasma following a dose of the drug. Quantitative polymerase chain reaction (qPCR) was used to determine Cmax by detecting the JCAR017 transgene. "99999" = N/A	
Baseline is defined as the last available recorded value on or prior to the date of JCAR017 infusion.	
End point type	Secondary
End point timeframe:	
At baseline and up until 24 months post JCAR017 infusion	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	22	10	1
Units: Copies/ug				
geometric mean (geometric coefficient of variation)	23132.1 (± 434.6)	21960.0 (± 278.1)	17337.8 (± 894.4)	51121.0 (± 99999)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Copies/ug				
geometric mean (geometric coefficient of variation)	7661.6 (± 1730.0)	32027.1 (± 101.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Peak Concentration (Tmax) of JCAR017 by qPCR

End point title	Time to Peak Concentration (Tmax) of JCAR017 by qPCR
End point description: Time to maximum concentration (Tmax) is the time it takes for a drug to reach the maximum concentration (Cmax) after administration. Quantitative polymerase chain reaction (qPCR) was used to determine Tmax by detecting the JCAR017 transgene. Baseline is defined as the last available recorded value on or prior to the date of JCAR017 infusion.	
End point type	Secondary
End point timeframe: At baseline and up until 24 months post JCAR017 infusion	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	22	10	1
Units: Days				
median (full range (min-max))	11.6 (3.0 to 28.0)	9.0 (7.0 to 14.0)	84.1 (7.0 to 733.0)	10.0 (10.0 to 10.0)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Days				
median (full range (min-max))	9.0 (7.0 to 14.0)	12.2 (10.0 to 21.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Exposure to JCAR017 as Measured by Area Under the Curve (AUC) of JCAR017 by qPCR

End point title	Total Exposure to JCAR017 as Measured by Area Under the Curve (AUC) of JCAR017 by qPCR
End point description: Area Under the Curve (AUC) represents the total exposure of participants to study drug. Quantitative polymerase chain reaction (qPCR) was used to determine AUC by detecting the JCAR017 transgene. "99999" = N/A Baseline is defined as the last available recorded value on or prior to the date of JCAR017 infusion.	
End point type	Secondary
End point timeframe: At baseline and up until 24 months post JCAR017 infusion	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	22	10	1
Units: Days*copies/ug				
geometric mean (geometric coefficient of variation)	185586.667 (\pm 325.6)	157499.362 (\pm 211.9)	134819.085 (\pm 1268.9)	286119.439 (\pm 99999)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Days*copies/ug				
geometric mean (geometric coefficient of variation)	64945.715 (\pm 1345.7)	199731.737 (\pm 136.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants with Presence of JCAR017 Transgene in Peripheral Blood by qPCR

End point title	Percent of Participants with Presence of JCAR017 Transgene in Peripheral Blood by qPCR
End point description: Persistence is defined as a transgene count greater than or equal to the lower limit of detection (LLOD) of 5 copies per reaction. Data obtained after the start of a new anti-cancer therapy were excluded. qPCR	

= Quantitative polymerase chain reaction

End point type	Secondary
End point timeframe:	
At Day 29 and Months 2, 3, 6, 9, 12, 18, and 24 post JCAR017 infusion.	

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	21	10	1
Units: Percent of Participants				
number (not applicable)				
Day 29	88.2	95.2	100.0	100.0
Month 2	70.0	66.7	100.0	100.0
Month 3	61.5	50.0	100.0	100.0
Month 6	33.3	45.5	71.4	0.0
Month 9	41.7	40.0	60.0	0.0
Month 12	40.0	57.1	100.0	0.0
Month 18	25.0	57.1	75.0	0.0
Month 24	28.6	50.0	100.0	0.0

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Percent of Participants				
number (not applicable)				
Day 29	80.0	100.0		
Month 2	100.0	62.5		
Month 3	100.0	37.5		
Month 6	100.0	16.7		
Month 9	100.0	25.0		
Month 12	66.7	0.0		
Month 18	100.0	20.0		
Month 24	100.0	20.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European Organisation for Research and Treatment of Cancer – Quality of Life C30 questionnaire (EORTC QLQ-C30) Scores

End point title	Change from Baseline in European Organisation for Research and Treatment of Cancer – Quality of Life C30 questionnaire (EORTC QLQ-C30) Scores
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End point description:

The EORTC QLQ-C30 consists of five functional scales (physical, role, emotional, cognitive, social), three symptom scales (fatigue, nausea/vomiting, pain), a global health status/health-related quality of life (HRQoL) scale, and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties). The questionnaire is scored on a 4-point Likert scale: 1 = not at all, 2 = a little, 3 = quite a bit, 4 = very much. The raw score is the average of the items contributing to the scale. The final scores are calculated via linear transformation of raw scores and range from 0 to 100. For functional scales higher scores indicate better QoL. For symptom scales and single items lower scores indicate fewer symptoms, i.e. better QoL. Baseline the last available recorded scores on or prior to the date of JCAR017 infusion. Only global health, fatigue, physical and cognitive functioning subscales were assessed. "99999" = N/A

End point type	Secondary
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End point timeframe:

At baseline and Day 1, 29, 60, 90, 180, 270, 365, 545, and 730 post JCAR017 infusion.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	23	10	1
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Global Health Status: Change from baseline Day 1	-4.41 (± 17.070)	-5.07 (± 17.898)	-6.67 (± 10.244)	-8.33 (± 99999)
Global Health Status: Change from baseline Day 29	-1.26 (± 14.301)	0.00 (± 18.002)	-4.17 (± 17.236)	0.00 (± 99999)
Global Health Status: Change from baseline Day 60	5.00 (± 14.778)	7.84 (± 17.547)	4.17 (± 16.457)	0.00 (± 99999)
Global Health Status: Change from baseline Day 90	2.47 (± 14.766)	1.28 (± 22.527)	-5.95 (± 17.817)	0.00 (± 99999)
Global Health Status: Change from baseline Day 180	6.94 (± 13.685)	1.04 (± 23.332)	-13.10 (± 35.635)	-16.67 (± 99999)
Global Health Status: Change from baseline Day 270	6.25 (± 20.140)	9.72 (± 9.742)	-3.33 (± 26.745)	0.00 (± 99999)
Global Health Status: Change from baseline Day 365	-6.67 (± 20.337)	3.57 (± 11.664)	-12.50 (± 25.909)	0.00 (± 99999)
Global Health Status: Change from baseline Day 545	-6.48 (± 18.530)	3.57 (± 26.726)	-5.56 (± 24.056)	0.00 (± 99999)
Global Health Status: Change from baseline Day 730	-11.11 (± 12.975)	-4.17 (± 12.638)	-6.25 (± 7.979)	0.00 (± 99999)
Physical Functioning: Change from baseline Day 1	-3.33 (± 20.970)	-6.09 (± 21.074)	-3.33 (± 11.440)	-6.67 (± 99999)
Physical Functioning: Change from baseline Day 29	-2.63 (± 18.555)	-4.21 (± 10.706)	-10.00 (± 14.824)	6.67 (± 99999)
Physical Functioning: Change from baseline Day 60	3.11 (± 15.135)	-0.39 (± 21.275)	-4.44 (± 15.587)	0.00 (± 99999)
Physical Functioning: Change from baseline Day 90	3.46 (± 16.781)	3.59 (± 12.054)	-5.71 (± 11.174)	6.67 (± 99999)
Physical Functioning: Change from baseline Day 180	7.78 (± 12.975)	-8.33 (± 31.219)	-5.71 (± 19.024)	-6.67 (± 99999)

Physical Functioning: Change from baseline Day 270	3.33 (± 10.050)	1.11 (± 19.052)	-2.67 (± 22.410)	6.67 (± 99999)
Physical Functioning: Change from baseline Day 365	0.67 (± 16.163)	0.95 (± 16.069)	-16.67 (± 20.000)	6.67 (± 99999)
Physical Functioning: Change from baseline Day 545	-3.70 (± 26.690)	-1.90 (± 19.135)	-13.33 (± 23.094)	6.67 (± 99999)
Physical Functioning: Change from baseline Day 730	1.11 (± 15.785)	-8.89 (± 28.493)	-3.33 (± 8.607)	6.67 (± 99999)
Cognitive Functioning: Change from baseline Day 1	-3.43 (± 17.301)	-3.62 (± 17.376)	-1.67 (± 9.461)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 29	-2.53 (± 16.203)	3.51 (± 14.250)	3.33 (± 13.147)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 60	2.78 (± 12.444)	0.98 (± 10.978)	0.00 (± 27.889)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 90	0.00 (± 13.074)	-1.28 (± 12.659)	4.76 (± 20.893)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 180	-2.78 (± 15.624)	-2.08 (± 5.893)	11.90 (± 20.893)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 270	0.00 (± 22.473)	0.00 (± 0.000)	3.33 (± 13.944)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 365	-11.67 (± 22.292)	0.00 (± 0.000)	-4.17 (± 8.333)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 545	-7.41 (± 18.840)	2.38 (± 11.501)	-5.56 (± 19.245)	0.00 (± 99999)
Cognitive Functioning: Change from baseline Day 730	-1.39 (± 18.060)	-5.56 (± 8.607)	-4.17 (± 15.957)	0.00 (± 99999)
Fatigue: Change from baseline Day 1	1.63 (± 26.959)	1.45 (± 16.173)	3.33 (± 20.320)	0.00 (± 99999)
Fatigue: Change from baseline Day 29	3.03 (± 24.418)	2.34 (± 12.046)	5.56 (± 17.568)	-11.11 (± 99999)
Fatigue: Change from baseline Day 60	-9.63 (± 18.623)	-1.31 (± 20.743)	3.70 (± 31.946)	11.11 (± 99999)
Fatigue: Change from baseline Day 90	-4.53 (± 19.795)	-4.27 (± 17.881)	4.76 (± 35.635)	-11.11 (± 99999)
Fatigue: Change from baseline Day 180	-8.33 (± 21.254)	2.78 (± 34.503)	-4.76 (± 38.946)	22.22 (± 99999)
Fatigue: Change from baseline Day 270	-9.26 (± 15.594)	0.00 (± 22.222)	-6.67 (± 14.907)	-11.11 (± 99999)
Fatigue: Change from baseline Day 365	-3.33 (± 14.861)	-4.76 (± 20.141)	13.89 (± 33.179)	-11.11 (± 99999)
Fatigue: Change from baseline Day 545	4.94 (± 25.526)	-1.59 (± 19.698)	-3.70 (± 27.962)	-11.11 (± 99999)
Fatigue: Change from baseline Day 730	0.93 (± 22.947)	3.70 (± 9.072)	5.56 (± 14.344)	-11.11 (± 99999)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Global Health Status: Change from baseline Day 1	8.33 (± 25.685)	-7.41 (± 12.108)		
Global Health Status: Change from baseline Day 29	16.67 (± 11.785)	-1.85 (± 14.299)		

Global Health Status: Change from baseline Day 60	13.89 (± 26.788)	9.26 (± 8.784)		
Global Health Status: Change from baseline Day 90	22.22 (± 41.107)	4.63 (± 8.448)		
Global Health Status: Change from baseline Day 180	25.00 (± 22.048)	2.78 (± 8.607)		
Global Health Status: Change from baseline Day 270	25.00 (± 22.048)	3.33 (± 9.501)		
Global Health Status: Change from baseline Day 365	30.56 (± 26.788)	3.33 (± 7.454)		
Global Health Status: Change from baseline Day 545	0.00 (± 47.140)	1.67 (± 9.129)		
Global Health Status: Change from baseline Day 730	20.83 (± 29.463)	-2.08 (± 21.916)		
Physical Functioning: Change from baseline Day 1	-2.67 (± 19.777)	-3.70 (± 14.948)		
Physical Functioning: Change from baseline Day 29	-8.33 (± 16.667)	-8.15 (± 18.493)		
Physical Functioning: Change from baseline Day 60	-2.22 (± 10.184)	-2.96 (± 10.062)		
Physical Functioning: Change from baseline Day 90	11.11 (± 23.413)	-0.74 (± 18.692)		
Physical Functioning: Change from baseline Day 180	15.56 (± 27.756)	-2.22 (± 24.825)		
Physical Functioning: Change from baseline Day 270	24.44 (± 27.756)	-6.67 (± 31.972)		
Physical Functioning: Change from baseline Day 365	22.22 (± 26.943)	5.33 (± 11.926)		
Physical Functioning: Change from baseline Day 545	13.33 (± 47.140)	9.33 (± 11.155)		
Physical Functioning: Change from baseline Day 730	3.33 (± 42.426)	-3.33 (± 11.547)		
Cognitive Functioning: Change from baseline Day 1	-3.33 (± 13.944)	-1.85 (± 10.015)		
Cognitive Functioning: Change from baseline Day 29	8.33 (± 21.517)	-7.41 (± 12.108)		
Cognitive Functioning: Change from baseline Day 60	33.33 (± 44.096)	-1.85 (± 13.029)		
Cognitive Functioning: Change from baseline Day 90	11.11 (± 19.245)	0.00 (± 8.333)		
Cognitive Functioning: Change from baseline Day 180	16.67 (± 28.868)	-5.56 (± 8.607)		
Cognitive Functioning: Change from baseline Day 270	33.33 (± 44.096)	3.33 (± 7.454)		
Cognitive Functioning: Change from baseline Day 365	22.22 (± 38.490)	6.67 (± 9.129)		
Cognitive Functioning: Change from baseline Day 545	-41.67 (± 82.496)	3.33 (± 7.454)		
Cognitive Functioning: Change from baseline Day 730	-16.67 (± 23.570)	-4.17 (± 8.333)		
Fatigue: Change from baseline Day 1	-20.00 (± 30.832)	1.23 (± 18.794)		
Fatigue: Change from baseline Day 29	-13.89 (± 27.778)	6.17 (± 14.815)		
Fatigue: Change from baseline Day 60	-14.81 (± 35.717)	0.00 (± 17.568)		
Fatigue: Change from baseline Day 90	-37.04 (± 12.830)	-3.70 (± 22.906)		
Fatigue: Change from baseline Day 180	-37.04 (± 23.130)	0.00 (± 33.702)		
Fatigue: Change from baseline Day 270	-29.63 (± 42.066)	-2.22 (± 34.605)		

Fatigue: Change from baseline Day 365	-44.44 (± 22.222)	-13.33 (± 14.487)		
Fatigue: Change from baseline Day 545	-5.56 (± 23.570)	-11.11 (± 15.713)		
Fatigue: Change from baseline Day 730	-16.67 (± 7.857)	-8.33 (± 16.667)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Cancer Treatment-Lymphoma "Additional Concerns" Subscale (FACT-LymS) Scores

End point title	Change from Baseline in Functional Assessment of Cancer Treatment-Lymphoma "Additional Concerns" Subscale (FACT-LymS) Scores
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End point description:

The Functional Assessment of Cancer Treatment-Lymphoma "Additional concerns" subscale (FACT-LymS) consists of the FACT-General scale and a 15-item lymphoma-specific additional concerns subscale (LYM). This scale addresses symptoms and functional limitations that are important to lymphoma patients. Only the LYM subscale was administered in this study. The LYM items are scored on a 0 ("Not at all") to 4 ("Very much") response scale. Items are aggregated to a single score on a 0-60 scale. Lower scores indicate better health outcomes. Baseline the last available recorded scores on or prior to the date of JCAR017 infusion. "99999" = N/A

End point type	Secondary
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End point timeframe:

At baseline and Day 1, 29, 60, 90, 180, 270, 365, 545, and 730 post JCAR017 infusion.

End point values	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 3: Japan Specific	Cohort 4: Newly Diagnosed High-Grade B- cell Lymphoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	23	10	1
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Change from baseline Day 1	0.7 (± 8.17)	0.1 (± 7.05)	1.9 (± 5.92)	1.0 (± 99999)
Change from baseline Day 29	-1.7 (± 7.14)	-2.7 (± 4.56)	1.3 (± 7.24)	-4.0 (± 99999)
Change from baseline Day 60	-2.8 (± 5.42)	-2.0 (± 4.20)	-3.3 (± 9.99)	-4.0 (± 99999)
Change from baseline Day 90	-0.4 (± 5.42)	-2.8 (± 3.83)	0.6 (± 9.25)	-5.0 (± 99999)
Change from baseline Day 180	0.6 (± 5.14)	-1.8 (± 5.65)	-3.6 (± 10.20)	2.0 (± 99999)
Change from baseline Day 270	-0.3 (± 6.78)	-3.7 (± 2.25)	-1.0 (± 10.07)	-8.0 (± 99999)
Change from baseline Day 365	1.3 (± 7.01)	-3.3 (± 3.30)	2.0 (± 12.03)	-6.0 (± 99999)
Change from baseline Day 545	0.7 (± 7.14)	-3.7 (± 4.35)	-4.7 (± 4.16)	-3.0 (± 99999)
Change from baseline Day 730	1.4 (± 7.12)	-0.8 (± 1.33)	-1.8 (± 5.32)	-2.0 (± 99999)

End point values	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 7: Outpatient Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Change from baseline Day 1	-4.0 (± 6.52)	-1.2 (± 11.08)		
Change from baseline Day 29	-6.5 (± 8.10)	1.0 (± 9.08)		
Change from baseline Day 60	-4.7 (± 8.33)	-0.4 (± 9.95)		
Change from baseline Day 90	-6.7 (± 8.50)	-1.7 (± 8.67)		
Change from baseline Day 180	-8.0 (± 7.00)	1.0 (± 7.27)		
Change from baseline Day 270	-10.00 (± 12.53)	2.4 (± 5.22)		
Change from baseline Day 365	-6.7 (± 10.69)	1.4 (± 7.33)		
Change from baseline Day 545	3.5 (± 6.36)	-1.0 (± 4.85)		
Change from baseline Day 730	-1.5 (± 12.02)	-1.5 (± 1.29)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for All-Cause Mortality, Serious Adverse Events and Other (Not Including Serious) Adverse Events from the date of leukapheresis until study completion (assessed up to approximately 25 months).

Adverse event reporting additional description:

All-Cause Mortality, Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that underwent leukapheresis and may or may not have received at least 1 dose of JCAR017.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Reporting group title	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Reporting group title	Cohort 7: Outpatient Treatment
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Reporting group title	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Reporting group title	Cohort 5: Primary Central Nervous System Lymphoma
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Reporting group title	Cohort 3: Japan Specific
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Reporting group description:

JCAR017 was infused at a dose of 100×10^6 JCAR017-positive transduced viable T cells (50×10^6 CD8+ CAR+ T cells and 50×10^6 CD4+ CAR+ T cells), on Day 1 (2 to 7 days after completion of Lymphodepleting chemotherapy).

Serious adverse events	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 7: Outpatient Treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 45 (42.22%)	8 / 32 (25.00%)	1 / 11 (9.09%)

number of deaths (all causes)	32	22	4
number of deaths resulting from adverse events	2	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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			
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	7 / 45 (15.56%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	7 / 7	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	2 / 45 (4.44%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			

subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Respiratory failure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Bradyphrenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Confusional state			
subjects affected / exposed	5 / 45 (11.11%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	5 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Cardiac disorders			

Cardiac failure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Aphasia			
subjects affected / exposed	4 / 45 (8.89%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	4 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amnesia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Depressed level of consciousness			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Dysarthria			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Dyskinesia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Somnolence			
subjects affected / exposed	2 / 45 (4.44%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Memory impairment			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Stupor			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Tremor			
subjects affected / exposed	5 / 45 (11.11%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	5 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	4 / 45 (8.89%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Neutropenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Thrombocytopenia			

subjects affected / exposed	1 / 45 (2.22%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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			
Abdominal pain			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Constipation			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Gastric haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (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
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (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
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	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	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Back pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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			
Conjunctivitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Clostridium colitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Candida sepsis			

subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (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
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Device related sepsis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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
Cytomegalovirus infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Septic shock			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (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
Staphylococcal sepsis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 32 (0.00%)	0 / 11 (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

Serious adverse events	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 3: Japan Specific
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	2 / 14 (14.29%)
number of deaths (all causes)	0	5	9
number of deaths resulting from adverse events	0	0	1

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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			
Capillary leak syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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			
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Bradyphrenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Delirium			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Disorientation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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

Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Amnesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Dysarthria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Dyskinesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (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
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Memory impairment			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Stupor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Eye disorders			

Ulcerative keratitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Gastric haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Melaena			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (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
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Clostridium colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Candida sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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

Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Device related sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Cytomegalovirus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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
Staphylococcal sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (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

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

Non-serious adverse events	Cohort 1: Diffuse B-cell Lymphoma Failed ≥ 2 Lines of Therapy	Cohort 2: Transplant Ineligible Diffuse B-cell Lymphoma	Cohort 7: Outpatient Treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 45 (88.89%)	25 / 32 (78.13%)	9 / 11 (81.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Peritumoural oedema subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Skin papilloma subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	1 / 11 (9.09%) 1
Tumour flare subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 32 (3.13%) 1	1 / 11 (9.09%) 1
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	3 / 32 (9.38%) 3	0 / 11 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	1 / 32 (3.13%) 1	1 / 11 (9.09%) 1
Asthenia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	2 / 32 (6.25%) 2	1 / 11 (9.09%) 2
Catheter site related reaction subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	20 / 45 (44.44%) 21	10 / 32 (31.25%) 11	1 / 11 (9.09%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	5 / 32 (15.63%) 5	0 / 11 (0.00%) 0
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	12 / 45 (26.67%) 12	12 / 32 (37.50%) 12	0 / 11 (0.00%) 0
Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 6	3 / 32 (9.38%) 3	0 / 11 (0.00%) 0

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 45 (8.89%)	0 / 32 (0.00%)	3 / 11 (27.27%)
occurrences (all)	6	0	3
Hypoxia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	2 / 32 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 45 (0.00%)	1 / 32 (3.13%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 45 (0.00%)	2 / 32 (6.25%)	0 / 11 (0.00%)
occurrences (all)	0	4	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 32 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Allergic transfusion reaction			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Nervous system disorders			
Seizure			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Post herpetic neuralgia			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Hemiparesis			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Headache			
subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 8	4 / 32 (12.50%) 4	0 / 11 (0.00%) 0
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Anaemia			
subjects affected / exposed occurrences (all)	21 / 45 (46.67%) 35	8 / 32 (25.00%) 15	2 / 11 (18.18%) 2
Leukopenia			
subjects affected / exposed occurrences (all)	9 / 45 (20.00%) 12	5 / 32 (15.63%) 8	2 / 11 (18.18%) 6
Lymphopenia			
subjects affected / exposed occurrences (all)	9 / 45 (20.00%) 12	4 / 32 (12.50%) 8	0 / 11 (0.00%) 0
Hypofibrinogenaemia			
subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Febrile neutropenia			
subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 6	1 / 32 (3.13%) 1	0 / 11 (0.00%) 0
Eosinophilia			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	35 / 45 (77.78%) 54	22 / 32 (68.75%) 40	9 / 11 (81.82%) 14
Thrombocytopenia subjects affected / exposed occurrences (all)	16 / 45 (35.56%) 20	11 / 32 (34.38%) 16	3 / 11 (27.27%) 3
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Eye disorders Keratopathy subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 6	2 / 32 (6.25%) 2	0 / 11 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 7	2 / 32 (6.25%) 2	0 / 11 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 7	3 / 32 (9.38%) 3	1 / 11 (9.09%) 1
Diarrhoea subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 8	3 / 32 (9.38%) 3	2 / 11 (18.18%) 2
Vomiting subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 5	2 / 32 (6.25%) 2	0 / 11 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Dermatitis acneiform			

subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	1 / 32 (3.13%) 1	0 / 11 (0.00%) 0
Renal and urinary disorders Micturition disorder subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 32 (3.13%) 1	1 / 11 (9.09%) 1
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	0 / 32 (0.00%) 0	1 / 11 (9.09%) 1
Bone pain subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4	0 / 32 (0.00%) 0	1 / 11 (9.09%) 1
Neck pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	2 / 32 (6.25%) 2	0 / 11 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Infections and infestations Varicella zoster virus infection subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4	0 / 32 (0.00%) 0	0 / 11 (0.00%) 0
Escherichia urinary tract infection subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	3 / 32 (9.38%) 3	0 / 11 (0.00%) 0
COVID-19			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 32 (0.00%) 0	1 / 11 (9.09%) 1
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	6 / 45 (13.33%)	1 / 32 (3.13%)	1 / 11 (9.09%)
occurrences (all)	7	1	1
Hypokalaemia			
subjects affected / exposed	6 / 45 (13.33%)	3 / 32 (9.38%)	1 / 11 (9.09%)
occurrences (all)	6	9	1
Decreased appetite			
subjects affected / exposed	2 / 45 (4.44%)	1 / 32 (3.13%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Hypophosphataemia			
subjects affected / exposed	3 / 45 (6.67%)	3 / 32 (9.38%)	0 / 11 (0.00%)
occurrences (all)	4	4	0

Non-serious adverse events	Cohort 4: Newly Diagnosed High-Grade B-cell Lymphoma	Cohort 5: Primary Central Nervous System Lymphoma	Cohort 3: Japan Specific
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	5 / 7 (71.43%)	12 / 14 (85.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoural oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin papilloma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tumour flare			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	4 / 14 (28.57%)
occurrences (all)	0	0	4
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	6 / 14 (42.86%)
occurrences (all)	0	3	7
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	4 / 14 (28.57%)
occurrences (all)	0	0	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Delirium subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 2
Confusional state subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 7 (28.57%) 2	0 / 14 (0.00%) 0
Blood fibrinogen decreased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Injury, poisoning and procedural complications Post procedural haemorrhage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Allergic transfusion reaction subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	2 / 14 (14.29%) 2
Nervous system disorders Seizure subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	0 / 14 (0.00%) 0
Post herpetic neuralgia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Hemiparesis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	0 / 14 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	0 / 14 (0.00%) 0

Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 7 (42.86%)	10 / 14 (71.43%)
occurrences (all)	0	8	10
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	11 / 14 (78.57%)
occurrences (all)	0	0	34
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypofibrinogenaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	4 / 14 (28.57%)
occurrences (all)	0	0	5
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	5 / 7 (71.43%)	11 / 14 (78.57%)
occurrences (all)	3	7	37
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	3 / 7 (42.86%)	11 / 14 (78.57%)
occurrences (all)	1	7	12
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Keratopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Nausea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	2 / 14 (14.29%) 2
Vomiting subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	2 / 14 (14.29%) 4
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Pruritus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Renal and urinary disorders			
Micturition disorder subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0

Neck pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	0 / 14 (0.00%) 0
Infections and infestations			
Varicella zoster virus infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	0 / 14 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Escherichia urinary tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0
Metabolism and nutrition disorders			
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 7 (14.29%) 1	1 / 14 (7.14%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Decreased appetite subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	1 / 14 (7.14%) 1
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 7 (0.00%) 0	0 / 14 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2018	Restricted transformed indolent B-NHL to transformed follicular lymphoma - Revised definition of TNE subjects - Revised eligibility criteria for Cohort 3 (Japan only), Cohort 5(PCNSL), Cohort 6 (Richter's transformation) - Added safety run-in for Cohort 3 - Revised inclusion criterion for subjects with secondary DLBCL CNS involvement
28 December 2018	An ad hoc DSMB meeting (14-Dec-2018) held after a Grade 5 respiratory failure on 10-Dec-2018. Implemented an urgent safety measure following trial pause with revision of I/E criteria; enrollment restricted to subjects with ECOG PS 0 to 1(except TNE subjects) and excluded subjects with vascular tumor invasion, DVT or PE within 3 mos, or requiring therapeutic levels of anticoagulation. - Added requirement for subjects to be clinically stable prior to liso-cel infusion, including absence of active infection, supplemental oxygen, uncontrolled cardiac arrhythmias, and vasopressor support - Clarified the selection of subjects with primary or secondary CNS involvement
21 November 2019	Cohort 4 (HGBCL) clarified to allow for consolidation with liso-cel after 1L therapy; Cohort 5 modified to 2L population; Cohort 6 removed; Cohort 7 added - Updated criteria for pausing/stopping the study, patient interviews, inclusion criteria, and pregnancy risk - Removed exclusion criteria of DVT/PE/ anticoagulation; added statements on stable disease/ anticoagulation - Added 2 exclusion criteria per HA requirements: - Excluded subjects with known severe hypersensitivity to DMSO or dextran - Excluded systemic immunostimulatory agents (including but not limited to IFN and IL-2) ≤ 6 wks or 5 half-lives of the drug, whichever was shorter, prior to liso-cel infusion. - Updated planned sample size from 124 to 116 - Added new conditions to be reported as SAEs
16 November 2020	Modified Cohort 2 sample size from ≥ 28 to ≤ 28 subjects - Revised Cohort 2 primary analysis to be descriptive without formal hypothesis testing. Analysis triggered when last subject treated with liso-cel was followed for at ≥ 1 post-baseline efficacy assessment instead of 6 months - Pooled analysis from Cohort 2 and Study 017006 (PILOT) to be reported outside of the BCM-001 CSR - Aligned screening, baseline, and post-baseline evaluations for Cohort 5 with standardized evaluations for PCNSL - Added inclusion criterion #8 back for subjects with NHL: "For subjects with NHL (except Cohort 5): Subjects must have PET-positive disease as per Lugano Classification
12 August 2021	Cohort 2 sample size was modified from a maximum of 28 to approximately 28 subjects. Specified that Cohort 2 will have formal hypothesis testing at the time of the primary analysis. Cohort 5 inclusion criteria were amended to allow for enrollment of subjects who failed to proceed to HDCT and ASCT following induction therapy. Timing of cohort 7 analysis was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported