Newcastle University

E-CLAD UK

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E-CLAD UK

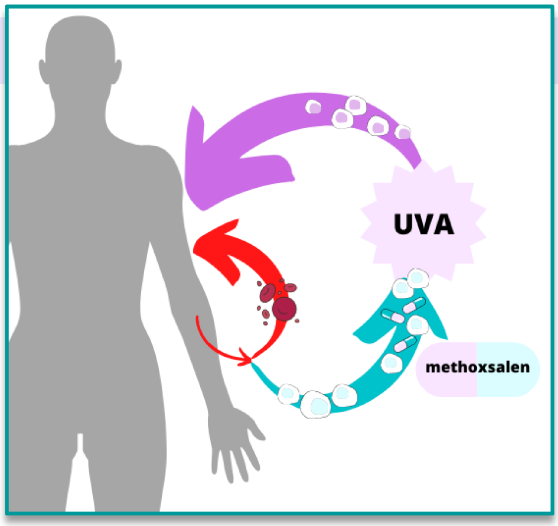
A research study to help improve treatment of chronic rejection after lung transplant

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 5 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.

This leaflet gives a short introduction to E-CLAD UK. Please ask your transplant team if you would like to find out more.



What is ECP?

ECP treatment involves passing a patient's blood through a machine that separates out the white blood cells. The red blood cells are returned to the body straight away.

The white blood cells are sensitised to light with a drug called methoxsalen, then exposed to UV (ultraviolet) light. This all happens inside the machine. The treated white blood cells are then returned to the body, where they trigger changes in the immune system.

This can help to stop the immune system from attacking the lungs, potentially slowing down or stopping the progression of CLAD.

What does the trial involve?

To find out if ECP can be used to treat CLAD, we need to compare its effects with the current usual treatment for CLAD that is available at the moment through the NHS.

The trial will involve 90 patients, who will all receive usual care for CLAD. On top of that, half of these patients will also receive a course of ECP treatment. When patients join the trial, they will be randomly allocated to one of these groups.

Standard care group → **45 patients will receive standard care (usual NHS treatment for CLAD) for 24 weeks**

ECP group → **45 patients will receive standard care (usual NHS treatment for CLAD) + a course of ECP therapy for 24 weeks**

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

E-CLAD Short PIS V2.0 14.10.2022 IRAS Ref: 1005642

Both groups will continue all their routine clinic appointments with their transplant team

Both groups will have monthly appointments with the research team to collect additional information and some additional blood samples

Both groups will be regularly monitored and treated appropriately throughout, including a **review after 12 weeks**. If the treatment you have been allocated doesn't seem to be working for you, you won't be stuck in the trial for 6 months– your doctor would explain other treatment options and you could leave the trial to access them at any point

Are there any benefits to taking part?

We can't promise that taking part in this trial would benefit you directly, although there is the possibility that the treatment you are allocated (either standard care or ECP) may help to treat your CLAD. We hope that the information we get from this trial will help improve treatment for patients with CLAD in the future.

Are there any risks to taking part?

There are always risks with undergoing any trial procedure and all medical treatments can lead to side effects. Your doctors and the research team will monitor your health regularly to ensure your wellbeing.

The main known side effect of ECP is that it will temporarily make you more sensitive to sunlight, meaning that you would 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.

Would I need to travel?

For both groups, your monthly appointments with the research team would be coordinated with your usual clinic appointments whenever possible.

If you are in the ECP group, you would need to travel to your lung transplant centre (or their nearby ECP unit) for your treatment. Treatment is given on 2 consecutive days, and travel and accommodation costs (if required) would be covered for you and a carer.

Would taking part in the trial delay my treatment?

No, you would receive treatment as soon as it can be arranged. You wouldn't have to wait until all 90 patients have joined the trial – we will recruit on a rolling basis, so you would get started on treatment as soon as possible.

What would happen at the end of the trial?

Altogether, you would be in the trial for 24 weeks. After that, you would continue to be cared for by your usual clinical team. Please note that ECP treatment cannot be provided by the trial after your participation in the trial has ended. Access to ECP treatment outside of the trial might be possible but it would depend on local arrangements and funding. Please discuss whether this would be an option for you with your clinical transplant team.

How will my information be used?

In this research study we will use information from you and your medical records. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. At the end of the study we will save some of the data in case we need to check it. We will make sure that no-one can work out who you are from the reports we write. The full information sheet tells you more about this.

Who can I speak to for more information?

Please speak to your transplant team who will be able to give you more details, including a full information sheet, and discuss the trial with you. Alternatively, scan this QR code with your smart phone or device for more information.

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Extracorporeal Photopheresis in the treatment of Chronic Lung Allograft Dysfunction (E-CLAD UK)

Participant Information Sheet

Why have I been invited to take part?

Chronic lung allograft dysfunction or CLAD for short, is a condition that affects how well transplanted lungs work and is caused by damage inflicted by the body's own immune system.

You have been given this information sheet because your transplant doctors think you may have developed CLAD, or because you were previously diagnosed with CLAD which is now worsening.

This means you may be eligible to take part in a research trial of a potential treatment and this sheet explains why this research is being done and what it would involve for you if you took part.

You can talk to your friends and family, transplant team or GP to help you decide if you want to take part. You will be given a minimum of 24 hours to think about it but can take as long as you need to make a decision.

A member of the research team will go through this information sheet with you and answer any questions you may have. If anything is unclear, or you need more information, please ask.

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Contents

1. What is the purpose of the trial?

People who have received a lung transplantation may experience a drop in their lung function months or years following their transplant. In some cases, this drop in lung function is because they have developed chronic lung allograft dysfunction (CLAD). CLAD happens when some of the white blood cells that normally make up your own immune system change their behaviour and attack your transplanted lungs reducing how well the lungs work.

One treatment currently used to treat a variety of different conditions affecting the immune system is called extracorporeal photopheresis (ECP). A few studies have used ECP to treat CLAD and these have shown promise at slowing the progression of CLAD. However, these studies were carried out in single hospitals in very selected patients and without careful comparison to those patients not getting ECP. This means there is currently not enough high-quality evidence that ECP is effective in treating CLAD for the NHS to use it routinely.

This clinical trial will assess if ECP can be successfully used to stop, or slow, the damage caused by CLAD and prevent lung function from deteriorating further. It will also help us to understand specifically how ECP works in the treatment of CLAD, which patients are most likely to benefit and ultimately help the NHS decide if ECP should be routinely used to treat CLAD.

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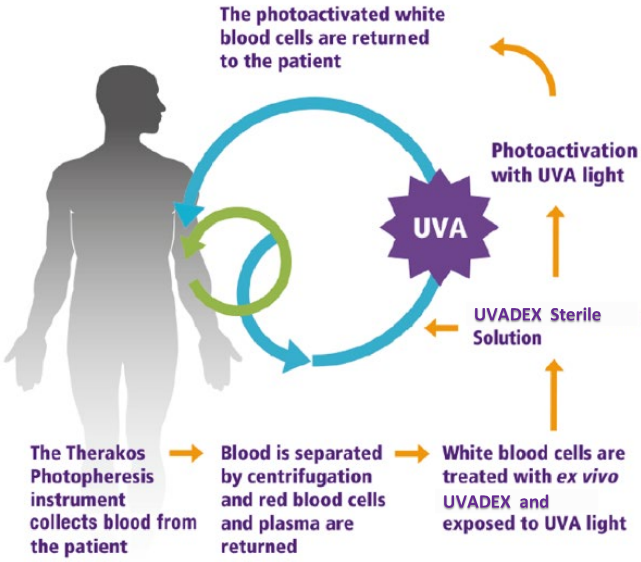
2. What is extracorporeal photopheresis (ECP)?

Extracorporeal photopheresis (ECP) is a treatment where some of your blood is taken from your vein, then circulated through an ECP machine (THERAKOS CELLEX System®) where the treatment of the white blood cells occurs before it is returned back into your vein.



Inside the ECP machine, your blood will be combined with a blood thinner (such as heparin) that will prevent it from clotting. Your blood is then passed through a centrifuge (that spins the blood) which separates the red blood cells and white blood cells. The red blood cells are then returned to your body immediately while the white blood cells are treated.

The white blood cells are combined with a drug called Methoxsalen (also called UVADEX), which makes them very sensitive to the effects of ultraviolet light. These white blood cells are then exposed to ultraviolet A (UVA) light inside the machine which causes them to shut down before being returned to your bloodstream. UVA light is found naturally in sunlight.

Some of the white blood cells called lymphocytes play an important part in regulating your immune system. The ultraviolet light modifies the function of the lymphocytes to stop your immune system from inflicting damage which may help to slow down the progression of CLAD.

3. Do I have to take part?

No, it is up to you to decide whether you want to take part in this trial. If you agree to take part, we will ask you to sign a consent form. If you decide not to take part, this will not affect your medical care and you will continue to receive the standard care for CLAD arranged by your doctor.

4. What would taking part in the trial involve?

This trial will recruit a total of 90 double lung transplant patients with CLAD from across all 5 adult lung transplant centres in the UK (Newcastle, Birmingham, London (Harefield), Cambridge and Manchester). Patients who have had a single lung transplant or are currently awaiting re-transplant will not be eligible to take part. Your doctor will fully discuss with you whether you are eligible to

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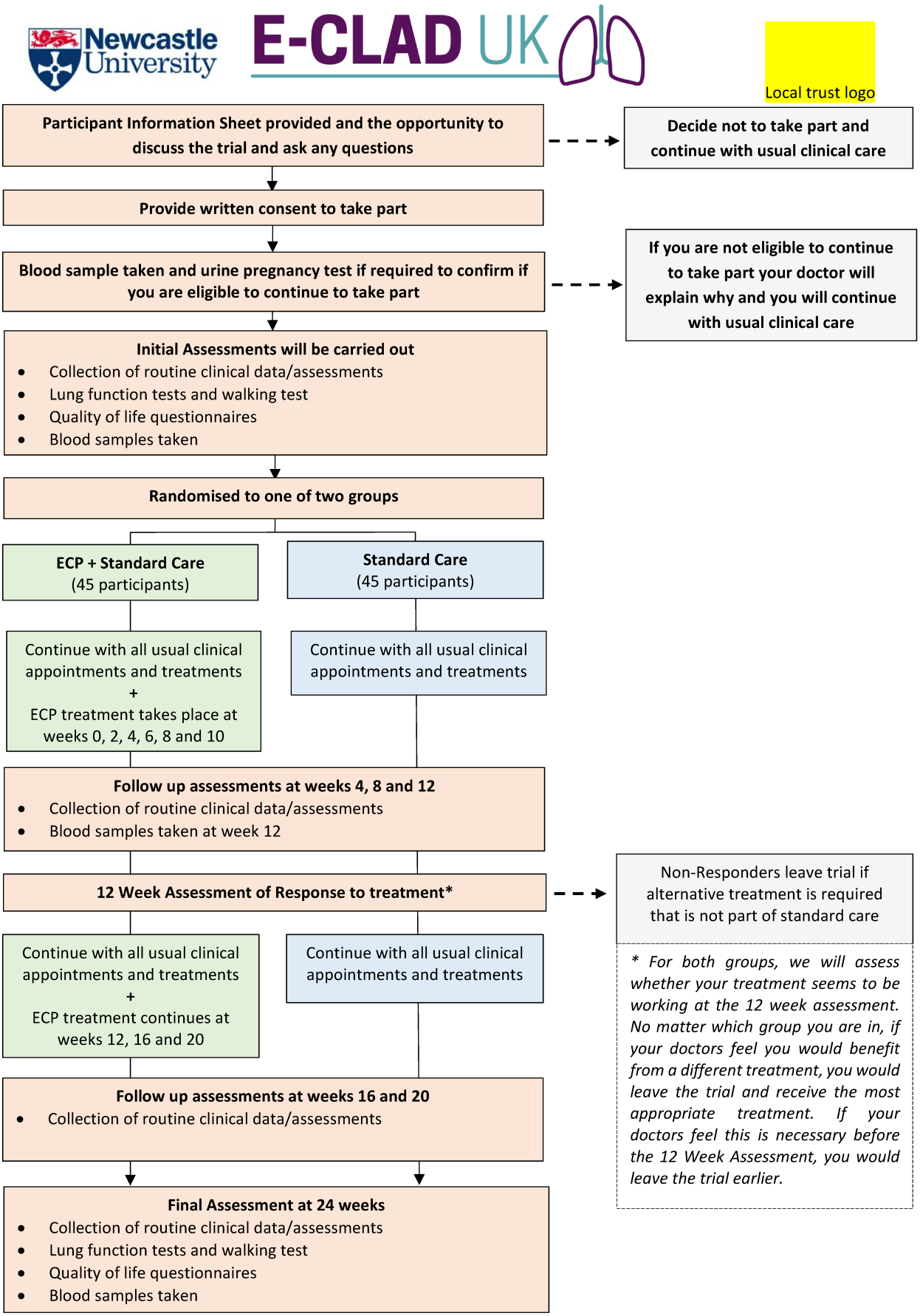
take part. Recruitment will take place on a rolling basis meaning that the treatment you are allocated will begin as soon as you have agreed to take part – you will not have to wait until all 90 participants are recruited before treatment begins.

Patients who are suitable to take part and give their consent will be randomly allocated by a computer to one of two groups.

One group will receive current usual treatment for CLAD, and the other group will receive ECP treatment in addition to current usual treatment. Both groups will be followed up closely to allow the research team to monitor what happens to lung function in the two groups.

Taking part in this trial involves attending between 7-11 hospital appointments over a 6-month period depending on if you are allocated to receive standard care or standard care and ECP. Where possible the trial assessments will take place when you are already attending your routine appointments in the transplant clinic. However, you will be required to attend additional appointments if you are randomised to receive ECP therapy.

The following flow chart outlines how you would progress through the trial depending on which group you are allocated to.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Participant Information Sheet provided and the opportunity to discuss the trial and ask any questions
Decide not to take part and continue with usual clinical care
Provide written consent to take part
Blood sample taken and urine pregnancy test if required to confirm if you are eligible to continue to take part
If you are not eligible to continue to take part your doctor will explain why and you will continue with usual clinical care
Initial Assessments will be carried out
Collection of routine clinical data/assessments
Lung function tests and walking test
Quality of life questionnaires
Blood samples taken
Randomised to one of two groups
ECP + Standard Care (45 participants)
Standard Care (45 participants)
Continue with all usual clinical appointments and treatments + ECP treatment takes place at weeks 0, 2, 4, 6, 8 and 10
Continue with all usual clinical appointments and treatments
Follow up assessments at weeks 4, 8 and 12
Collection of routine clinical data/assessments
Blood samples taken at week 12
12 Week Assessment of Response to treatment*
Non-Responders leave trial if alternative treatment is required that is not part of standard care
Continue with all usual clinical appointments and treatments + ECP treatment continues at weeks 12, 16 and 20
Continue with all usual clinical appointments and treatments
Follow up assessments at weeks 16 and 20
Collection of routine clinical data/assessments
Final Assessment at 24 weeks
Collection of routine clinical data/assessments
Lung function tests and walking test
Quality of life questionnaires
Blood samples taken
* For both groups, we will assess whether your treatment seems to be working at the 12 week assessment. No matter which group you are in, if your doctors feel you would benefit from a different treatment, you would leave the trial and receive the most appropriate treatment. If your doctors feel this is necessary before the 12 Week Assessment, you would leave the trial earlier.

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5. Initial Assessment

If you decide to take part in the trial, the research team will arrange to see you at your next clinic appointment. At this appointment a member of the trial team will talk through this information sheet and answer any questions that you have. If you still want to take part, you will be asked to give written informed consent and the trial team will check that you meet all the suitability criteria for the trial before carrying out any trial assessments.

Due to the potential side effects of ECP, you cannot take part in this trial if you are pregnant. People who have the potential to become pregnant will need to provide a urine sample for pregnancy testing at this first visit. Once the result of this pregnancy test is available your clinical team will let you know the result. If you have a positive pregnancy test you will not be able to take any further part in the trial.

You will be asked to provide a blood sample to check that it would be safe for you to potentially receive ECP treatment. Should the blood test reveal the need for additional caution or procedures connected to the ECP procedure then the research team will discuss this with you and whether you wish to continue in the study or not.

Collection of routine data

There are a number of tests or assessments that are carried out as part of routine care for people with CLAD. Rather than re-doing these tests as part of this trial, with your permission, we will collect the results from the routine tests already done, to use in the trial. These routine tests include:

- Blood test results
- Chest X-rays
- Lung Function Tests
- Physical assessments at clinic or in hospital

We will also collect some additional information from your medical notes including relevant medical history, current and previous medications and the results of lung function tests taken during the 3 months before your participation in this trial.

Research assessments

At this initial assessment you will also be asked to complete:

- Two questionnaires about how CLAD is affecting your quality of life
- A walking test to assess your ability to exercise
- Additional more detailed lung function tests

You will also be asked to provide four additional blood samples. We will collect approximately 17ml of blood (approx. 3 teaspoons).

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Randomisation

When these initial assessments are complete you will be randomly allocated by computer to one of the two groups:

1. Standard care group – who will receive usual (standard) care offered to patients with CLAD
2. ECP plus standard care group – who will receive usual (standard) care and ECP treatment

You will have an equal chance of being allocated to each group and the research team will explain which group you have been allocated to and what this means for you.

This initial assessment will take approximately 60 minutes in addition to your routine appointment.

6. What happens if I am allocated to standard care?

What happens if I am allocated Standard Care?

- You will continue to receive the current standard care for CLAD
- You will be seen by the research team approximately every four weeks (approximately 4, 8, 12, 16, 20 and 24 weeks after your initial assessment)
- At each of these assessments results from your routine blood tests, x-rays and lung function tests will be collected
- A 12 week assessment will be carried out to check if you are responding to treatment
- The research team will also document any relevant information from your medical notes, ask you about any changes to your health, including any changes in your treatments and medications and additional hospital visits you have attended
- The following additional research assessments will be carried out:
    - Four additional blood samples totalling approximately 17ml will be collected at your week 12 and 24 appointments only
- At your last appointment at 24 weeks, you will be asked to repeat the following research assessments:
    - Two questionnaires about how CLAD is affecting your quality of life
    - A walking test to assess your exercise tolerance
    - Additional lung function tests

You may also be approached before your involvement in this trial ends, to ask your permission to collect longer term follow up information. This is not compulsory and you can say no. If you do say no this will not impact on your care in any way.

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What does standard care involve?

Standard care consists of all the usual treatments and care you receive from your transplant centre to help maintain your overall health, your lung health and the best treatments currently available within the NHS for the treatment of CLAD. The specific choice of treatment will be led by your usual transplant doctors depending on how your condition progresses and will focus on treating the symptoms. This may include oxygen and medication to prevent or treat any infections. Physical rehabilitation and emotional support are also provided where required. A radiotherapy treatment called Total Lymphoid Irradiation or TLI which is sometimes used to treat CLAD won't be used during the trial as it might interfere with ECP. However, TLI may be available to use for any participant who leaves the trial because their CLAD has worsened.

7. What happens if I am allocated to receive ECP?

What happens if I am allocated ECP?

In addition to all the activity in the previous standard care section,

- You will also receive a course of up to 9 ECP treatment cycles over a 20 week period (each cycle will consist of 2 individual treatments which will be given on consecutive days - each treatment will last 2-3 hours)
- ECP treatment cycles will take place at 2 week intervals for the first three months (week 0, 2, 4, 6, 8, 10 and 12) and then every 4 weeks for the remainder of the treatments (week 16 and 20)*
- At each of these treatments results from your routine blood tests, x-rays and lung function tests will be collected
- You will be monitored for an additional 4 weeks after your last ECP treatment. This is to ensure your safety. This will be done via review of your medical records – you will not need to attend any additional hospital appointments as part of this.

  * Your first ECP treatment should take place within 2 weeks of your initial assessment. If for some reason your ECP treatment cannot start until after 2 weeks, you will be asked to repeat your initial lung function tests

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Wherever possible trial visits will take place at the same time as your routine clinical visits. For those in the ECP group, ECP treatments will take place at a dedicated NHS ECP unit where the clinical staff are specialists trained to deliver the treatment. This unit may be at the same hospital where you received your transplant, or it may be at another unit or hospital close by. Your local ECP site is XXXXXXXXXXXX. If you are required to travel between sites on the same day, transport will be arranged where required.

Preparing for ECP treatment

- In the couple of days leading up to your treatment you should ensure that you are well hydrated by drinking plenty of fluids such as water or juice and avoiding caffeine and alcohol.
- In the evening before and morning of your treatment you should avoid high-fat foods (eg cream, fried food, cheese etc).

What will happen on the day of ECP treatment?

- On the first day of your ECP treatment the clinical team supervising the procedure will ask you to sign a clinical consent form for treatment.
- You will then have blood samples taken (about two teaspoons or 9ml) to ensure that it is safe to treat you.
- One or sometimes two tubes (cannulas) will be inserted into veins in your right or/and left arm on the day of treatment. This is decided by the clinical team after assessing your veins.
- Blood will be removed through one cannula, circulated through the ECP machine and returned to you either via the same cannula or a second cannula. After each round of treatment the cannulas will be removed.

It can sometimes be difficult to reliably insert cannulas into the veins or sometimes these cannulas don't allow sufficient blood flow for ECP treatment to be completed successfully. If this happens a separate procedure may be required to insert a long-term fine tube into a large vein in your neck and tunnel the fine tube under the skin coming out in the upper chest. This is called a central venous catheter and is inserted under local anaesthetic. These are commonly used in patients who require treatments that regularly need access to blood including ECP. If a central venous catheter is required, it will stay in place for the duration of the ECP treatment (up to 20 weeks). This approach is required in approximately 30 % of patients receiving ECP.

If you have a central venous catheter this will be flushed and dressed as appropriate after each treatment. You will be able to have a shower or bath when the central venous catheter is in place, but some simple precautions will be required, in particular that the line must not be immersed in water. Specific guidance will be provided by your clinical team on how to look after your catheter to reduce the risk of infections. There is the possibility that a central cannula could become blocked, infected or stop working requiring it to be replaced. Should this be the case, your doctor will discuss this with you.

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8. Will you check that the treatment is working?

All participants will be reviewed 12 weeks after joining the trial to assess if they have responded to their treatment. This is to ensure the treatment is given enough time to take effect. For patients in the ECP group, this review will take place before you have the 7th cycle of ECP treatment.

However routinely collected lung function tests will be reviewed throughout the trial and if these suggest a significant progression of CLAD before the 12 week assessment then your doctor can stop the trial treatment straight away and discuss alternative treatments with you. The same will also apply after the 12 week review up to your completion of the trial.

Your doctor will not keep you on trial treatment if your lung function continues to decline significantly and they will discuss all treatment options with you throughout the trial. Taking part in this trial will not mean you are unable to access other treatments available to you. Should you stop trial treatment and commence any further treatment that is not current standard care for CLAD, you will be withdrawn from the trial. This will not affect your medical care in any way.

9. What happens after I have finished trial treatment?

You will continue to be cared for by your usual clinic team in the transplant centre after your final research visit at 24 weeks. Please note that ECP treatment cannot be provided by the trial team after your participation in the trial has ended. Access to ECP treatment outside of the trial might be possible but this will be dependent on your transplant team being able to make arrangements for this locally. Not all hospitals are able to offer ECP treatment so please discuss whether this would be an option for you with your clinical team. At present the effect of long term ECP treatment is not known in comparison to a set course of ECP treatment.

10. Are there any possible benefits of taking part?

We cannot promise that this trial will help you directly, although there is the possibility that the treatment you are allocated may help treat your CLAD. The information we get from this trial may also help improve the treatment of people with CLAD in the future. If you want to find out more about taking part in research studies, you can visit the NHS Choices website https://www.nhs.uk/conditions/clinical-trials/

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11. Are there any risks to my health in taking part?

There are always risks with undergoing a trial procedure and all treatments, regardless of any medicine used, can lead to side effects. If you feel unwell or feel that your health is being affected in any way, it is important that you inform the research team as soon as possible. Any side effects will be carefully recorded and treated. Allergic reactions may also occur and your clinical team will be able to treat you for this should it occur. Risks associated with taking a sample of blood from your arm include pain, bruising, light-headedness and on rare occasions, infection. Any medications you are taking will be reviewed by the research team at each visit to ensure any potential interactions are identified.

Risks involved with Central Venous Catheters

If you need a central venous catheter inserting to deliver the ECP treatment, then you will be shown how to look after it. As with anything that sits inside the body there is an added risk of infection. You will be told the signs of infection to look out for. On rare occasions it might be necessary to remove an infected catheter and reinsert a new one. You may initially experience slight pain, bruising and discomfort.

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What are the possible side effects of ECP?

ECP treatment is generally well tolerated, however a small number of patients may experience some side effects.

UVADEX, which is used in the ECP treatment, will make your whole body temporarily more sensitive to sunlight. You must therefore avoid sunlight both during and after the administration of your treatment. After treatment you should avoid sunlight for at least 24 hours because it may damage your skin by causing burning or, in the long term, premature ageing. When you go outside you should cover your skin, use a strong sun-blocking cream and wear wrap-around UVA-blocking sunglasses. These glasses should be worn for 24 hours after your treatment, to avoid the light damaging your eyes by causing cataracts to form. You will be provided with an ECP starter pack that includes key items such as sunglasses and sunscreen. This will be provided to you by your local research team prior to starting ECP.

Mild side effects seen with ECP include:

- Tiredness for about 12 hours after treatment
- You may also feel slightly dizzy or faint for a short time. You should arrive for treatment well hydrated and then eat and drink normally on the day of your treatment to minimise these effects.
- You may have a mildly raised temperature for a short time after the treatment. This does not normally interfere with your normal activities.
- A temporary (short-lived) tingling sensation around the extremities.

Although most patients receiving ECP have no significant problems, other side effects reported include:

- low blood pressure
- nausea (feeling sick)
- vomiting (being sick)
- infections
- damage to veins (as a result of repeated insertion of needle to the veins)

It is very unlikely that you would ever be given more UVADEX than you should be, however, if this were to happen, you may need to remain in a darkened room for 24 hours or longer as part of your treatment.

Please also note participants must not donate blood or sperm until one month after the final ECP treatment.

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12. What happens if I feel unwell?

If you feel unwell at any time please contact your transplant centre who can make an appointment for you to come into the unit if needed or refer you to other colleagues such as your GP as necessary. It will also be important that the research team know about any problems that you have, so please make sure that you also keep them informed by contacting them on the number at the end of this information sheet or on the patient safety card. If you experience a medical emergency, you should seek urgent medical attention as you would normally.

13. Pregnancy and contraception

The study drug UVADEX may cause fetal harm if given to somebody who is pregnant. Therefore, you must not enter this trial if you are pregnant or breast feeding. If you are sexually active and it's possible for you to become pregnant, you must agree to use appropriate methods of contraception throughout the trial. For the purposes of this trial a person is considered of child-bearing potential (fertile), following their first menstrual cycle up until becoming post-menopausal, unless they are permanently sterile. Any participants with a partner who could become pregnant must also agree to use contraception throughout the trial. Details of contraception options recommended for participants in this trial are listed at the end of this sheet.

14. What if relevant new information becomes available?

If, during the course of the trial, new information about ECP treatment or other CLAD treatments becomes available that is relevant to you, we will tell you about it. We will discuss whether you should or would like to stop the trial treatment or withdraw from the trial.

15. Given the Coronavirus pandemic, is it safe for me to take part?

We can reassure you that the study will follow all local and national NHS guidelines for Coronavirus. This trial does involve additional visits to hospital but wherever possible we will try to ensure that these take place when you are due to attend a routine appointment. For all visits the teams will follow all safety measures in place at that time regarding COVID-19. This may involve having to conduct lateral flow or PCR tests before attending for treatment or having to complete a period of self-isolation prior to attending for treatment. Your local team will inform you of any requirements but if you have any questions, at any time, about this study and Coronavirus please speak to your local team. Their contact details are listed at the end of this document.

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16. Optional Interviews

If you decide to take part in the E-CLAD UK trial you may be asked to take part in an additional interview. We would like to speak to approximately one third of those taking part in the trial to find out about people's views and experiences of taking part in the trial as well as their experiences of CLAD and its treatment. This will be done in an interview with a trained researcher. Interviews would take place in your own home by video conference (eg Zoom, Microsoft Teams) or by telephone. This is separate to the main trial, so you can still take part in the trial without agreeing to be interviewed.

You will be asked to indicate on the consent form if you would be willing to be contacted to take part in an interview. If you are selected, a member of your local research team will provide you with further information about how the interviews will be carried out. You will only be contacted with the opportunity to take part in the interview if you confirm on the consent form that you are happy to be approached. You can change your mind at any time and decide not to take part in the interviews.

17. What will happen to the samples collected?

Blood and urine samples that are routinely sent to the local hospital laboratory for analysis as part of your standard clinical care will be destroyed once a result has been confirmed in line with routine hospital practice. Blood samples that are collected for research purposes will be processed and some sent to a laboratory at Newcastle University for analysis and some to a commercial laboratory called Melio Health. If there is any research blood sample left over at Newcastle University after testing, these will be placed into a Newcastle University biobank called The Newcastle Institute of Transplantation Tissue Biobank for long term storage and future related analysis. Melio Health will destroy any remaining blood after analysis in line with national regulations.

At the start of the study you will be allocated a unique study ID number which will be used instead of your name on study documents. Only your local team will know this number links to you (more information provided in section 20 below).

All research samples will be also only use this unique study ID so that neither laboratory will be able to identify you.

18. Will my GP be informed of my participation in the trial?

If you become a trial participant, with your consent we will send your GP a letter informing them that you are taking part in the trial. This is so that your medical records at your GP practice and in the hospital contain documentation that you are taking part in a clinical trial. Any test results from taking part in the trial will be added to your medical notes.

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If you need to see your GP for any reason during the trial, please remind them that you are taking part in a research trial. We may also contact your GP if we need any information about you during the trial that is not available from your medical notes at the transplant hospital.

19. Will I receive any travel expenses and payments?

If you are randomised to ECP treatment for this trial, you will need to receive each ECP treatment on two consecutive days. The trial will provide reasonable travel and overnight accommodation costs for you and a carer (if appropriate) whilst you are receiving these ECP treatments. Your trial team will manage any payments to reimburse costs to you and you may be asked to provide receipts for your travel. Please speak to a member of the trial team for more details about this. No additional payments will be made for taking part in the trial.

20. Will I be able to withdraw from the trial?

Should you decide to, you would be free to withdraw at any time. You would not have to give a reason for withdrawing, but it is helpful to the trial if you do to help us to understand ways it can be improved.

If you withdraw from the trial before 24 weeks, or are withdrawn by your doctor for any reason, the information and any blood samples collected up to this point will be retained for analysis. We will ask you to complete the research assessments scheduled for the final week 24 visit at the time of your withdrawal. These are the full lung function tests, 6 minute walk test and quality of life questionnaires. If you withdraw or are withdrawn before the week 12 visit, we will also ask for your permission to collect a set of research blood samples at your final visit. You will also be asked if you are happy for us to continue collecting information from your medical notes where relevant to the trial. These are all entirely optional.

If you wish to withdraw from the trial, please contact the research team at the details below:

Telephone:

Email:

Address:

21. How will we use information about you?

We will need to use information from you and your medical records for this research project.

This information will include your name, date of birth, NHS number and contact details as per routine hospital practice. People will use this information to do the research or to check your records to make sure that the research is being done properly.

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People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. Only the trial team at your hospital will be able to link this number back to you using your date of birth, name and NHS number.

Where information needs to be shared with the wider research team, we will only use your Unique Subject ID, gender, ethnicity and age to identify you (not your name or NHS number).

Some parts of your medical records and the data collected for the trial may be looked at by authorised persons from the Sponsor (Newcastle upon Tyne Hospitals NHS Foundation Trust) and the Newcastle Clinical Trials Unit to check that the trial is being conducted to the correct standards. All will have a duty of confidentiality to you as a trial participant.

Your data which leaves the NHS Trust where you are being treated will be stored both electronically and in paper form. During the trial this will be held securely in databases, operated by a third party (called Sealed Envelope), but only accessible to the research team.

Once we have finished the study, we will keep some of the data so we can check the results. At the end of the trial, all trial information will be kept in a secure storage area (this is called archiving) for at least 5 years. This ensures any queries about the running of the trial can be answered. All information will be held in a way that ensures we protect your confidentiality, after which it will be safely destroyed.

When we publish the results of this trial or any research related to this trial, we will write our reports in a way that no-one can work out that you took part in the study.

22. What are your choices about how your information is used?

You can stop being a part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we will not be able to let you see or change the data we hold about you.

23. What will happen to the results of the trial?

The final results of the trial will be written for publication in medical journals and presented at meetings to other doctors, nurses, researchers and patients. A final report will be written for the trial funder and a patient and public advisory group will help the trial team develop a report

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specifically for patients and the public. You will be able to request a copy of the summary of the results from your trial hospital.

All trial data that is published will be anonymous. Fully anonymised data may also be made available to other researchers to help inform other research studies. Your identity will always be protected.

24. Who has reviewed the trial?

The trial has been reviewed by an NHS Research Ethics Committee. The Committee needs to be satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given sufficient information on which to make an informed decision to take part or not. The East Midlands- Derby Committee has reviewed this trial and agreed that it is ethical to proceed. This trial has also been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA), which is responsible for regulating clinical trials within the UK.

25. Who is organising and funding the research?

The trial is the responsibility of the Newcastle Upon Tyne Hospitals NHS Foundation Trust and is run in collaboration with Newcastle Clinical Trials Unit. Newcastle Clinical Trials Unit is based at Newcastle University.

The trial is funded by The National Institute for Health Research (NIHR) EME programme (reference NIHR130612). This body is funded by the UK government to carry out research for the benefit of the NHS and its patients.

26. What if something goes wrong?

We do not expect anything to go wrong as a result of you taking part in this research trial. If you have been harmed by taking part in this trial, you may have grounds for legal action and could seek compensation through the research sponsors, Newcastle upon Tyne NHS Foundation Trust, who have appropriate insurance-related arrangements in place. If the harm is due to routine clinical treatment or negligence, then the NHS indemnity arrangements will apply.

If you have a concern about any aspect of this trial, you can speak to a member of the trial team who will do their best to answer your questions. Further contact details are included at the end of this information leaflet.

If you prefer to raise your concerns with someone not involved in your care, you can contact the Patient Advice and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202

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Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department through any of the details below:

Telephone:

Email:

Address:

27. Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- in our leaflet available from https://www.newcastle-hospitals.nhs.uk/help/privacy/privacy-notice-for-patients/
- by asking one of the research team
- by sending an email to the Sponsor Data Protection Officer at nuth.dpo@nhs.net
- by ringing the Newcastle upon Tyne Hospital Data Protection Officer on 0191 223 1474

28. Contact for further information

For further information regarding the trial, or if you wish to discuss any matters related to the trial with a member of the research team, please contact us as detailed below:

Enter full address of recruiting NHS Trust

Enter contact details of lead Transplant specialist at the recruiting NHS Trust

Enter contact details of the research nurse team at the recruiting NHS Trust

You can also contact the Research and Development Department at the Trust for general advice using the following details:

Enter contact details of the R&D department at the recruiting NHS Trust

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As well as being able to contact the trial team for support at any point during the trial, there are also external organisations that you can approach to get support such as:

- The Samaritans Telephone: 116 123

General information about the study as well as updates on trial progress can be found on the publicly available website *website address*.

Thank you for taking the time to read this information

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Appendix 1 – Additional Research Blood Samples

We will also ask a small group of participants from Newcastle upon Tyne Hospitals NHS Foundation Trust for additional blood samples which will be taken both before and after ECP treatments. These samples will be used to help us understand how the ECP treatment works in the treatment of CLAD. Each sample will be for 20 ml of blood (approx. 4 teaspoons) and a sample will be taken both before and after your ECP treatment (2 x 20ml).

You will be asked to give written consent to these additional samples and giving these additional blood samples is entirely optional. You will still be able to remain in the trial if you do not consent to giving these additional blood samples.

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Appendix 2 - Description of contraceptive methods

For **participants who can become pregnant**, the following contraceptive methods are allowed:

- combined hormonal contraception (oral, intravaginal, transdermal)
- progestogen only hormonal contraception (oral, injectable, implantable)
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)
- bilateral tube occlusion or hysterectomy
- vasectomised partner
- practice true abstinence in line with preferred and usual lifestyle

In addition, their partner should use one of the following contraception forms from entry into the trial up until after the end of the ECP treatment:

- condom
- vasectomy
- practice true abstinence in line with preferred and usual lifestyle

If you become pregnant during the course of the trial, you must tell your trial doctor **immediately** so appropriate action can be discussed.

Any **participants with a partner who could become pregnant** must use contraception from entry into the trial up until after the end of the ECP treatment. In this case, the following contraceptive methods are allowed:

- condom
- vasectomy
- practice true abstinence in line with preferred and usual lifestyle

In addition to these acceptable methods of contraception, their partner also needs to use one of the following contraceptive methods:

- combined hormonal contraception (oral, intravaginal, transdermal)
- progestogen only hormonal contraception (oral, injectable, implantable)
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)
- bilateral tubal occlusion
- practice true abstinence in line with preferred and usual lifestyle

For participants whose partner could become pregnant:

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- If your partner becomes pregnant during the course of the trial, you must tell your trial doctor **immediately** so appropriate action can be discussed.
- If your partner becomes pregnant during the trial, we will ask them to sign a consent form. This will allow the trial team to collect safety information about the outcome of their pregnancy.

Trust headed paper

Extracorporeal Photopheresis in the treatment of Chronic Lung Allograft Dysfunction: a randomised controlled trial (E-CLAD UK)

Informed Consent Form

(confidential once completed)

Site Number: _____ Principal Investigator: _____

Participant Identification Number for this trial: _____

Please INITIAL the boxes below if you agree:

1.	I confirm that I have read and understood the E-CLAD UK Participant Information Sheet version_____, dated _____. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that I do not have to take part in this trial. I know that I can withdraw at any time and do not have to give a reason. I know that this will not affect my standard medical care or legal rights. I understand that if I withdraw from the trial, the information collected from me until that point will be retained and used.	
3.	I understand that parts of my medical records and data collected during the trial may be looked at by responsible people. I give my permission for these people to have access to my medical records. This includes people from the Newcastle Clinical Trials Unit, Newcastle University, trial Sponsor, regulatory authorities and local NHS Trusts where it is relevant to my taking part in research.	
4.	I understand that any personal information collected about me for the trial will be kept confidential and will not be made public. I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers. I understand I will not be directly identified in the published results of the trial.	
5.	I agree to my General Practitioner (GP) being informed of my participation in the E-CLAD UK trial.	
6.	I understand that the information provided in this trial is being managed by the Newcastle Clinical Trials Unit.	
7.	I agree to the information provided and this signed consent form being stored for 5 years after the end of the trial.	
8.	I understand that the research blood samples collected as part of this trial will be processed and sent to a central laboratory either Melio Health or Newcastle University where they will be immediately analysed.	
9.	I understand that at the end of study any leftover research blood samples held at Newcastle University will be transferred to The Newcastle Institute of Transplantation Tissue Biobank for long term storage and further related analysis outside of the trial. These samples will be anonymised.	
10.	I understand that blood and urine samples left over after analysis at either the local hospital laboratory or at Melio Health will be destroyed in line with national regulations and routine practice.	
11.	I understand that a copy of this consent form will be submitted to Newcastle Clinical Trials Unit for the purposes of central monitoring and will be destroyed following a documented check of the form. I give permission for these individuals to receive a copy of this form.	
12.	I understand that I may be approached regarding collection of longer term follow up information.	

For participants of childbearing potential		
13.	I understand that if I am of childbearing potential, I will need to provide a urine sample at the first visit to make sure that I am not pregnant. I understand that this is for safety reasons.	
14.	I understand that ECP treatment is contraindicated during pregnancy due to the potential risk to the unborn child from the treatment. If I am randomised to the ECP group, I agree that I have been informed about this and that it is my responsibility to use an appropriate form of contraception as has been explained to me, if sexually active.	
15.	I understand that if I become pregnant during participation in the trial, I must inform the research team as soon as possible. I consent to allow the research team to follow my pregnancy to completion.	

For participants with partners of childbearing potential		
16.	If I am randomised to the ECP group, I understand that I will have to agree to use the forms of contraception that have been explained to me, if sexually active. I understand that this is for safety reasons.	
17.	I understand that if my partner becomes pregnant during my participation in the trial, I must inform the research team as soon as possible. I understand that they will be approached to provide consent to allow the research team to follow their pregnancy to completion.	

Optional for ALL participants		
18.	I confirm that I am happy to be approached regarding the possibility of taking part in an interview and that relevant details can be passed to Newcastle Clinical Trials Unit and the qualitative research team at Newcastle University so that I can be contacted regarding this. I understand that not everyone who consents to be approached about taking part in interviews may actually be contacted.	
19.	I would like a summary of the results to be sent to me when the trial has finished.	

Optional for Newcastle participants		
20.	I confirm that I would be willing provide additional blood samples for research studies (before and after ECP treatment) if required.	

ALL participants		
21.	**I agree to take part in the E-CLAD UK trial.**	

STOP AND CHECK Please make sure you have initialled the boxes if you agree.

Name of participant	Signature	Date
Name of person taking consent	Signature	Date

When completed - original copy for Investigator Site File, 1 copy for patient and 1 copy for hospital records.