



Clinical trial results: CD19-TARGETING 3RD GENERATION CAR T CELLS FOR REFRACTORY B CELL MALIGNANCY – A PHASE II TRIAL

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-004043-36 |
| Trial protocol | SE |
| Global end of trial date | 14 January 2022 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 19 April 2023 |
| First version publication date | 19 April 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 004:TCELL |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03068416 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Uppsala University |
| Sponsor organisation address | Dag Hammarskjöldsväg 20, Uppsala, Sweden, 751 85 |
| Public contact | Jamileh Hashemi, Department of Immunology, Genetics and Pathology , Uppsala University, Sweden, 0046 186110203, jamileh.hashemi@igp.uu.se |
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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 | 07 October 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 January 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the feasibility and safety of two administrations of CAR T cells to patients with disseminated B cell lymphoma or leukemia.
- To evaluate long-term toxicity of CAR T cells by an extended follow-up period (12-24 months) when patients are analyzed even if they have progressed in their disease and/or received another therapy.
- To evaluate whether two courses of gemcitabine given in association with CAR T cells can increase the effect of CAR T cell therapy.

Protection of trial subjects:

The main serious risks for patients treated with CAR T cells are fever, cytokine release syndrome, dyspnea, Platelet count decreased and risk of infection due to low immunoglobulin level. The patients have been closely monitored and tocilizumab (anti-IL6R) was successfully used to limit cytokine release syndrome.

Background therapy:

The study protocol included bridging therapy of the treating clinician's choice. Prior CAR T-cell injection, the patients may treated with chemotherapy and/or radiotherapy for 4-8 weeks to reduce the tumour burden and control the disease. Thereafter the patients are preconditioned for 3 days with Fludarabine and Cyclophosphamide. CAR T-cell injection followed by 2 cycles of gemcitabine (800 mg/m²) in order to suppress myeloid derived suppressor cells (MDSC) thought to hamper CAR T-cell function).

Evidence for comparator:

No comparator was used.

| | |
|---|--|
| Actual start date of recruitment | 10 April 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety, Ethical reason, Regulatory reason, Scientific research |
| Long term follow-up duration | 24 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Sweden: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 1 |
| Adults (18-64 years) | 12 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 2017-2020 in Sweden. The trial site was in Uppsala but some patients were referred to by other hospitals.

Pre-assignment

Screening details:

24 patients met eligibility criteria. Four of 28 (4/28) recruited patients failed to receive treatment. Main reason for failing screening of three patients was too short expected survival that would result in patients not surviving long enough for the CAR T cells to be manufactured. It was not possible to manufacture CAR T cell for one (1) patient.

Pre-assignment period milestones

| | |
|------------------------------|-------------------|
| Number of subjects started | 28 ^[1] |
| Number of subjects completed | 24 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-----------------------|
| Reason: Number of subjects | Protocol deviation: 4 |
|----------------------------|-----------------------|

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Enrollment is defined as patients randomised to a treatment arm. Pre-assignment is the screening period prior to initiation of treatment.

Period 1

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

Blinding implementation details:

Blinding was not applicable.

Arms

| | |
|-----------|-------------|
| Arm title | CAR-T cells |
|-----------|-------------|

Arm description:

Two doses CAR-T cells infusion in patients who did not respond or relapsed after initial response and two courses of gemcitabine in association with CAR-T cells.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | CAR T cells |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

2x10⁸ cells/m²

| Number of subjects in period 1 | CAR-T cells |
|---------------------------------------|-------------|
| Started | 24 |
| Completed | 24 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|--|---------------|-------|--|
| Number of subjects | 24 | 24 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 1 | 1 | |
| Adults (18-64 years) | 12 | 12 | |
| From 65-84 years | 11 | 11 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 63 | | |
| full range (min-max) | 14 to 77 | - | |
| Gender categorical | | | |
| Female | | | |
| Male | | | |
| Units: Subjects | | | |
| Female | 13 | 13 | |
| Male | 11 | 11 | |

Subject analysis sets

| | |
|---|-----------------------------|
| Subject analysis set title | Received CART treatment |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| Started treatment with CAR T | |
| Subject analysis set title | One week |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Protein Levels measured 1 week after treatment | |
| Subject analysis set title | Three weeks |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Protein levels measured three weeks after treatment | |

| Reporting group values | Received CART treatment | One week | Three weeks |
|---|-------------------------|----------|-------------|
| Number of subjects | 24 | 24 | 24 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| median | 63 | 63 | |
| full range (min-max) | 14 to 77 | 14 to 77 | |
| Gender categorical | | | |
| Female | | | |
| Male | | | |
| Units: Subjects | | | |
| Female | 13 | | |
| Male | 11 | | |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | CAR-T cells |
| Reporting group description: Two doses CAR-T cells infusion in patients who did not respond or relapsed after initial response and two courses of gemcitabine in association with CAR-T cells. | |
| Subject analysis set title | Received CART treatment |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: Started treatment with CAR T | |
| Subject analysis set title | One week |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Protein Levels measured 1 week after treatment | |
| Subject analysis set title | Three weeks |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Protein levels measured three weeks after treatment | |

Primary: Tumor response measured as best response and over all response

| | |
|---|---|
| End point title | Tumor response measured as best response and over all response ^[1] |
| End point description: Patients received two administrations of CAR T cells are grouped as overall responder and best responder at 1 month after the first CAR-T infusion. Tumor metrics total structural burden (V total) for the pre-therapy scan (t0) and post therapy scan (t1) are presented. | |
| End point type | Primary |
| End point timeframe: From study inclusion to the end of study participation | |
| 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: It is one-arm study therefore statistical analysis has not been presented. | |

| End point values | CAR-T cells | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 | | | |
| Units: Number of patients | | | | |
| Overall response | 9 | | | |
| Best response | 12 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Determination of tumor size and the tumor marker CD19

| | |
|-----------------|---|
| End point title | Determination of tumor size and the tumor marker CD19 |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From treatment to maximum 24 months post treatment

| End point values | CAR-T cells | Received CART treatment | | |
|-------------------------------|---------------------|-------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 24 | | | |
| Units: ml | | | | |
| median (full range (min-max)) | 34.7 (4.0 to 219.9) | 17.6 (3.4 to 202.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Determination of the level CAR T cell in blood

| | |
|-----------------|--|
| End point title | Determination of the level CAR T cell in blood |
|-----------------|--|

End point description:

Patients who received two administrations of CAR T cells (14 patients) were divided in two groups as increased vs not increased CAR T copy number in blood. Only 4 out of the 14 patients who got 2 doses had an increase of CAR-Ts in their blood after the second infusion.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From treatment to maximum 24 months post treatment

| End point values | Received CART treatment | One week | Three weeks | |
|--------------------------------------|-------------------------|-------------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 14 | 14 | 14 | |
| Units: Copy number | | | | |
| arithmetic mean (standard deviation) | | | | |
| Not increased CAR T cell | 2379.349 (± 3146.384) | 1269.0323 (± 1567.2802) | 260.831 (± 430.951) | |
| Increased CAR T cell | 97.9 (± 79.6) | 157.93 (± 108.70) | 310.366 (± 357.00) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Determination of the of the presence of immunological markers in blood and biopsies

| | |
|-----------------|---|
| End point title | Determination of the of the presence of immunological markers in blood and biopsies |
|-----------------|---|

End point description:

Protein levels found in plasma of patients, before CAR T infusion, after one week and three weeks of CAR T treatment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From treatment to maximum 24 months post treatment

| End point values | CAR-T cells | One week | Three weeks | |
|----------------------------------|--------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 24 | 24 | 24 | |
| Units: NPX | | | | |
| arithmetic mean (standard error) | | | | |
| TNFRSF9 | -0.3567 (± 0.6191) | -0.7712 (± 0.4819) | -1.6148 (± 0.4694) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Enrollment to last visit (maximum 24 months post CAR T cell infusion)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

| | |
|--------------------|---|
| Dictionary version | 5 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events | Overall trial | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 24 (54.17%) | | |
| number of deaths (all causes) | 16 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Creatinine increased | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences causally related to treatment / all | 3 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| White blood cell decreased | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |

| | | | |
|--|-----------------|--|--|
| Hypotension | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tremor | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fever | | | |
| subjects affected / exposed | 7 / 24 (29.17%) | | |
| occurrences causally related to treatment / all | 14 / 14 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalized edema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Throat pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhea | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomach pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnea | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Confusion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hallucinations | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Infections and infestations | | | |
| Bladder infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device-related infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection Suspicion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Unknown infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cath-a-port | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection Bronchial | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Overall trial | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 24 (45.83%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal-cell cancer | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Tumor in left leg | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Common cold | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Edema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 5 | | |
| Fever | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Flu like symptoms subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | | |
| Neurological pain right arm subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 3 / 24 (12.50%) 3 | | |
| Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | | |
| Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Decreased leukocytes subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Hypogammaglobulenemi subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 5 / 24 (20.83%) 5 | | |
| White blood cell decreased subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | | |
| Cardiac disorders | | | |

| | | | |
|--|---|--|--|
| Palpitations subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | | |
| Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) | 3 / 24 (12.50%) 3 | | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Eye disorders dry eye subjects affected / exposed occurrences (all) Glaucoma subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Diarrhea subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 1 / 24 (4.17%) 1 | | |
| Hepatobiliary disorders | | | |

| | | | |
|--|---|--|--|
| Portal vein thrombosis subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | | |
| Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Redness under both eyes subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Discomfort left eyebrow subjects affected / exposed occurrences (all) Flank pain subjects affected / exposed occurrences (all) Groin discomfort subjects affected / exposed occurrences (all) Muscle strain left thigh subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | | |
| Infections and infestations Bronchial infection subjects affected / exposed occurrences (all) Herpes simplex reactivation subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 02 January 2019 | <p>(1) The number of patients has been changed to "<25" from "<15". This change is motivated by the fact that although CD19-CAR T cell therapy is now approved within the EU and will be available as standard care therapy in Sweden, the introduction of this therapy into Swedish hospitals will take time. For many patients it will then be too late. Since we still have virus left from the batch used for production and also have financing for treating more patients we would like to do that.</p> <p>(2) Following the possibility to include 10 more patients the planned trial period has been extended with one year and the trial time table has been extended with one year for the last patient in and last patient out.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36575477>