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Long-term follow-up after "ready-made" CAR T cells

Submission date 19/01/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 10/09/2024	**Overall study status** Ongoing	
Last Edited 06/06/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
In this observational study, we are monitoring the long-term patients who previously received ‘ready-made’ CAR T cells within phase 1 clinical trials. ‘Ready-made’ CAR T cells are universal cellular products that derive from healthy donor white blood cells. As they are created by using special gene editing techniques, they are called "genome-edited allogenic CAR-T cells". They aim to fight and reduce leukaemia ahead of bone marrow transplant (BMT) and they are administered to patients with relapsed/refractory acute lymphoblastic or myeloid leukaemia. They are not expected to persist after BMT. This study aims to monitor long-term outcomes and adverse effects after ‘ready-made’ CART cells and bone marrow transplants. To date, three different ‘ready-made’ CAR T have been used in phase I trials at Great Ormond Street Hospital, which are PBLTT52CAR19 for B-cell acute lymphoblastic leukaemia, BE-CAR7 for T-cell acute lymphoblastic leukaemia and BE-CAR33 for acute myeloid leukaemia.

Who can participate?
Children previously administered with one of the mentioned products and who have completed the treatment study will be eligible to participate in this long-term study.

What does the study involve?
Up to 20 patients will be included in this study which will take place at Great Ormond Street Hospital. The start of this study will be after the treatment study, 12 or 24 months after allogeneic BMT (depending on which treatment study patients were enrolled). As long-term persistence of CAR T cells beyond SCT is not anticipated, only routine blood tests are required. Patients will be monitored with yearly visits up to 15 years after BMT. This study will use arrangements already in place in BMT long-term follow-up. Study visits will match with the planned ones and blood samples will be collected as part of normal routine care.

What are the possible benefits and risks of participating?
There is no foreseeable risk to participants as this is a follow-up and monitoring study. No IMP administrations are expected. Moreover, the study will align with the already in-place BMT long-term follow-up and will not add extra blood tests, clinical examinations or procedures. Follow-up visits will take place together with standard planned visits.

Where is the study run from?
Great Ormond Street Hospital for Children NHS Foundation Trust

When is the study starting and how long is it expected to run for?
January 2024 to September 2042

Who is funding the study?
Great Ormond Street Hospital for Children NHS Foundation Trust

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009055

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
23IC21, IRAS 1009055

Study information

Scientific Title
An observational, long-term post-transplant follow-up after allogeneic genome edited lentiviral transduced CAR T cells

Acronym
LTalloCAR

Study objectives
The primary objective is to detect long-term effects after genome edited lentiviral transduced allogeneic universal CAR T cell therapy, including the following Investigational Medicinal Products (IMPs), PBLTT52CAR19, BE-CAR7 and BE-CAR33.

The secondary objectives of the trial are:
- To track mononuclear cell chimerism for the recipient, transplant donor, and IMP (CAR-T) donor signals
- To confirm non-persistence of IMP (by chimerism assay)
- To monitor progression-free survival
- To assess overall survival

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/03/2024, London – West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8241; westlondon.rec@hra.nhs.uk), ref: 24/LO/0005

Study design
Observational long-term post-transplant follow-up study

Primary study design
Observational

Secondary study design

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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

Health condition(s) or problem(s) studied
Relapsed/refractory acute myeloid leukaemia and relapsed/refractory acute lymphoblastic leukaemia

Interventions
This study is a long-term observational follow-up of patients who received allo-CAR Investigational Medicinal Products (IMPs) after allogeneic stem cell transplantation (allo-SCT). The study aims to assess the long-term safety of these therapies, with follow-up lasting 15 years from the date of IMP administration. Routine blood tests will be conducted annually to monitor safety, with the first visit 24-36 months post-transplant.

Participants: Eligible participants are those who have completed Phase 1 of their treatment with specific CAR T cells:
• PBLTT52CAR19 for B-ALL
• BE-CAR7 for T-ALL
• BE-CAR33 for AML
Assessments:
• Routine blood tests to monitor chimerism, immune recovery, infections, and graft-versus-host disease (GVHD).
• Safety assessments include tracking new hematologic disorders, immune recovery, and disease outcomes.
Follow-up Schedule:
The follow-up will integrate into the standard of care for patients post-SCT, aligning with existing long-term monitoring practices. The first follow-up visit will occur 24-36 months after allo-HSCT, according to the original treatment study schedule. Inclusion status will be confirmed at the time of enrolment. Follow-up visits will be conducted annually from Year 2 or Year 3 until Year 15, with a window of ±1 month.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Allogeneic genome edited lentiviral transduced CAR T cells. [For BE CAR33 T cells: TCRαβ-CAR33+ T For BE CAR7 T cells: CAR7+TCRαβ-_T-cells For PBLTT52CAR19 T cells: CAR19+TCRαβ-_T-cells]

Primary outcome measure
The identification and documentation of long-term adverse effects following genome-edited allogeneic universal CAR T cell therapy and allogeneic transplant (PBLTT52CAR19, BE-CAR7, and BE-CAR33), including non-persistence of IMP beyond allo-SCT (via chimerism testing), the occurrence of new haematologic disorders (cytopenia, malignancies), autoimmune disorders, immune recovery (T-cell, B-cell aplasia, immunoglobulins), severe viral infections, engraftment, chimerism status, and new or ongoing GVHD grade 3 or higher, assessed annually from year 2 or 3 through year 15 (+/- 1 month)

Secondary outcome measures
The tracking of mononuclear cell chimerism for the recipient, transplant donor, and IMP (CAR-T) donor signals to confirm the non-persistence of IMP (by chimerism assay). Chimerism status in blood will be performed annually from year 2 or 3 through year 15 (+/- 1 month)

Overall study start date
12/01/2024

Completion date
30/09/2042

Eligibility

Key inclusion criteria
The principal inclusion criteria are:
1. Written informed consent obtained prior to any study-specific procedure (patient or parent(s) or legal representative)
2. Patients affected by advanced lymphoid or myeloid leukemia, who have been administered with allogenic genome edited lentiviral CAR T cells and had allo-SCT over 12 months ago

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
20

Total final enrolment
30

Key exclusion criteria
Not meeting the inclusion criteria

Date of first enrolment
10/01/2025

Date of final enrolment
01/06/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

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Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Great Ormond Street Hospital for Children

Alternative Name(s)
GOSH

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

1. Peer reviewed scientific journals
2. Internal report
3. Conference presentation
The trial will comply with the Data Protection Act. If the Patient, parents/guardian 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

Intention to publish date
30/09/2040

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