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Study of EN-374 gene therapy in participants with X-linked chronic granulomatous disease

Submission date 02/05/2025	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol
Registration date 08/04/2026	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 07/05/2026	**Condition category** Genetic Diseases	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Chronic granulomatous disease (CGD) is a rare primary immune deficiency disorder characterized by recurrent bacterial or fungal infections starting in infancy. The x-linked form of CGD (X-CGD) is caused by mutations in the CYBB gene.
EN-374 is a helper-dependent adenoviral (HDAd)-based gene therapy in development for the treatment of X-CGD using an in vivo gene therapy approach.
Adult participants with X-CGD will be enrolled into the dose-escalation part of the study. Following completion of the adult cohorts, then pediatric participants will be enrolled into the dose-expansion part of the study

Who can participate?
Male patients with X-CGD who meet all inclusion and exclusion criteria listed below

What does the study involve?
EN-374 is administered by IV infusion to genetically modify hematopoietic stem cells (HSCs) to express a wild-type CYBB gene. The EN-374 treatment regimen includes HSC mobilization, immune prophylaxis, EN-374 administration, and enrichment of genetically modified HSCs.

What are the possible benefits and risks of participating?
Taking part in this study may or may not help treat participants with X-CGD. EN-374 is being studied for the first time in humans. The participants' health could improve, stay the same, or get worse. However, the data we get from the participants during this study may help doctors learn more about the study drug and the disease, and this may help future CGD patients.
Possible risks from similar gene therapy treatments include immune reactions, small blood clots, and abnormal cell growth. There are risks associated with each of the medications in the overall treatment regimen that are available in the Summary of Product Characteristics for each medication that is approved for other uses.

Where is the study run from?
Catalyst Clinical Research (UK)

When is the study starting and how long is it expected to run for?
August 2025 to December 2027

Who is funding the study?
Ensoma (USA)

Who is the main contact?
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Contact information

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Scientific, Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06876363

Integrated Research Application System (IRAS)
1011755

Central Portfolio Management System (CPMS)
67191

Protocol serial number
EN-374-101

Study information

Scientific Title
A Phase I/II open-label, single-ascending-dose study of EN-374, a helper-dependent adenoviral-based gene therapy, in participants with X-linked chronic granulomatous disease

Study objectives
Primary objective:
To evaluate the safety of the EN-374 treatment regimen and identify a dose level for further evaluation in participants with x-linked chronic granulomatous disease.

Secondary objective:
To evaluate the effect of the EN-374 treatment regimen on the production of functional neutrophils with NADPH oxidase activity.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/11/2025, South Central - Oxford A Research Ethics Committee (Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8241; oxforda.rec@hra.nhs.uk), ref: 25/SC/0165

Primary study design
Interventional

Study design
Non-randomized study

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
X-linked chronic granulomatous disease

Interventions
A single dose of EN-374 administered by intravenous infusion after mobilization and followed by enrichment

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
EN-374, O6BG [6-(phenylmethoxy)-1H-purin-2-amine]

Primary outcome(s)
Incidence rate across all age groups of treatment-emergent adverse events (TEAEs), treatment-related TEAEs (TRAEs), and serious adverse events (SAEs) recorded throughout the participants' involvement in the study

Key secondary outcome(s)
1. The percentage of dihydrorhodamine (DHR)+ neutrophils measured using flow cytometry at screening, day 15, day 29, day 57, day 85, month 4, month 5, month 6, month 9, month 12
2. The percentage of participants with ≥10%, 20%, 30%, 40%, or 50% DHR+ neutrophils measured using flow cytometry at screening, day 15, day 29, day 57, day 85, month 4, month 5, month 6, month 9, month 12

Completion date
01/12/2027

Eligibility

Key inclusion criteria
1. Male
2. Age: ≥18 years at the time of signing the informed consent form (ICF)
3. Diagnosis of X-CGD with DHR+ cells ≤5% and a pathogenic mutation in the CYBB gene
4. History of at least one severe infection requiring medical intervention or chronic inflammatory disorder
5. Does not have a suitable, available, and willing human leukocyte antigen (HLA)-matched (10/10) related donor
6.EN-374 capsid total antibody titer below threshold
7. Use of highly effective contraception
8. Informed consent
9. Adequate organ function as indicated by the criteria in the Protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Months

Upper age limit
100 Years

Sex
Male

Total final enrolment
0

Key exclusion criteria
1. Active bacteremia or fungemia
2. History of human immunodeficiency virus (HIV), hepatitis B, or hepatitis C
3. History or clinical evidence of any medical or social issues likely to put the participant at additional risk or to interfere with study conduct
4. History of HSCT or granulocyte transfusions
5. Known hypersensitivity to elements in the treatment regimen
6. Undergone investigational gene therapy
7. Treated with another investigational drug product within 30 days (or 5 half-lives) within 30 days before screening
8. Unable to comply with the visit and requirement of the protocol

Date of first enrolment
05/08/2025

Date of final enrolment
30/06/2027

Locations

Countries of recruitment
United Kingdom

England

United States of America

Study participating centre
University College London
-
London
England
WC1E 6BT

Sponsor information

Organisation
Catalyst Clinical Research

Funder(s)

Funder type
Industry

Funder Name
Ensoma

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date