



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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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 |
| Consent withdrawn by subject | 2 | 1 |
| Physician decision | 14 | 8 |
| 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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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/m²/day on day -7 through day -5 and fludarabine at a dose of 30 mg/m²/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 occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 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 occurrences (all) | 4 / 7 (57.14%) 5 | 0 / 21 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Serum ferritin increased subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Urine output decreased subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 3 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 6 / 7 (85.71%) 7 | 0 / 21 (0.00%) 0 | 2 / 6 (33.33%) 3 |
| Injury, poisoning and procedural complications Radiation necrosis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vascular access complication subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Tachycardia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Atrial flutter subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 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 occurrences (all) | 2 / 7 (28.57%) 2 | 1 / 21 (4.76%) 1 | 2 / 6 (33.33%) 3 |
| Dysgeusia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 5 / 7 (71.43%) 6 | 1 / 21 (4.76%) 1 | 5 / 6 (83.33%) 5 |
| Leukopenia subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 3 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 3 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 3 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pancytopenia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 21 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Eye disorders | | | |
| Dry eye subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Lacrimation increased subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 21 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 21 (0.00%) 0 | 1 / 6 (16.67%) 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 occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 21 (0.00%) 0 | 0 / 6 (0.00%) 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 8×10^9 to 15×10^9 in order to maximize the delivery of cells for participants whose manufacture yields $>8 \times 10^9$ 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. |
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Notes: