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CAR T cells to fight acute myeloid leukaemia

Submission date
11/01/2023

Recruitment status
No longer recruiting

Registration date
01/12/2023

Overall study status
Ongoing

Last Edited
08/07/2025

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This phase I study will treat children aged 6 months up to 16 years old with acute myeloid leukaemia (AML), which has come back (relapsed). The new product is made from white blood cells (T cells) collected from a healthy donor and changed so they can kill leukaemia cells. These 'ready-made' CAR T cells have been made using a new technique called Base Editing and have been given the code name 'BE CAR-33'. They look for and attack cells showing a flag called 'CD33'. This technique allows them to work after chemotherapy and also disarms them to prevent effects against normal cells. The main purpose of this study is to assess the safety of the 'BE CAR-33' therapy and to see if ready-made CAR T cells can get rid of leukaemia ahead of a planned bone marrow transplant that will hopefully prevent the leukaemia from returning.

Who can participate?
Children aged from 6 months up to 16 years old with relapsed AML

What does the study involve?
Up to 10 patients will be included in this trial. Patients will undergo careful screening to confirm that this treatment is adequate for them. If deciding to join the study, the researcher will need to wipe out their existing immune system with chemotherapy prior to BE CAR-33 infusion, as past research indicates that this improves the ability of T-cells to establish and grow. Patients will then receive a single infusion of the BE CAR-33 cells. Participants will be closely monitored via blood and bone marrow tests for safety and to check the levels of BE CAR-33 and leukaemia cells. Patients are expected to be in the hospital for 5 weeks for the BE CAR-33 therapy and the transplant will be scheduled 4 weeks after the end of BE CAR33. Patients will be monitored every month for the first three months and then every 6 months.

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 subsequent bone marrow transplant (BMT). Leukaemia is less likely to come back after BMT 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.
The following are the risks associated with study participation:
1. Immediate infusion reaction, rarely, hypersensitivity reactions may occur shortly after the administration. Patients will be pre-medicated with paracetamol and intravenous

chlorphenamine.
2. Cytokine release syndrome. Signs and symptoms include fevers, nausea headache, rash, rapid heartbeat, low blood pressure, and dyspnoea. Tocilizumab is the preferred first-line treatment agent for the treatment of severe CRS.
3. Neurotoxicity, after CAR therapy can include obtundation, seizures, dysphasia, mental status changes confusion, disorientation, agitation, tremor, dysgraphia, increased intracranial pressure, papilloedema and cerebral oedema. Management includes e.g.: Imaging by CT/MRI, EEG, CSF examination, also IV steroid therapy, Tocilizumab and Anakinra may be considered.
4. Tumour lysis syndrome (TLS) may lead to hyperuricemia, hyperkalaemia, hyperphosphatemia, and hypocalcaemia. It is recommended to use hydration, allopurinol or Asparinase/Rasburicase and oral phosphate binders.
5. Graft versus host disease (GVHD). Residual TCR T cells in the BE-CART product could mediate GVHD. Limited skin GVHD will be managed with topical therapies. GVHD >grade II of the skin or involving the liver may require prednisolone therapy.
6. Cytopaenia and Aplasia. Aplasia and lymphopenia should resolve after allogeneic stem cell transplantation (Allo-SCT). Patients may receive GCSF for neutropenia. Hospital SOPs will be followed for viral, bacterial and fungal cover.
7. Veno-occlusive disease (VOD), sinusoidal obstruction syndrome, which may be exacerbated following allo-SCT. The pathophysiology may result from the effects of calicheamicin on CD33+ sinusoidal endothelial cells, and additional risk factors include myeloablative regimens, previous liver disease and age extremes. As mitigation, all patients will be closely monitored for VOD, including hepatomegaly, weight gain, rise in bilirubin and ascites. Liver function will be monitored daily, along with baseline and pre-SCT ultrasound scans. Prophylactic ursodeoxycholic acid will be considered in all patients.
8. Genotoxicity & Transformation. The two main risks associated with the use of HIV-based Lentiviral vectors include the capability of generation of replication-competent lentivirus (RCL) and potential oncogenesis through insertional mutagenesis. Third generation lentiviral vectors mitigate the risk of RCL production.
9. Risks from base editing, associated with ‘conventional’ CRISPR/Cas9 mediated genome editing include off-target cleavage and on-target effect. These have been largely mitigated by the switch to BE and seamless C>T editing.

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 2023 to June 2026

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Prof Waseem Qasim, w.qasim@ucl.ac.uk (UK)

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-004311-66

Integrated Research Application System (IRAS)

1007053

ClinicalTrials.gov (NCT)
NCT05942599

Protocol serial number
18IC13, IRAS 1007053, CPMS 55915

Study information

Scientific Title
Phase I study of base-edited CAR T cells against acute myeloid leukaemia (AML): deep conditioning ahead of allogeneic stem cell transplantation

Acronym
CARAML

Study objectives
The primary objective is to evaluate the safety of BE-CAR33 in paediatric patients with relapsed CAR33+ acute myeloid leukaemia (AML).
The secondary objective is to determine if BE-CAR33 can mediate complete remission ahead of scheduled allo-SCT at 28 days.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 15/03/2023, London - West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8098, (0) 207 104 8007, (0)207104 8256; westlondon.rec@hra.nhs.uk), ref: 23/LO/0014

Study design
Phase I study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Paediatric relapsed CAR33+ acute myeloid leukaemia

Interventions
In this study, all patients will receive a single dose of a CAR33+ T cell treatment (BE CAR-33) given through an intravenous infusion. The amount of BE CAR-33 T cells given will be based on the patient's weight, and the treatment will last for 28 days. There will be no randomization of patients, and patients will be followed up for 12 months after the treatment.

Intervention Type

Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
BE-CAR33

Primary outcome(s)
Safety monitored at baseline, lymphodepletion, D0 (investigational medicinal product infusion day), D7, D17, D21, D28 post-infusion, at GD-1 (one day before bone marrow transplant (BMT) and additional points in following months: M1, M2, M3, M6 and M12 post-BMT will include:
1. Clinical examination and vital signs
2. Standard blood parameters
3. Oxygen saturation & cardiac assessment
4. Cytokines
5. Infections
National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) will be used to grade events. Specialized grading scales for cytokine release syndrome and graft versus host disease will be applied

Key secondary outcome(s))
Ability of BE-CAR33 to achieve myeloablation and disease remission ahead of allogeneic stem cell transplantation (Allo-SCT). Disease response assessed between D21-D28 will include:
Bone marrow examination for disease levels measured using flow cytometry and/or molecular minimal residual disease tests

Completion date
01/06/2026

Eligibility

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

Medical and therapeutic criteria:
1. Relapsed AML ahead of planned allogeneic haematopoietic stem cell transplantation (allo-SCT). Morphologically confirmed with leukemic blasts in the bone marrow (>5%) or a quantifiable minimal residual disease (MRD) load (by multiparameter flow cytometry and/or quantitative polymerase chain reaction)
2. CD33+ (>95%) blast 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) and Eastern Cooperative Oncology Group ECOG performance status < 2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
6

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 kgs
7. Presence of donor-specific anti-HLA antibodies directed against BE-CAR33
8. GvHD requiring systemic therapy
9. Systemic steroid therapy prednisolone >0.5mg/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 anti-fungal 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 T cell therapy known to be associated with ≥Grade 3 cytokine release syndrome (CRS) or ≥Grade 3 drug-related CNS toxicity

Date of first enrolment
21/07/2023

Date of final enrolment
01/06/2025

Locations

Countries of recruitment
United Kingdom

England

Germany

Study participating centre
Great Ormond Street Hospital
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Sponsor information

Organisation
Great Ormond Street Hospital for Children NHS Foundation Trust

ROR
https://ror.org/03zydm450

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

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

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes