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Transplanting patches of skin with lung transplants to help prevent and detect rejection

Submission date
27/10/2023

Recruitment status
Recruiting

Registration date
22/11/2023

Overall study status
Ongoing

Last Edited
04/11/2025

Condition category
Other

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Transplanted organs such as lungs, hearts, kidneys and pancreases are subject to attack by the immune system causing rejection of the transplanted organ. Rejection is prevented by immunosuppression medication that interferes with the body's immune system and hinders rejection. Despite these medications rejection still occurs. If rejection is not detected and treated early enough the transplanted organ scars and stops working. Detecting rejection is difficult as it does not have specific features. In lung transplants attempts are made to detect rejection by frequent hospital visits for chest x-rays, blood tests and biopsies of the transplanted lung performed by putting a tube into the airway down into the lung. These tests are performed very regularly or of the patient has symptoms of lung disease such as cough. All these tests can show are if there is inflammation but there is no specific measure of rejection until the rejection is very severe.
We discovered when we were doing intestinal transplants which included skin transplants that the skin displayed a easily visible rash when rejection was occurring, and that this sign was present before the intestine transplant rejected. The skin was visible continuously, so we did not have to rely on intermittent biopsies or other tests, but only performed these when the skin indicated there was rejection. As a result of this we began a trial, transplanting a patch of skin with pancreas and kidney transplants. Our preliminary results show that the skin not only acts as a monitor for rejection but also reduces the risk of rejection in transplants.
We wish to repeat this study in lung transplants to see if a skin transplant can act as a rejection monitor for lung transplants, reduce the immune suppression drug levels, and avoid rejection injury to the lungs.
The aim of the SENTINEL study is to find out whether transplanting both lung and a patch of skin (called a sentinel skin flap) from the same donor helps to reduce rejection of the lung.
The skin will be transplanted onto the under-surface of the lower arm.

Who can participate?
Adults over 18 years, scheduled for lung transplant surgery.

What does the study involve?
SENTINEL is a randomised study: We are making a direct comparison between people who have lung transplant only or lung transplant and sentinel skin flap. Patients who agree to participate

in the study will be randomly allocated to one of the treatment groups. We are inviting everyone who is waiting for lung transplant to consider taking part. The study will transplant 152 people: half will get a skin flap with their lung transplant, and the other half will not. We will follow patients up over 12 months. They will attend their usual hospital visits 3, 6 and 12 months after transplant. At these visits, clinical and research biopsies and other samples will be collected. We will record lung function and quality of life measures as well. We will investigate any suspected episodes of rejection, and we will record data and take samples on these occasions.

What are the possible benefits and risks of participating?
The only extra tests we do as part of the study are blood tests and skin biopsies taken at standard appointments. There is a risk that patients may not like the skin flap. If this is the case, we can remove it. This study will provide evidence which we hope will change the pathway for lung transplant and improve outcomes for patients. It could also help pave the way for skin flap transplant to be used in all organ transplants.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
March 2023 to September 2028

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

Who is the main contact?
Professor Henk Giele, henk.giele@nds.ox.ac.uk, Henk.giele@mac.com
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Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
318347

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 55602, NIHR130899, IRAS 318347

Study information

Scientific Title
Efficacy and mechanism of sentinel skin flap reduction of solid organ (lung) transplant rejection: A randomised controlled trial

Acronym
SENTINEL

Study objectives
Sentinel Skin Flaps will reduce the incidence of lung transplant rejection in the first 12 months compared to lung transplant alone

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/05/2023, London - Queen Square Research Ethics Committee (HRA NRES Centre Bristol, 3rd floor, block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 207 104 8284; queensquare.rec@hra.nhs.uk), ref: 23/LO/0248

Study design

Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Organ rejection

Interventions
The participant will be randomised either to receive lung alone or lung and skin flap transplantation. If randomised to lung and skin flap transplantation then at the time of their lung transplant a sentinel skin flap measuring 10 by 3 cm will be placed into an incision on the under surface of their forearm. None of the patient's skin will be removed so that should the patient wish the sentinel skin flap can be easily removed at the end of the study under local or general anaesthetic and all the patients will be left with will be a linear scar 10-12 cm in length under the forearm.
At the time of the operation a small biopsy of the patient's skin taken from the edge of the incision and from the edge of the donor flap will be stored. A blood sample as well as a sputum sample and sample of the removed diseased lung will also be taken for analysis. Before the patient is discharged, they will be taught what skin changes to look for and given contact numbers of the transplant and study team to contact if they have any questions or feel they may have a change in the skin.
Subsequently skin biopsies from the skin flap will be taken (without local anaesthetic as the skin is numb) when the patient visit for their routine post-lung transplant follow ups and tests, 3,6 and 12 months after the transplant. These routine skin biopsies will be analysed and reported by the local pathology service with the results of the routine tests also reported to the research team, Skin microbiological swabs of the skin flap and adjacent native skin as well as 10 mls of blood taken at the same time as the routine tests will be taken for analysis by the research team in Oxford.
Should the patient notice any rash or symptoms suggestive of lung rejection they will attend the transplant unit and undergo the usual investigations of the transplanted lung, and in addition a biopsy of the skin flap will be performed.
The biopsies will be assessed for rejection by the local pathology service and stored for later analysis in Oxford.

If randomised to lung only, then no skin biopsies will be taken but skin microbiological swabs and 10 mls of blood will be taken at the routine visits at 3,6 and 12 months and sent to Oxford for later analysis. Any lung biopsies taken as part of routine care in either group may be later analysed, but no study specific lung biopsies will be performed.
At the end of the 12-month study period the patients will be offered removal of the skin flap (which can be done under local or general anaesthetic) or they may choose to retain it.
We intend to randomise 152 patients, 76 patients into each arm of the study. We have performed sentinel skin flaps in 30 patients so far with pancreas transplants and 37 in combination with intestinal transplants and based on the expected rejection rate in lung transplants which compares to those in pancreas and intestinal transplants indicates the numbers required to reliably demonstrate effectiveness. Each patient will be enrolled in the study for 12 months.
There will be no increase in hospital visits as samples will be collected during routine planned

visits or when the possibility of rejection indicates a hospital visit is needed. We predict that we should be able to recruit all the patients required for the study within 36 months.
This study has been designed with the help of the transplant surgeons and physicians, immunologists, NHSBT and specialist nurses for organ donation, as well as transplant patients (and their carers) some of whom have had a sentinel skin flap.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Lung rejection event in the first 12 months, diagnosed by clinical criteria and/or biopsy (ISHLT grade A≥1 for lung)

Key secondary outcome(s))
1. Diagnostic accuracy (sensitivity, specificity, negative predictive value and positive predictive value) of the sentinel skin flap compared to current reference standard (biopsy and/or clinical diagnosis): collected over 12 months
2. Safety of SSF transplant: number of rejection events:
2.1. Number and severity of skin flap rejection episodes (defined by biopsy BANFF grade ≥ 1) and time to first rejection diagnosis measured using biopsy in the first 12 months after transplant
2.2. Transplanted lung and patient survival measured at 12 months
2.3. Transplant lung function measured using lung function tests at 12 months
2.4. Surgical complications and complications relating to the SSF (such as infection, skin loss, nerve injury) measured using clinical parameters at 12 months
2.5. Development of de-novo donor specific antibodies measured using blood tests at 12 months
2.6. Development of graft versus host disease measured using blood chimerism at 12 months
2.7. Evidence of chronic rejection in lung measured using international criteria at 12 months
3. Immunosuppression levels and requirements measured using drug monitoring at 12 months
4. HRQoL as measured by the following validated questionnaires: SF-36; EQ-5D-5L and DAS-24 at baseline, 6 and 12 months.

Completion date
01/09/2028

Eligibility

Key inclusion criteria
1. Intended recipient of a lung transplant
2. Aged 18 years or over
3. Capable of giving informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the study, or may influence the result of the study, or the participant’s ability to comply with trial procedures
2. Severe peripheral vascular disease with no vessels available for inset of the skin flap

Date of first enrolment
15/12/2023

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
Harefield Hospital
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
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United Kingdom
SE1 7EH

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way

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B15 2GW

Study participating centre
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The Newcastle upon Tyne Hospitals NHS Foundation Trust
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High Heaton
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NE7 7DN

Study participating centre
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Manchester University NHS Foundation Trust
Cobbett House
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR EME

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	19/04/2023	15/11/2023	No	Yes
Participant information sheet	Summary participant information sheet version 1.0	14/02/2023	15/11/2023	No	Yes
Participant information sheet	version 2.0	01/12/2023	28/02/2024	No	Yes
Participant information sheet	version 3.0	14/02/2024	28/03/2024	No	Yes
Participant information sheet	version 4.0	13/06/2025	19/08/2025	No	Yes
Protocol file	version 1.1	27/04/2023	15/11/2023	No	No
Protocol file	version 2.0	15/11/2023	28/02/2024	No	No
Protocol file	version 3.0	07/02/2024	28/03/2024	No	No
Protocol file	version 4.0	13/06/2025	19/08/2025	No	No