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Extracorporeal Photopheresis (light treatment of white blood cells) in the treatment of Chronic Lung Allograft Dysfunction (chronic rejection): a randomised controlled trial

Submission date 27/08/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 03/11/2022	**Overall study status** Ongoing	
Last Edited 10/05/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Chronic lung allograft dysfunction (CLAD) is a complication that can happen after a lung transplant. CLAD develops when the immune system causes damage to the transplanted lungs, and lung function drops. It is also called chronic rejection. E-CLAD UK is a research study that aims to find out if a therapy called extracorporeal photopheresis (ECP) treatment can be used to treat CLAD. The research is being done by a team of specialists from all five UK adult lung transplant centres. ECP is currently used to treat various conditions involving the immune system. There have been a few small studies that suggest ECP could also help in the treatment of CLAD. However, there is currently not enough evidence for the NHS to say whether or not it should be used routinely to treat CLAD. The E-CLAD UK trial has been set up to answer this question.

Who can participate?
Double lung or heart and double lung transplant recipients aged 16 years and over with a confirmed diagnosis of CLAD.

What does the study involve?
The trial will involve 90 patients, who will all receive usual care for CLAD for 24 weeks. On top of that, half of these patients will also receive a course of ECP treatment. A course of ECP therapy involves 9 cycles of ECP treatment, every 2 weeks for 12 weeks and then 4 weekly until week 20. Each cycle involves 2 treatments, lasting between 2-3 hours on consecutive days. Both groups will continue all their routine clinic appointments with their transplant team.

What are the possible benefits and risks of participating?
The researchers can’t promise that taking part in this trial will benefit participants directly, although there is the possibility that the allocated treatments (either standard care or ECP) may help to treat CLAD. It is hoped that the information we get from this trial will help improve treatment for patients with CLAD in the future.

There are always risks with undergoing any trial procedure and all medical treatments can lead to side effects. The research team will monitor participants' health regularly to ensure their wellbeing. The main known side effect of ECP is that it will temporarily make patients more sensitive to sunlight, meaning that they will have to take extra care of the sun for at least 24 hours after treatment. Other side effects can include tiredness, dizziness, feeling cold and a mildly raised temperature for a short time following treatment.

Where is the study run from?
Newcastle Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
August 2022 to June 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Newcastle Clinical Trials Unit, e-clad@newcastle.ac.uk

Study website
https://research.ncl.ac.uk/e-claduk/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-002659-20

IRAS number
1005642

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
R&D10000/NU-000947, IRAS 1005642, CPMS 53956

Study information

Scientific Title
Extracorporeal photopheresis in the treatment of chronic lung allograft dysfunction: a randomised controlled trial

Acronym
E-CLAD UK

Study objectives
Primary objective:
To determine if extracorporeal photopheresis (ECP) therapy plus standard of care (SOC) is more effective at stabilising lung function in lung transplant recipients with chronic lung allograft dysfunction (CLAD) compared to SOC alone.

Secondary objectives:
1 To determine how the treatment strategies of ECP therapy plus SOC and SOC alone affect the following outcomes over a 24-week period
2. Change in rate of decline in lung allograft function between 12 weeks before (available from

clinical records) and 24 weeks after randomisation, measured by change in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC)
3. Absolute change in lung allograft dysfunction from baseline to 24 weeks, measured by FEV1 and FVC
4. Change in exercise capacity from baseline to 24 weeks measured by 6-minute walk test
5. Change in disease severity from baseline to 24 weeks measured by International Society for Heart and Lung Transplantation (ISHLT) CLAD Stage (1-4)
6. Change in health-related quality of life from baseline to 24 weeks measured by SF-36 v2 and EQ-5D-5L
7. Survival at 24 weeks after randomisation (end of study)
8. AEs and serious adverse events (SAEs) from randomisation to 24 weeks

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/10/2022, East Midlands - Derby Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 1048210; derby.rec@hra.nhs.uk), ref: 22/EM/0218

Study design
Open randomized controlled parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
https://research.ncl.ac.uk/e-claduk/ecladtrial/

Health condition(s) or problem(s) studied
Chronic lung allograft dysfunction

Interventions
Participants will be randomly allocated by a computer (Sealed Envelope) to one of two groups. One group will receive the current usual treatment for CLAD, and the other group will receive extracorporeal photopheresis (ECP) in addition to the current usual treatment. ECP involves the temporary removal of blood through a machine where white blood cells are separated, combined with a drug which makes them sensitive to ultraviolet light and then exposed to ultraviolet A light causing them to shut down before being returned to the bloodstream. ECP treatment will involve a course of up to 9 treatment cycles over a 20-week period with each cycle consisting of 2 individual treatments lasting 2-3 hours given on consecutive days. All participants will be closely monitored over a 24-week period.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
UVADEX [Methoxsalen]

Primary outcome measure
Lung function stabilisation is measured using change in FEV1 and FVC at 12 and 24 weeks compared to baseline at study entry

Secondary outcome measures
1. Rate of decline in lung allograft function measured using spirometry (FEV1 and FVC) at baseline and 24 weeks
2. Exercise capacity measured using distance walked in the 6 Minute Walk Test at baseline and 24 weeks
3. Disease severity measured by CLAD classification as per ISHLT guideline at baseline and 24 weeks
4. Health-related quality of life measured by the SF-36 v2 and EQ-5D-5L questionnaires at baseline and 24 weeks
5. Survival collected from medical records at 24 weeks
6. Safety measured by collecting details of adverse events and serious adverse events occuring between baseline and 24 weeks

Overall study start date
25/08/2022

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Adults (≥16 years of age) with body weight ≥30 kg
2. Bilateral lung or heart and (bilateral) lung transplant recipients
3. Confirmed diagnosis of CLAD stages 1, 2 or 3 as per ISHLT 2019 consensus definition
4. New CLAD diagnosis or prior diagnosis with evidence of current progressive disease
5. Exclusion of non-CLAD causes for decline in lung function by high-resolution computed tomography (HRCT) thorax and bronchoscopy +/- transbronchial biopsy within 12 weeks of first CLAD diagnoses
6. Adequate treatment of potential non-CLAD causes of a decline in lung function (e.g. acute cellular or acute humoral rejection, infections, airway anastomotic strictures and medical treatment for gastroesophageal reflux)
7. ≥3 recorded FEV1 and FVC measurements including home spirometry obtained at intervals of ≥3 weeks during the 26 weeks preceding randomisation
8. Progressive decline in FEV1 (≥10%) while on azithromycin for ≥6 weeks
9. Capacity to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
90

Key exclusion criteria
1. Single lung transplant recipients
2. Female patients who are breastfeeding, pregnant or planning to become pregnant during the timeframe of study participation
3. Current treatment with or past history of TLI completed within the last 12 months
4. ≤1-month wash-out from any other investigational therapies for CLAD
5. Inability to perform lung function tests or adhere to study protocol as judged by supervising clinician
6. History of Hematopoietic Stem Cell Transplantation (HSCT)
7. Patients who are on a retransplant waiting list
8. Current participation in another interventional clinical trial, or participation in a clinical trial of an investigational agent in the previous 4 weeks from consent
9. Patients with inadequate vascular access options to perform ECP
10. Any contraindication to receiving ECP. These include:
10.1. Previous allergic reaction to Methoxsalen, another psoralen compound, or any of the other UVADEX® ingredients
10.2. Co-existing untreated skin cancer (melanoma, basal cell or squamous cell cancer) if the patient deemed at higher risk of harm due to exposure to UVADEX or from their CLAD diagnosis
10.3. Any disease which involves sensitivity to light such as porphyria, systemic lupus erythematosus or albinism
10.4. Previous removal of spleen
10.5. Blood clotting disorder or an increased white blood cell count >25 x 10e9 per litre
10.6. Significant heart disease or severe anaemia causing inability to tolerate blood volume shifts associated with ECP
10.7. Aphakia or lens removed from either eye (unless already blind in eye without a lens)
10.8. Sexually active men and women of childbearing potential unless adequate contraception is used during treatment

Date of first enrolment
31/01/2023

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Harefield Hospital
Hill End Road
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United Kingdom
UB9 6JH

Study participating centre
Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Birmingham

United Kingdom
B15 2GW

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

Sponsor details
Joint Research Office
Regent Centre
Newcastle upon Tyne
England
United Kingdom
NE3 3HD
+44 (0)191 2825959
tnu-tr.sponsormanagement@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.newcastle-hospitals.org.uk/

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

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. Conference presentation
3. Publication on website
4. Submission to regulatory authorities

In alignment with the ethos of open science data from the study, with reasonable request a fully anonymised data set will be made available to independent researchers following the publication of the main outputs from the trial. Requests for data sharing will be reviewed by a Data Access Committee and subject to completion of a Data Sharing Agreement.

Intention to publish date
30/06/2027

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available upon request by bona fide teams at the end of the trial from Newcastle University. Requests will be considered by a Data Access Committee, and subject to presenting a clear plan of what the data will be used for, how the data will be analysed, how the results will be disseminated, and who the authors will be. Data transfer will be subject to the completion of a Data Sharing Agreement between Newcastle University and the end users.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol article		09/05/2024	10/05/2024	Yes	No