Clinical trial results:
A Phase 1b/2a Pilot Randomized Study to Evaluate the Safety and Tolerability of Autologous T-Cells Expressing Enhanced TCRs (T-Cell Receptors) Specific for NY-ESO-1/LAGE-1a (GSK3377794) Alone, or in Combination with Pembrolizumab in HLA-A2+ Participants with NY-ESO-1- or LAGE-1a-Positive Advanced or Recurrent Non-Small Cell Lung Cancer

Summary

EudraCT number	2018-003949-42
Trial protocol	GB NL ES
Global end of trial date	04 November 2022

Results information

Result version number	v1 (current)
This version publication date	08 July 2023
First version publication date	08 July 2023

Trial information

Trial identification

Sponsor protocol code	208471

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03709706
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	24 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of autologous genetically modified T-cells (GSK3377794) in human leukocyte antigen (HLA) HLA-A*02:01, HLA-A*02:05 and/or HLA-A*02:06 positive participants with NY-ESO-1 and/or LAGE-1a positive advanced NSCLC alone [Arm A] or GSK3377794 in combination with pembrolizumab in participants with NSCLC with patients lacking or patients with actionable genetic aberrations.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 December 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	15 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	34
EEA total number of subjects	13

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)	20
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Open-label study that evaluated the safety and tolerability of autologous T-cells expressing enhanced T-cell receptors (TCRs) that were specific for New York esophageal squamous cell carcinoma (NY-ESO)-1 and/or Cancer testis antigen 2 (LAGE-1a) (GSK3377794, Lete-cel) in participants with Advanced or Recurrent Non-Small Cell Lung Cancer.

Pre-assignment

Screening details:

34 participants with Advanced/Recurrent NSCLS with Human Leukocyte Antigen (HLA)-A02:01, HLA-A02:05,and/or HLA-A*02:06 were enrolled, out of which 13 received Lete-cel infusion. The study was terminated due to reasons pertaining to feasibility. As a result of early termination, no participants were assigned to Arm B, thus no analysis was performed

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Lete-cel monotherapy

Arm description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T- cell receptors (TCR) specific for NY-ESO-1/LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel. Participants who had disease progression within 25 weeks of Lete-cel infusion were offered therapy with Pembrolizumab following benefit-risk evaluation. Pembrolizumab 200 mg was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until subsequent disease progression or intolerable toxicity. Pembrolizumab therapy was not allowed if disease progression occurred post 25 weeks of Lete-cel infusion.

Arm type	Experimental
Investigational medicinal product name	Lete-cel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T- cell receptors (TCR) specific for NY-ESO-1/LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel. Participants who had disease progression within 25 weeks of Lete-cel infusion were offered therapy with Pembrolizumab following benefit-risk evaluation. Pembrolizumab 200 mg was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until subsequent disease progression or intolerable toxicity. Pembrolizumab therapy was not allowed if disease progression occurred post 25 weeks of Lete-cel infusion.

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors

(TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Arm title	Arm C: Lete-cel + pembrolizumab

Arm description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Lete-cel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Number of subjects in period 1	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab
Started	20	14
Intent-to-Treat (ITT) Population	20	14
Modified - Intent to Treat Population	7	6
No Treatment	13	8
Completed	3	3
Not completed	17	11
Physician decision	14	8
Consent withdrawn by subject	2	1
Adverse event, non-fatal	-	1
Death Prior to Lete-Cel Infusion	1	1

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Lete-cel monotherapy

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T- cell receptors (TCR) specific for NY-ESO-1/LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel. Participants who had disease progression within 25 weeks of Lete-cel infusion were offered therapy with Pembrolizumab following benefit-risk evaluation. Pembrolizumab 200 mg was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until subsequent disease progression or intolerable toxicity. Pembrolizumab therapy was not allowed if disease progression occurred post 25 weeks of Lete-cel infusion.

Reporting group title	Arm C: Lete-cel + pembrolizumab

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Reporting group values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab	Total
Number of subjects	20	14	34
Age categorical Units: Subjects			
19-64 years	11	9	20
>=65 years	9	5	14
Age continuous Units: years			
arithmetic mean	62.1	59.4	
standard deviation	± 8.90	± 10.25	-
Sex: Female, Male Units: Participants			
Female	8	9	17
Male	12	5	17
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	1
White	19	12	31
Unknown or Not Reported	1	1	2

End points

End points reporting groups

Reporting group title	Arm A: Lete-cel monotherapy

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T- cell receptors (TCR) specific for NY-ESO-1/LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel. Participants who had disease progression within 25 weeks of Lete-cel infusion were offered therapy with Pembrolizumab following benefit-risk evaluation. Pembrolizumab 200 mg was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until subsequent disease progression or intolerable toxicity. Pembrolizumab therapy was not allowed if disease progression occurred post 25 weeks of Lete-cel infusion.

Reporting group title	Arm C: Lete-cel + pembrolizumab

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Primary: Number of participants with treatment-emergent adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with treatment-emergent adverse events (AEs) and serious adverse events (SAEs)[1]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, other situations which involve medical or scientific judgment or is associated with liver injury and impaired liver function. AEs which start or worsen on or after T-cell infusion are defined as treatment-emergent. Modified Intent-to-Treat (mITT) population included all participants who received Lete-cel infusion.

End point type	Primary

End point timeframe:

Up to approximately 10 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: The primary endpoint of the study was planned to analyses with only descriptive statistics. Hence, no statistical analysis were performed.

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Participants				
AEs	7	6		
SAEs	5	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with treatment-emergent adverse events of Special Interest (AESI)

End point title	Number of participants with treatment-emergent adverse events of Special Interest (AESI)[2]

End point description:

AESI included cytokine release syndrome (CRS), pneumonitis/pneumonia, graft vs host disease (GvHD), guillain barre syndrome (GBS) or acute inflammatory demyelinating polyneuropathy (AIDP), pancytopenia/aplastic anemia (including analysis of all hematopoietic cytopenias), immune effector cell-associated neurotoxicity syndrome (ICANS) and treatment-related inflammatory response at tumor site. AEs which start or worsen on or after T-cell infusion are defined as treatment-emergent. mITT population.

End point type	Primary

End point timeframe:

Up to approximately 10 months

Notes:

[2] - 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: The primary endpoint of the study was planned to analyses with only descriptive statistics. Hence, no statistical analysis were performed.

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Participants	6	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with treatment-emergent adverse events and serious adverse events based on maximum severity grades

End point title	Number of participants with treatment-emergent adverse events and serious adverse events based on maximum severity grades[3]

End point description:

An AE is any untoward medical occurrence in a clinical investigation, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, other situations which involve medical or scientific judgment or is associated with liver injury and impaired liver function. AEs which start or worsen on or after T-cell infusion are defined as treatment-emergent. Severity was reported during study and was assigned a grade according to the NCI-CTCAE. AEs and SAEs severity were graded on a 5-point scale as: 1 = mild; discomfort noticed, 2 =

moderate discomfort, 3 = severe; inability to work or perform normal daily activity, 4 = life-threatening consequences and 5 = death related to AE. mITT population.

End point type	Primary

End point timeframe:

Up to approximately 10 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: The primary endpoint of the study was planned to analyses with only descriptive statistics. Hence, no statistical analysis were performed.

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Participants				
AEs, Grade 2	1	0		
AEs, Grade 3	1	3		
AEs, Grade 4	5	2		
AEs, Grade 5	0	1		
SAEs, Grade 3	4	2		
SAEs, Grade 4	1	0		
SAEs, Grade 5	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) Per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 by investigator assessment

End point title	Overall Response Rate (ORR) Per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 by investigator assessment[4]

End point description:

Overall response rate (ORR) defined as the percentage of participants with a complete response (CR) or partial response (PR) via investigator assessment per RECIST (Response Evaluation Criteria in Solid Tumors Criteria) v1.1 relative to the total number of participants in the analysis population. Partial response is defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. Complete response is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 millimeters (mm). Confidence intervals (CI) were calculated using the exact (Clopper-Pearson) method. mITT population.

End point type	Primary

End point timeframe:

Up to approximately 10 months

Notes:

[4] - 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: The primary endpoint of the study was planned to analyses with only descriptive statistics. Hence, no statistical analysis were performed.

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0 to 41)	0 (0 to 45.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants AEs leading to dose delays

End point title	Number of Participants AEs leading to dose delays[5]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with AEs leading to dose delays were summarized. Modified Intent-to-Treat (mITT) population.

End point type	Primary

End point timeframe:

Up to approximately 10 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: The primary endpoint of the study was planned to analyses with only descriptive statistics. Hence, no statistical analysis were performed.

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Participants	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) per RECIST version 1.1 by investigator assessment

End point title	Progression-free survival (PFS) per RECIST version 1.1 by investigator assessment

End point description:

Progression free survival was defined as the interval between the date of T cell infusion and the earliest date of disease progression or death due to any cause. Progressive disease (PD) is defined as at least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. PFS based on responses assessed by investigator per RECIST v1.1 is presented. Kaplan-Meier Median and 95% confidence intervals are presented. Confidence intervals were calculated using the Brookmeyer-Crowley method. mITT population.

End point type	Secondary

End point timeframe:

Up to approximately 10 months

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Months				
median (confidence interval 95%)	5.32 (1.45 to 5.52)	1.48 (0.62 to 2.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR) per RECIST version 1.1 by investigator assessment

End point title	Disease control rate (DCR) per RECIST version 1.1 by investigator assessment

End point description:

DCR was defined as the percentage of participants with a confirmed complete response (CR), partial response (PR), or stable disease (SD) for at least 6 months as per RECIST v1.1. Partial response is defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. Complete response is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 millimeters (mm). SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease. Confidence intervals (CI) were calculated using the exact (Clopper-Pearson) method. mITT population.

End point type	Secondary

End point timeframe:

Up to approximately 10 months

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0 to 41)	0 (0 to 45.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (Tmax) of lete-cel

End point title	Time to Cmax (Tmax) of lete-cel

End point description:

Tmax was defined as time to reach peak cell expansion during the study. Blood samples were collected for analysis of Tmax of lete-cel. Pharmacokinetic (PK) population.

End point type	Secondary

End point timeframe:

Day 1 to Day 15

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Days				
median (full range (min-max))	3 (1 to 15)	7.9 (1 to 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) per RECIST version 1.1 by investigator assessment

End point title	Duration of response (DOR) per RECIST version 1.1 by investigator assessment

End point description:

Duration of response was defined as the interval between the initial date of confirmed response (PR/CR) and the date of progressive disease or death among participants with a confirmed response per RECIST 1.1. Partial response is defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. Complete response is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 millimeters. mITT population. Only participants with CR or PR were included in the analysis.

End point type	Secondary

End point timeframe:

Up to approximately 10 months

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[6] - No participant achieved CR or PR, hence the number of participants analyzed is 0.

[7] - No participant achieved CR or PR, hence the number of participants analyzed is 0.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response (TTR) per RECIST version 1.1 by investigator assessment

End point title	Time to response (TTR) per RECIST version 1.1 by investigator assessment

End point description:

Time to response was defined as the interval of time between the date of T-cell infusion and the first documented evidence of the confirmed response (PR or CR), in the subset of participants with a confirmed PR or CR as their best confirmed overall response. Partial response is defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. Complete response is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 mm. mITT population. Only participants with CR or PR were included in the analysis.

End point type	Secondary

End point timeframe:

Up to approximately 10 months

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[8] - No participant achieved CR or PR, hence the number of participants analyzed is 0.

[9] - No participant achieved CR or PR, hence the number of participants analyzed is 0.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum transgene expansion (Cmax) of lete-cel

End point title	Maximum transgene expansion (Cmax) of lete-cel

End point description:

Cmax was defined as peak cell expansion during the study. Blood samples were collected for analysis of Cmax of lete-cel. Pharmacokinetic (PK) population included all participants in the mITT population from whom at least one PK sample was obtained, analyzed, and was measurable.

End point type	Secondary

End point timeframe:

Day 1 to Day 15

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Copies per microgram genomic DNA				
geometric mean (geometric coefficient of variation)	155712.1398 (± 55.21519)	127343.0679 (± 34.95574)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve to day 28 (AUC0-28d) of lete-cel

End point title	Area under the plasma concentration-time curve to day 28 (AUC0-28d) of lete-cel

End point description:

Area under the cell expansion-time curve from first T-cell infusion to Day 28. Blood samples were collected to measure AUC (0-28 days). Pharmacokinetic (PK) population.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Arm A: Lete-cel monotherapy	Arm C: Lete-cel + pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Days*copies per microgram genomic DNA				
geometric mean (geometric coefficient of variation)	1646416.5835 (± 109.45757)	1565617.646 (± 46.16918)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) were collected up to approximately 10 months

Adverse event reporting additional description:

All cause mortality, SAEs and non-serious adverse events were reported for the Intent to Treat (ITT) population that includes all participants who started the leukapheresis procedure. Participants in the "No Treatment" arm started the leukapheresis procedure but did not receive lymphodepletion chemotherapy or Lete-cel infusion.

Assessment type	Systematic

Dictionary used

Dictionary name	V25.1
Dictionary version	25.1

Reporting groups

Reporting group title	Arm A: Lete-cel monotherapy

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T- cell receptors (TCR) specific for NY-ESO-1/LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel. Participants who had disease progression within 25 weeks of Lete-cel infusion were offered therapy with Pembrolizumab following benefit-risk evaluation. Pembrolizumab 200 mg was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until subsequent disease progression or intolerable toxicity. Pembrolizumab therapy was not allowed if disease progression occurred post 25 weeks of Lete-cel infusion.

Reporting group title	No Treatment

Reporting group description:

Participants who underwent leukapheresis but did not go on to receive lymphodepletion chemotherapy or T-cell infusion.

Reporting group title	Arm C: Lete-cel + pembrolizumab

Reporting group description:

Eligible participants underwent leukapheresis to manufacture autologous T cells bearing T-cell receptors (TCR) specific for NY-ESO-1 /LAGE-1a. Lymphodepleting chemotherapy was administered, consisting of cyclophosphamide at a dose of 900 mg/m^2/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m^2/day on day -8 through day -5. On day 1, participants received a single infusion of Lete-cel followed by pembrolizumab 200 mg starting on Day 22 (Week 4 Day 1). Pembrolizumab was administered every three weeks (Q3W) for up to 35 cycles (up to Week 106) or until disease progression, whichever occurred first.

Serious adverse events	Arm A: Lete-cel monotherapy	No Treatment	Arm C: Lete-cel + pembrolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	2 / 21 (9.52%)	4 / 6 (66.67%)
number of deaths (all causes)	3	5	1
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	1 / 21 (4.76%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 21 (4.76%)	0 / 6 (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
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Nervous system disorders			
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 7 (0.00%)	1 / 21 (4.76%)	0 / 6 (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
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Small intestinal obstruction			

subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Biliary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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

Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (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
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Arm A: Lete-cel monotherapy	No Treatment	Arm C: Lete-cel + pembrolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	3 / 21 (14.29%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tumour pain			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Orthostatic hypotension			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	2
Face oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Facial pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	4 / 7 (57.14%)	1 / 21 (4.76%)	2 / 6 (33.33%)
occurrences (all)	4	1	2
Malaise			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	5 / 7 (71.43%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Chills			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	4 / 7 (57.14%)	0 / 21 (0.00%)	4 / 6 (66.67%)
occurrences (all)	4	0	5
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	3 / 7 (42.86%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Haemoptysis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Pulmonary embolism			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pulmonary oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Hallucination			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Depression			
subjects affected / exposed	3 / 7 (42.86%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Insomnia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 21 (4.76%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Persistent depressive disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Neutrophil count decreased			
subjects affected / exposed	3 / 7 (42.86%)	0 / 21 (0.00%)	4 / 6 (66.67%)
occurrences (all)	4	0	4
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			

subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	3
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Blood fibrinogen decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood methaemoglobin present			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	7 / 7 (100.00%)	1 / 21 (4.76%)	4 / 6 (66.67%)
occurrences (all)	8	1	4
Platelet count decreased			

subjects affected / exposed	4 / 7 (57.14%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Serum ferritin increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urine output decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
White blood cell count decreased			
subjects affected / exposed	6 / 7 (85.71%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	7	0	3
Injury, poisoning and procedural complications			
Radiation necrosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vascular access complication			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Atrial flutter			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dysarthria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cognitive disorder			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 21 (4.76%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Intraventricular haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
IIIrd nerve paralysis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Headache			

subjects affected / exposed	2 / 7 (28.57%)	1 / 21 (4.76%)	2 / 6 (33.33%)
occurrences (all)	2	1	3
Dysgeusia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 7 (71.43%)	1 / 21 (4.76%)	5 / 6 (83.33%)
occurrences (all)	6	1	5
Leukopenia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Lymphopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Neutropenia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Pancytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	3 / 7 (42.86%)	0 / 21 (0.00%)	3 / 6 (50.00%)
occurrences (all)	3	0	3
Dry mouth			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lip dry			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Oral disorder			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertransaminasaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Dermatitis acneiform			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	4 / 7 (57.14%)	0 / 21 (0.00%)	3 / 6 (50.00%)
occurrences (all)	4	0	3
Rash maculo-papular			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	3
Rash morbilliform			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rash erythematous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oliguria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Chronic kidney disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			

subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	4
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Sacral pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neck pain			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash pustular			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	5 / 7 (71.43%)	1 / 21 (4.76%)	3 / 6 (50.00%)
occurrences (all)	6	1	3
Hyperchloraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Hyperkalaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypervolaemia			

subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 21 (4.76%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Hypocalcaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Hypokalaemia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 21 (4.76%)	1 / 6 (16.67%)
occurrences (all)	4	1	1
Hypomagnesaemia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 21 (4.76%)	0 / 6 (0.00%)
occurrences (all)	6	1	0
Hyponatraemia			
subjects affected / exposed	4 / 7 (57.14%)	0 / 21 (0.00%)	2 / 6 (33.33%)
occurrences (all)	12	0	2
Malnutrition			
subjects affected / exposed	1 / 7 (14.29%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 21 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 October 2018	Changes made to the protocol were requested by Regulatory Agency as a result of safety events which included 2 reports of Guillain-Barré syndrome in subjects who have received chemotherapy and GSK3377794 during clinical trials
13 February 2019	Study Arm C was added. Changes were made for clarity, at the request of sponsor partners and because they were requested by the Regulatory Agency.
01 October 2019	Removal of randomization to Arm A and Arm B, clarification of aspects related to participant enrollment and clarification regarding study stopping and pausing rules.
29 October 2019	Addition of fresh biopsy collection to perform antigen expression screening, in the absence of archival tumor tissue.
21 February 2020	Add clarification regarding measurable lesion, to remove docetaxel as exclusion criterion and add platinum-based combination chemotherapy as an inclusion criterion. Docetaxel therapy was removed as supportive therapy between leukapheresis and the start of lymphodepletion.
17 May 2021	Simplify/enhance screening and enrollment efforts Broaden participant eligibility Include additional safety tests and measures.
04 November 2022	Implementation of additional safety monitoring measures for Lete-cel Increase the upper end of the target dose range of transduced T cells from to 8×109 to 15×109 in order to maximize the delivery of cells for participants whose manufacture yields >8×109 transduced T cells.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated for reasons pertaining to feasibility.

Notes: