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Observational long-term follow- up study for patients previously treated with ex vivo gene therapy

Submission date 08/03/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 11/06/2025	**Overall study status** Ongoing	
Last Edited 10/09/2025	**Condition category** Genetic Diseases	

Plain English summary of protocol

Background and study aims
Great Ormond Street Hospital (GOSH) is running clinical trials to test new gene therapies for children with inherited immune system conditions like Chronic Granulomatous Disease and Severe Combined Immunodeficiency. These conditions make it hard for the body to fight infections. The gene therapy works by correcting the faulty gene in the patient's own blood stem cells and returning them to the body to help rebuild the immune system.
After receiving gene therapy, patients are monitored for 2 to 3 years. However, to make sure the treatment is safe in the long term, patients need to be followed for up to 15 years. This study helps GOSH meet that requirement by continuing to monitor patients for any long-term side effects and to see how well the treatment is working over time.

Who can participate?
Patients can take part if they:
-Received gene therapy as part of a GOSH clinical trial.
-Were treated with gene therapy at GOSH through compassionate use (outside of a trial).
-Were in a commercial follow-up study at GOSH that has since ended.

What does the study involve?
Participants will continue with their usual medical care and follow-up appointments at GOSH. The study mainly involves reviewing medical records and collecting information from routine check-ups. In some cases, extra blood samples may be taken. Rarely, a bone marrow sample might be needed, but this would be discussed in advance.

What are the possible benefits and risks of participating?
There are no direct benefits to the patient, as this study is for monitoring purposes only. However, participation will:
• Help doctors better understand the long-term safety of gene therapy.
• Allow for early detection of any potential issues, ensuring the best possible care for patients.
• Contribute to future improvements in gene therapy, benefiting other patients with similar conditions.

Because this study follows patients over many years, it provides valuable information to help researchers and doctors develop safer and more effective gene therapies for the future.
This study involves minimal risk, as it mainly consists of reviewing existing medical records and routine check-ups. Blood tests may cause mild pain or bruising, but a numbing cream can be used to reduce discomfort. There is also a small chance of minor bleeding or infection, though these risks are uncommon. If any side effects occur, they will be treated appropriately.

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

When is the study starting and how long is it expected to run for?
March 2025 To June 2042

Who is funding the study?
Great Ormond Street Hospital (GOSH) (UK)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1009819

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Protocol Number 24IC16, CTA Number: 17328/0238/001-0001

Study information

Scientific Title
Long term follow-up for patients with inborn errors of immunity treated with autologous ex vivo gene modified CD34+ advanced therapies at Great Ormond Street Hospital

Study objectives
Primary objective:
To characterize the long-term safety of the gene therapy treatment and detect potential gene therapy-related adverse events in participants who received an autologous ex vivo gene modified CD34+ advanced therapy at GOSH.

Secondary objective:
To evaluate long-term, sustained disease correction and clinical efficacy of the gene therapy treatment through collection of ‘standard of care’ assessment data.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/05/2025, London - West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, NG1 6FS, United Kingdom; +44 2071048075; westlondon.rec@hra.nhs.uk), ref: 25/LO/0188

Study design
Observational long -term follow-up post gene therapy

Primary study design
Observational

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied

Medical condition: X-linked SCID (SCID-X1); p47 deficient Autosomal Recessive Chronic Granulomatous Disease (AR-CGD) and Severe Combined Immunodeficiency Due to Adenosine Deaminase Deficiency (ADA-SCID)

Interventions
Patients will continue to receive routine medical care and follow-up appointments at GOSH, just as they normally would. This study will involve reviewing medical records and collecting information from standard medical check-ups. In some cases, additional blood samples may be taken. If needed, a bone marrow sample may be collected, but this would only happen in rare cases and would be discussed in advance with the patient and their family.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Cryopreserved lentiviral vector transduced patient CD34+ cells [G2SCID lentiviral vector transduced patient CD34+ cells, CD34+ cells transduced with pCCLChimp47, CD34+ HSCs transduced ex vivo with EFS LV]

Primary outcome(s)
Characterize the long-term safety of the gene therapy treatment and detect potential gene therapy-related adverse events in participants who received an autologous ex vivo gene modified CD34+ advanced therapy at GOSH. Monitoring will be performed during yearly visit from Year 3 or 4 to Year 15 post-infusion and will include documentation of the:
1. Adverse events (AEs), serious adverse events (SAEs), and/or adverse reactions
are measured through clinical assessments and review of medical records.
2. Overall survival (OS) and event-free survival (EFS)
are assessed through clinical review of survival status and defined clinical events (rescue HSCT, second gene therapy, mutagenic therapy exposure).
3. Vector copy number (VCN) in peripheral blood cell lineages, measured using quantitative PCR (qPCR).

Key secondary outcome(s))
Evaluate long-term, sustained disease correction and clinical efficacy of the gene therapy treatment through collection of ‘standard of care’ assessment data. Monitoring will be performed during yearly visit from Year 3 or 4 to Year 15 post-infusion and will include documentation of the:
1. Immune reconstitution, measured via laboratory assessments of blood cell counts, lymphocyte subsets (absolute numbers and percentages), and immunoglobulin levels.
2. Discontinuation of immunoglobulin replacement therapy, assessed through review of treatment records and time to discontinuation.

Completion date
30/06/2042

Eligibility

Key inclusion criteria
1. Participants must have previously received a CD34+ ATIMP through a clinical trial or compassionate use program at GOSH.
2. The patient displays persistent detectable gene marking.
3. The patient is not followed-up on another LTFU study for the same condition.
4. The patient or their guardian can provide informed consent.
5. Inclusion can be prospective or retrospective.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
Refusal to sign informed consent

Date of first enrolment
01/12/2025

Date of final enrolment
30/04/2030

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Great Ormond Street Hospital for Children NHS Foundation Trust

ROR

https://ror.org/03zydm450

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

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent 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