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CAR T cells to fight T cell leukaemia

Submission date 11/01/2022	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 06/04/2022	**Overall study status** Ongoing	
Last Edited 28/05/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
T-cell leukaemia is an uncommon type of blood cell cancer that affects white blood cells (T cells). This phase I clinical trial will treat patients aged 6 months and above with T cell leukaemia which has come back (relapsed) after chemotherapy or is not responding to chemotherapy (refractory). The cell therapy is made from white blood cells (T cells) collected from a healthy donor and changed so they can kill other T cells, including leukaemia cells. These 'ready-made' CAR T cells have been made using a new technique called CRISPR base editing to modify their DNA code and have been given the name BE CAR-7. This technique allows them to work after chemotherapy and also disarms them to prevent effects against normal cells. The main aim of this study is to assess the safety of the BE CAR-7 treatment and to see if ready-made CAR T cells can eradicate T cell leukaemia ahead of a planned bone marrow transplant.

Who can participate?
Patients aged 6 months and above with relapsed/refractory T cell leukaemia ahead of a planned bone marrow transplant.

What does the study involve?
Patients will undergo careful screening to confirm that this treatment is adequate for them. Chemotherapy will be given prior to BE CAR-7 infusion to improve the ability of T-cells to establish and grow. Patients will then receive a single infusion of the BE CAR-7 cells and will be closely monitored in hospital. Patients are expected to be in hospital for 4-6 weeks for the BE CAR-7 treatment and the transplant will be scheduled 2-4 weeks after the end of BE CAR7 if leukaemia cells are no longer detectable. Patients will be monitored on the study for 1 year after transplant and then long term in routine clinics.

What are the possible benefits and risks of participating?
Taking part in the study of testing 'ready-made' CAR T cells could help reduce the amount of disease and get the patient into remission before a bone marrow transplant. Leukaemia is less likely to come back after a bone marrow transplant if levels in the bone marrow are undetectable. The ready-made CAR T cells are being used to try and improve the chances of successful transplantation. Side effects may include low blood cell counts, infections, cytokine storm (severe immune reaction), graft versus host disease (where the donated cells attack the body) and other complications.

Where is the study run from?
Great Ormond Street Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2022 to May 2028

Who is funding the study?
1. Medical Research Council (MRC) (UK)
2. King's College Hospital (UK)

Who is the main contact?
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Plain English summary under review with external organization

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2021-004312-25

IRAS number
1004379

ClinicalTrials.gov number
NCT05397184

Secondary identifying numbers
19IC17, IRAS 1004379

Study information

Scientific Title
Phase I study of base edited CAR7 T cells to treat T cell malignancies (TvT CAR7)

Acronym
TvT CAR7

Study objectives
The primary objective is to assess the safety of base edited (BE)-CAR7s in patients experiencing relapsed/refractory CD7+ T-cell acute lymphoblastic leukemia (T-ALL).

The secondary objectives of the trial are to determine if BE-CAR7 can mediate remission ahead of allogeneic stem cell transplantation (Allo-SCT).

Efficacy endpoints are:
Bone marrow will be examined at D28 for disease levels by flow and/or molecular minimal

residual disease (MRD).
Disease remission is defined as morphological complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) with MRD <10e-3 by flow and/or PCR.

There are additional exploratory objectives:
1. To assess disease-free survival and overall survival.
2. To assess the time to remission and duration of remission/progression
3. To follow the immune recovery of patients after allogeneic hematopoietic stem cell transplantation (alloHSCT)
4. To track the expansion, persistence and elimination of BE-CAR7
5. To monitor for possible genotoxic side effects from BE modification
6. To record complications following BE-CAR7 treatment

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/03/2022, London - West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8007; westlondon.rec@hra.nhs.uk), ref: 22/LO/0001

Study design
Single-arm non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Relapsed/refractory T-cell acute lymphoid leukaemia

Interventions
Single-dose intravenous infusion (weight-based dosing) of a banded dose of CAR7+ T cells/kg BE-CAR7
Total duration of treatment: 28 days
Follow-up: 12 months

Patients will undergo careful screening to confirm that this treatment is adequate for them. Chemotherapy will be given prior to BE CAR-7 infusion to improve the ability of T-cells to

establish and grow. Patients will then receive a single infusion of the BE CAR-7 cells and will be closely monitored in hospital via blood and bone marrow tests for safety and to check the levels of BE CAR-7 and leukaemia cells. Patients are expected to be in hospital for 4-6 weeks for the BE CAR-7 therapy and the transplant will be scheduled 2-4 weeks after the end of BE CAR7 if leukaemia cells are no longer detectable. Patients will be monitored on the study for 1 year every month for the first 3 months and then every 6 months and then long term in routine clinics.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
BE-CAR7

Primary outcome measure
The safety of BE-CAR7s in patients experiencing relapsed/refractory CD7+ T-ALL; measured at baseline, lymphodepletion, day 0, day 28, and additional points for 12 months post bone marrow transplant (BMT) using:
1. Clinical examination and vital signs
2. Standard blood parameters
3. Oxygen saturation and cardiac assessment
4. Cytokines
5. Infections
National Cancer Institute Common Terminology Criteria for Adverse Event will be used to grade events. Specialized grading scales for cytokine release syndrome (CRS) and graft versus host disease (GVHD) will be applied.

Secondary outcome measures
Disease remission ahead of allo-SCT measured by bone marrow examination at day 28 for disease levels by flow and/or molecular MRD. Disease remission is defined as morphological complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) with MRD <10e-3 by flow and/or PCR.

Overall study start date
04/01/2022

Completion date
31/05/2028

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/05/2025:
Demographic characteristics:
1. Male or female patients
2. Aged 6 months and above

Medical and therapeutic criteria:
1. Relapsed/refractory T cell malignancy ahead of planned allogeneic haematopoietic stem cell transplantation (allo-SCT). Morphologically confirmed with leukemic blasts in the bone marrow (>5%) or a quantifiable MRD load (by multiparameter flow cytometry and/or quantitative polymerase chain reaction)
2. CD7+ (>99%) leukaemia-associated immunophenotype (LAIP)
3. Eligible and fit for allogeneic hematopoietic stem cells transplantation with suitable donor available
4. Estimated life expectancy ≥12 weeks
5. Lansky (age <16 years at the time of assent/consent) or Karnofsky (age ≥16 years at the time of assent/consent) performance status ≥70; Eastern Cooperative Oncology Group ECOG performance status <2

Previous inclusion criteria:
Demographic characteristics:
1. Male or female patients
2. Age ranging between 6 months and <16 years

Medical and therapeutic criteria:
1. Relapsed/refractory T cell malignancy ahead of planned allogeneic haematopoietic stem cell transplantation (allo-SCT). Morphologically confirmed with leukemic blasts in the bone marrow (>5%) or a quantifiable MRD load (by multiparameter flow cytometry and/or quantitative polymerase chain reaction)
2. CD7+ (>99%) leukaemia-associated immunophenotype (LAIP)
3. Eligible and fit for allogeneic hematopoietic stem cells transplantation with suitable donor available
4. Estimated life expectancy ≥12 weeks
5. Lansky (age <16 years at the time of assent/consent) or Karnofsky (age ≥16 years at the time of assent/consent) performance status ≥70; Eastern Cooperative Oncology Group ECOG performance status <2

Participant type(s)
Patient

Age group
Mixed

Lower age limit
6 Months

Sex
Both

Target number of participants
10

Key exclusion criteria
1. Patients/parents unwilling to undergo a follow-up for 15 years
2. Foreseeable poor compliance to the study procedures
3. Evidence of disease progression after cytoreduction
4. Uncontrollable CNS leukaemia or neurological symptoms defined as CNS grade 3 (per National

Comprehensive Cancer Network guidelines)
5. Absence of suitable HLA matched or mismatched donor
6. Weight <6 kg
7. Presence of donor-specific anti-HLA antibodies directed against BE-CAR7
8. GvHD requiring systemic therapy
9. Systemic steroid therapy prednisolone >0.5 mg/kg/day
10. Known hypersensitivity to any of the test materials or related compounds
11. Active bacterial, fungal or viral infection not controlled by standard of care anti-microbial or anti-viral treatment. Uncontrolled bacteraemia/ fungaemia is defined as the ongoing detection of bacteria/fungus on blood cultures despite antibiotic or antifungal therapy. Uncontrolled viraemia is defined as rising viral loads on two consecutive occasions despite antiviral therapy.
12. Risk of pregnancy or non-compliance with contraception (if applicable). Girls of childbearing potential must have been tested negative in a pregnancy test within 14 days prior to inclusion.
13. Lactating female participants unwilling to stop breastfeeding
14. Prior CAR therapy known to be associated with ≥Grade 3 cytokine release syndrome (CRS) or ≥Grade 3 drug-related CNS toxicity

Date of first enrolment
01/04/2022

Date of final enrolment
31/05/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
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Study participating centre
King's College Hospital
Denmark Hill
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
http://www.gosh.nhs.uk/

ROR
https://ror.org/00zn2c847

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Other publications
5. Protocol is not published yet. Protocol with redacted confidential information will be uploaded after study closeout.

Intention to publish date

30/09/2029

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication. The trial will comply with the Data Protection Act. If the patient, parents/guardians consent, anonymised data may be used for research and development including under commercial agreements reached by the hospital. The people who analyse the information will not be able to identify the subject and will not be able to find out the name, NHS number or contact details.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article		14/06/2023	15/06/2023	Yes	No
HRA research summary			28/06/2023	No	No