

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

<b>Submission date</b> 27/08/2022	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 03/11/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 31/07/2025	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## 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 2028

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

## Contact information

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Scientific

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**Additional identifiers****Clinical Trials Information System (CTIS)**

2022-002659-20

**Integrated Research Application System (IRAS)**

1005642

**Protocol serial number**

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

### **Study type(s)**

Treatment

### **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(s)**

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

### **Key secondary outcome(s)**

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 occurring between baseline and 24 weeks

**Completion date**

30/06/2028

## Eligibility

**Key inclusion criteria**

1. Adults ( $\geq 16$  years of age) with body weight  $\geq 30$  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.  $\geq 3$  recorded FEV1 and FVC measurements including home spirometry obtained at intervals of  $\geq 3$  weeks during the 26 weeks preceding randomisation
8. Progressive decline in FEV1 ( $\geq 10\%$ ) while on azithromycin for  $\geq 6$  weeks
9. Capacity to provide written informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

16 years

**Sex**

All

**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.  $\leq 1$ -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  $>25 \times 10^9$  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**

30/06/2027

## **Locations**

**Countries of recruitment**

United Kingdom

England

**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  
Harefield  
Uxbridge  
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

**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, Efficacy and Mechanism Evaluation (EME), EME

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## 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?
<a href="#">Protocol article</a>		09/05/2024	10/05/2024	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes