ISRCTN99737999 https://doi.org/10.1186/ISRCTN99737999

Topical alprostadil in patients with systemic sclerosis

Submission date
06/10/2025

Recruitment status
No longer recruiting

Registration date
22/10/2025

Overall study status
Completed

Last Edited
07/10/2025

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
Digital vasculopathy (damage to the blood vessels of the hands/fingers) is a key feature of Systemic Sclerosis (otherwise known as scleroderma) and can result in Raynaud's Phenomenon (cold hands/feet), digital (finger) ulcers and gangrene. The currently used treatments (a group of drugs called prostanoids) are administered intravenously, requiring a few days stay in hospital. Such treatments are poorly tolerated due to side effects and can require dose reduction or discontinuation of the medicine. There is an unmet need for locally acting, topical medicines (applied to the skin) to treat digital vasculopathy. These would likely be better tolerated (avoiding systemic administration), and more convenient (administered at home).

This is a physiological study to examine the effect of topical alprostadil (an analogue of prostaglandin E1), on digital vasculopathy in patients with Systemic Sclerosis (SSc).

Who can participate?
Patients with a confirmed diagnosis of systemic sclerosis (often referred to as 'scleroderma'), who are 18 years of age or older and who attend Salford Royal Hospital for their care can take part in this study.

What does the study involve?
Twenty patients with SSc will be recruited to the study. Participants will be asked to attend Salford Royal Hospital for a single (morning) study visit, lasting approximately two hours. Participants will be asked to sign consent, provide clinical data relating to their condition and have their finger skin thickness assessed (both manually, by a clinician, and automated, by High Frequency Ultrasound Imaging). Participants will then receive the treatment intervention. Alprostadil, placebo (dummy drug) and no treatment will be applied to the index, middle and ring fingers of each participant in a randomised order. Alprostadil and placebo (creams) will be applied manually by study investigators to the backs of participants fingers. This will be rubbed in for 60 seconds. Study investigators wish to understand how the skin (blood flow and temperature) reacts to the treatment intervention. To do this they will measure the blood flow (using Laser Doppler Imaging) and temperature (using Thermography) of the participants fingers immediately before, directly after, and then every 10 minutes for 90 minutes after the treatment intervention.

What are the possible benefits and risks of participating?
The study will not have any direct benefits for participants, but it will help researchers in their understanding of scleroderma. There will be no immediate benefit for participants from the 'one off' application of study drug, alprostadil. This is a physiological study to determine if local application of alprostadil to participant's fingers can increase blood flow (as measured by Laser Doppler imaging and thermography imaging techniques. This work will help the researchers understand if topical application of vasodilators may be a future therapeutic target for scleroderma vasculopathy.

The possible risks are minimal and not expected. The study drug (alprostadil) is licenced for the treatment of erectile dysfunction in men. However, it is being used ‘off licence’ for this study to examine the vasodilatory effect of blood vessels in in the fingers (does it cause more blood to flow to the fingers). The only known side effect of the drug (when applied topically, to the skin) may be a slight rash.

Where is the study run from?
The study is led by Dr Michael Hughes – Clinical Senior Lecturer & Honorary Consultant Rheumatologist. The study will be run by the Scleroderma Research Group at Northern Care Alliance NHS Foundation Trust, Salford Royal Hospital (UK).

When is the study starting and how long is it expected to run for?
The study is expected to start on 01/10/2025 and run for approximately 12 months. The end date as listed in IRAS is 01/09/2026

Who is funding the study?
The study will be internally funded by NIHR Manchester, Biomedical Research Centre (BRC), under the Next Generation Therapeutics (NGT) theme (UK).

Who is the main contact:
Mr Paul New (study co-ordinator):
Northern Care Alliance NHS Trust, Salford Royal Hospital, Salford, Manchester, M6 8HD, UK.
paul.new2@nca.nhs.uk

Contact information

Type(s)
Public

Contact name
Mr Paul New

Contact details
Northern Care Alliance NHS Foundation Trust
Clinical Science Building
Stott Lane
Salford
United Kingdom
M6 8HD
+44 161 206 4295
paul.new2@nca.nhs.uk

Type(s)
Scientific, Principal investigator

Contact name
Dr Michael Hughes

Contact details
University of Manchester
Manchester
United Kingdom
M13 9PT
+44 161 2064616
michael.hughes-6@manchester.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
359229

Protocol serial number
25/EE/0175

Study information

Scientific Title
A physiological study exploring the digital vascular response to topical alprostadil in patients with systemic sclerosis

Acronym
SScVAS

Study objectives
Principal research question: To investigate the acute physiological effects of topical alprostadil applied locally to the fingers of patients with SSc on digital vasculopathy / microcirculation.

Secondary research question: To tentatively explore the generalisability of disease-related factors including the severity of digital skin sclerosis (Skin thickness) and disease duration /subset on local response to alprostadil in patients with SSc.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/10/2025, East of England - Cambridge South Research Ethics Committee (Equinox House, City Link, Cambridge, NG2 4LA, United Kingdom; +44 207 104 8084; cambridgesouth.rec@hra.nhs.uk), ref: 25/EE/0175

Primary study design
Interventional

Study design
Single centre interventional blinded randomized controlled trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Systemic Sclerosis (SSc), scleroderma

Interventions
Treatment: One off topical application of study drug, alprostadil cream, to one of the fingers of the participant's dominant hand.

Placebo: One off topical application of study placebo, Lipobase cream, to a second finger of the participant's dominant hand.

No treatment: To a third finger of the participant's dominant hand

Treatment intervention:
The index, middle and ring fingers will be allocated to application of alprostadil, placebo, and no treatment, in a predetermined randomised order on successive patients. The patient's dominant hand shall be studied. The studied dose of alprostadil shall be 300 micrograms. Alprostadil and placebo shall be applied by a study investigator manually using a gloved hand. The alprostadil will be applied vertically along the dorsal aspect of the finger from the base of the finger to the nailbed, using a gentle rubbing motion up and down the length of the finger, for 60 seconds. Finally, any visible surplus remaining ointment shall be removed by the study investigator using gauze. The rationale for this is to avoid any deleterious impact on data acquisition from vascular imaging
through interaction or obstruction with the cream material.

Sequence of intervention
1. Alprostadil will be rubbed onto the dorsum of one finger for 1minute.
2. Placebo: same as alprostadil in colour, texture, odour and absorption, will be rubbed on the dorsum of a second
finger for 1minute.
3. No ointment will be applied to the dorsum of the third finger, in order to allow any systemic effect of the alprostadil to
be identified.

Outcome measures:
Study investigators wish to understand how the skin (blood flow and temperature) reacts to the treatment intervention. To do this they will measure the blood flow (using Laser Doppler Imaging) and temperature (using Thermography) of the participants fingers immediately before, directly after, and then every 10 minutes for 90 minutes after the treatment intervention.

Laser Doppler imaging (LDI)
LDI which measures blood flow allows a perfusion map (in arbitrary units) to be produced of the studied area. LDI will be performed immediately before and after the treatment intervention and then every 10 minutes for 90 minutes. LDI is non-invasive and painless.

Thermography
Thermographic assessment measures skin temperature and provides an indirect measure of small and large blood
vessel function. Standardised thermographic images shall be acquired immediately before and after treatment
intervention, and then every 10 minutes for 90 minutes. Thermography is non-invasive and painless.

The rationale of Laser Doppler imaging and Thermography is to demonstrate an objective localised increase in skin perfusion with the treatment intervention.

Assessment of digital skin fibrosis (skin thickness):
The extent of the finger skin sclerosis (skin thickening) on the treated hand shall be assessed by High Frequency Ultrasound (HFUS) to measures skin thickness of the hands and finger

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Alprostadil cream, Lipobase cream

Primary outcome(s)
Digital vasculopathy/microcirculation assessed by surrogate measurement of skin perfusion and temperature using Laser Doppler Imaging and Thermography respectively. This will be measured immediately before treatment and then every 10 minutes after treatment for 90 minutes.

Key secondary outcome(s)
1. Perfusion/temperature measured using laser Doppler imaging / Thermography before application of alprostadil, immediately after, and then every 10 minutes for 90 minutes after application
2. Patient skin score as measured by the modified Rodnan skin score (clinician assessed) and High Frequency ultrasound imaging (visual assessment of thickness) at a single time point
3. Disease duration (time since diagnosis/first symptoms) and disease subtype (localised or systemic) at a single time point

Completion date
01/09/2026

Eligibility

Key inclusion criteria
1. Clinician confirmed diagnosis of SSc-spectrum disorder
2. Eighteen years of age or older at the time of recruitment
3. Able to give full informed consent
4. Steady dose (for at least two weeks) of relevant prescribed oral drug (e.g., vasodilatory and vasoactive) therapies for SSc-associated vasculopathy

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Presence of digital ulcers on the fingers
2. Patients receiving treatment with intravenous vasodilatory/vasoactive therapy (e.g., iloprost)
3. Finger digital ulcers currently requiring hospital admission (e.g., to receive iloprost) or awaiting surgery for digital vasculopathy

Date of first enrolment
01/10/2025

Date of final enrolment
01/09/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
Salford
United Kingdom
M6 8HD

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
NIHR Manchester, Biomedical Research Centre (BRC), under the Next Generation Therapeutics (NGT) theme, Internally funded.

Results and Publications

Individual participant data (IPD) sharing plan
Data sharing statement to be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date