

Can the use of decellularised dermis allograft (DCD) help improve ulcer healing in patients with chronic venous leg ulceration?

Submission date 12/08/2019	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 13/08/2019	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 23/02/2024	Condition category Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

A large number of patients (around 1% of the adult population) suffer from an ulcer (break in the skin surface) near the ankle. In most people, such an injury should heal up within a week or two. However, many ulcers do not heal and may result in longstanding (chronic), painful, smelly and embarrassing wounds. Compression bandaging is the main standard of care for these patients, which corrects the underlying venous hypertension and helps the ulcer to heal. Skin grafting can act as an additional therapy to compression bandaging to aid healing. Skin grafts can be taken from the patient's own skin, from a donor or from tissue-engineered skin. Graft from the patient's own skin is often taken from the thigh but can result in scarring in the area from which it is taken and the procedure needs to be performed in a surgical theatre. Grafts from donor and animal skin have been successfully employed, but have the risk of being rejected and disease transmission. The DCD graft is made from human skin from deceased donors which has been processed to remove the human cells and leave a matrix behind. DCD contains no human cells, unlike other donated skin grafts, which means that it is unlikely to be rejected by the body. The graft is placed over the ulcer and secured into place with glue, staples or stitches and then covered with a dressing so that compression bandaging can be placed on top. The DCD acts as a scaffold into which the body's own cells can grow and generate new skin and therefore does not need to be removed. The aim of this study is to see if using DCD grafts in addition to compression bandaging can help leg ulcers to heal quicker.

Who can participate?

Patients aged 18 or over who have had a venous leg ulcer for longer than 6 months

What does the study involve?

Participants are randomly allocated to one of two treatments: either compression bandaging alone, or compression bandaging and a DCD graft. Participants are followed-up for 1 year and undergo routine leg ulcer care in community or hospital (or both) settings, in accordance with the local standard care. Participants attend clinic visits (in person until the ulcer has healed or by telephone once the ulcer has healed) at 1 week, 3 weeks, 6 weeks, 12 weeks, 6 months, 9 months and 12 months. Patients are contacted by telephone in between visits to check for ulcer

healing, and are invited for a visit to confirm healing if the patient reports that it has healed. Once healing has been confirmed, patients are contacted monthly by telephone to ask if the ulcer has returned. The researchers will look at the number of ulcers healed in both patient groups and the speed at which the ulcers healed and whether they came back. They also ask the patients to complete health questionnaires at the first visit, 12 weeks, 6 months and 12 months to see if there were any changes in their quality of life following treatment. Furthermore, they look at the costs of the two treatments.

What are the possible benefits and risks of participating?

The advantage of DCD allograft is that it can be applied to the wound without an admission for a procedure under general anaesthetic, and does not have a risk of scarring at the graft site. The decellularisation process removes the cells that could contain intracellular viruses and prions, and the graft undergoes a sterilisation process which means the graft is in the lowest risk category for disease transmission. It is possible that patients could have an allergic reaction to the graft, although to date there have been no documented cases of disease transmission or allergic reaction. In addition, the wound or graft could get infected or suffer from fluid buildup which could dislodge the DCD graft, although this can be minimized by making cuts into the graft prior to application.

Where is the study run from?

The study is sponsored by Imperial College London, where the trial manager is based. The data management and statistical support is provided by Edinburgh Clinical Trials Unit

When is the study starting and how long is it expected to run for?

April 2019 to March 2023 (updated 30/07/2021, previously: March 2022)

Who is funding the study?

The Jon Moulton Charitable Trust

Who is the main contact?

Valeria Balan, valeria.balan22@imperial.ac.uk

Contact information

Type(s)

Scientific

Contact name

Ms Valeria Balan

Contact details

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

NCT04021316

Secondary identifying numbers

42168

Study information

Scientific Title

Decellularised dermis allograft for the treatment of chronic venous leg ulceration

Acronym

DAVE

Study objectives

Chronic venous ulceration are open wounds on the lower limbs which have been present for at least six months and are caused by a poorly functioning venous system. They affect about 1% of the general population and about 4% of those over 65. The wounds cause pain, reduced movement, and can smell - greatly affecting the quality of life of leg ulcer patients. The standard care for these patients is compression bandaging, which requires changing several times a week by community or district nurses; this drives the high cost of leg ulcer care, which can amount to £2.5 billion per annum.

Skin grafting can be used alongside compression bandaging and can help the ulcers heal faster than compression alone. Grafts can be taken from the patient's own skin, from a donor or from tissue engineered skin. An autograft (using own skin) can cause scarring and the need for a formal surgical procedure in theatre so are not suitable for all ulcer patients. Allografts (donor skin) and xenografts (animal skin) have been used successfully, but present similar drawbacks to autografts, plus the potential for the body to reject the graft and disease transmission. Tissue engineered skin has several advantages as it has been processed to remove the cells, and therefore won't be rejected via the immune response. Human decellularised dermis (DCD) is generated from donated skin from deceased people and processed to remove the cells. It can be glued or sewn onto the skin under local anesthetic, in an outpatient setting. DCD has mainly been studied in patients with diabetic foot ulceration and has shown improved healing rates and quality of life.

This study will investigate the use of DCD in addition to compression therapy versus compression therapy alone in patients with chronic venous leg ulceration.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 15/08/2019, London - Bloomsbury Research Ethics Committee (HRA RES Centre Manchester, Barlow House 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; Tel: +44 (0) 2071048127; Email: nrescommittee.london-bloomsbury@nhs.net), REC ref: 19/LO/1271

Study design

Randomised; Interventional; Design type: Treatment, Surgery, Other

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Chronic venous leg ulceration

Interventions

Patients will be randomly allocated to one of two treatments: either compression bandaging alone, or compression bandaging and a DCD graft. Participants will be followed-up for 1 year and will undergo routine leg ulcer care in community or hospital (or both) settings, in accordance with the local standard care. Participants will attend clinic visits (in person until the ulcer has healed or by telephone once the ulcer has healed) at 1 week, 3 weeks, 6 weeks, 12 weeks, 6 months, 9 months and 12 months. Patients will be contacted by telephone in between visits to check for ulcer healing, and will be invited for a visit to confirm healing if the patient reports that it has healed. Once healing has been confirmed, patients will be contacted monthly by telephone to ask if the ulcer has returned. The researchers will look at the number of ulcers healed in both patient groups and the speed at which the ulcers healed and whether they came back. They will also ask the patients to complete health questionnaires at the first visit, 6 weeks, 6 months and 12 months to see if there were any changes in their quality of life following treatment. Furthermore, they will look at the costs of the two treatments.

Added 18/12/2020:

A qualitative sub-study has been embedded into the current study and will utilise the Theoretical Framework of Acceptability (TFA) to explore both participant and healthcare provider (HCP) attitudes towards the acceptability of the intervention, as well as general experiences. Semi-structured, one-to-one interviews will be held with patients assigned to the intervention arm and HCPs involved in applying the DCD graft. All the interviews will be audio-recorded (with consent) and transcribed verbatim. Two members of the team will participate in data analysis to ensure transparency and credibility of the themes that are identified and their interpretation. Data will be analysed using thematic analysis. The qualitative study will be conducted in line with and written up in accordance with the COREQ guidelines.

Intervention Type

Procedure/Surgery

Primary outcome measure

Proportion with a healed index ulcer assessed with ulcer photography at 12 weeks after randomisation

Secondary outcome measures

Current secondary outcome measures as of 16/04/2020:

1. Time to index ulcer healing from randomisation, assessed with ulcer photography at 12 months
2. The percentage change in index ulcer area in cm² measured with ulcer planimetry at 12 weeks from randomisation
3. The proportion of participants with a healed index ulcer assessed with ulcer photography at 12 months from randomisation
4. The proportion of participants whose index ulcer healed for whom an ulcer recurred at the index site assessed with telephone self-report within 12 months from randomisation
5. Generic quality of life measured using the EuroQol-5D (EQ-5D) questionnaire at 12 weeks, 6 months and 12 months from randomisation
6. Disease-specific quality of life measured using the Charing Cross Venous Ulcer Questionnaire (CCVUQ) at 12 weeks, 6 months and 12 months from randomisation
7. The cost for each patient, calculated from the healthcare resources used at 12 months
8. Incremental cost-effectiveness ratio (ICER) from the EQ-5D questionnaire with appropriate sensitivity analysis at 12 months

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Overall study start date

01/04/2019

Completion date

31/03/2023

Reason abandoned (if study stopped)

Objectives no longer viable

Eligibility

Key inclusion criteria

Current inclusion criteria as of 16/04/2020:

1. ≥ 18 years or older (no upper age limit)
2. The ability to consent to participation
3. A diagnosis of venous leg ulceration* (defined as 'colour duplex confirmation of superficial and or deep venous reflux with any break in the skin that has either: a) been present for more than 2 weeks, or b) occurred in a person with a history of venous leg ulceration)
4. A wound duration of at least 6 months
5. Documented venous incompetence on duplex ultrasound
6. Ulcer wound size $> 2 \text{ cm}^2$.
7. $\text{ABPI} \geq 0.8$, or if the ABPI is incompressible, other forms of clinical assessment must exclude peripheral arterial disease (peripheral pulse examination, toe pressure, duplex ultrasound, clinical judgment)

*if more than one ulcer is present, the largest ulcer will be chosen as the reference ulcer for the purposes of the trial

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1. ≥ 18 years or older (no upper age limit)
2. The ability to consent to participation
3. A diagnosis of venous leg ulceration* (defined as 'colour duplex confirmation of superficial and or deep venous reflux with any break in the skin that has either: a) been present for more than 2 weeks, or b) occurred in a person with a history of venous leg ulceration)
4. A wound duration of 6 to 24 months inclusive
5. Documented venous incompetence on duplex ultrasound
6. Ulcer wound size $> 2 \text{ cm}^2$.
7. $\text{ABPI} \geq 0.8$, or if the ABPI is incompressible, other forms of clinical assessment must exclude peripheral arterial disease (peripheral pulse examination, toe pressure, duplex ultrasound, clinical judgment)

*if more than one ulcer is present, the largest ulcer will be chosen as the reference ulcer for the purposes of the trial

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 196; UK Sample Size: 196

Total final enrolment

Key exclusion criteria

Current exclusion criteria as of 16/04/2020:

1. A diagnosis of sickle cell
2. Unable to receive one or more of the randomised treatment strategies for any reason at the discretion of the attending clinical team (e.g. known allergies to dCELL dermis preparation components)
3. A clinically infected ulcer defined as evidence of erythema, cellulitis or systemically unwell
4. Treatment with biomedical/topical growth factors within previous 30 days
5. Previous history of an inability to tolerate compression therapy
6. Foot ulcer (i.e. below the ankle)

Previous exclusion criteria:

1. A diagnosis of sickle cell
2. Known sensitivities to any of the reagents/antibiotics listed on the DCD package insert
3. A clinically infected ulcer defined as evidence of erythema, cellulitis or systemically unwell
4. Treatment with biomedical/topical growth factors within previous 30 days
5. Previous history of an inability to tolerate compression therapy
6. Foot ulcer (i.e. below the ankle)

Date of first enrolment

01/10/2019

Date of final enrolment

30/09/2022

Locations**Countries of recruitment**

England

United Kingdom

Study participating centre

Imperial College Healthcare NHS Trust

St Mary's Hospital

Praed Street

London

United Kingdom

W2 1NY

Study participating centre

Worcestershire Acute Hospitals NHS Trust

Worcestershire Royal Hospital

Charles Hastings Way

Worcester

United Kingdom
WR5 1DD

Study participating centre

Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

London North West University Healthcare NHS Trust
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre

Gloucestershire Hospitals NHS Foundation Trust
Trust HQ
Alexandra House
Cheltenham
United Kingdom
GL53 7AN

Study participating centre

North Cumbria University Hospitals NHS Trust
West Cumberland Hospital
Hensingham
Whitehaven
United Kingdom
CA28 8JG

Study participating centre

University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road

Plymouth
United Kingdom
PL6 8DH

Study participating centre
Taunton and Somerset NHS Foundation Trust
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Trust Offices
Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Basildon and Thurrock University Hospitals NHS Foundation Trust
Basildon University Hospital
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Sponsor information

Organisation

Imperial College of Science, Technology and Medicine

Sponsor details

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becky.ward@imperial.ac.uk

Sponsor type

University/education

ROR

<https://ror.org/041kmwe10>

Funder(s)**Funder type**

Charity

Funder Name

J P Moulton Charitable Foundation; Grant Codes: P79954

Results and Publications**Publication and dissemination plan**

1. The researchers aim to publish the protocol and will post the SAP to the trial website once finalised
2. Peer-reviewed scientific journals
3. Conference presentation
4. Publication on website
5. Participants will be informed of the results by a newsletter

Intention to publish date

31/03/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Sarrah Peerbux (s.peerbux@imperial.ac.uk). Raw anonymised data can be

requested after publication. Available for 10 years after end of trial. Requests will be approved by the Chief Investigator on a case by case basis.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		02/04/2021	06/04/2021	Yes	No
HRA research summary			28/06/2023	No	No