ISRCTN11180128 https://doi.org/10.1186/ISRCTN11180128

Capsaicin 8% patch treatment in non-freezing cold injury (NFCI)

Submission date
30/01/2024

Recruitment status
Recruiting

Registration date
02/02/2024

Overall study status
Ongoing

Last Edited
17/06/2026

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
Exposure of the limb extremities to cold, but above-freezing temperatures, may lead to chronic pain and persistent cold hypersensitivity. The condition now termed non-freezing cold injury (NFCI) was previously called trench foot, and it has been known since World Wars I and II to be a vaso-neuropathy. An underlying small fibre neuropathy with neuro-vascular changes has been demonstrated in skin biopsies, which may account for the symptoms. In lay terms, in NFCI there is damage to the small diameter nerves in the skin which mediate pain and temperature, and their interactions with blood vessels. Current treatments for neuropathic pain have limited benefits and significant side effects. An effective treatment, licensed in the UK/EU for neuropathic pain, is the Capsaicin 8% patch ("Qutenza 179 mg cutaneous patch"), which may relieve pain for up to 3 months after a single 30–60-minute application. This treatment is localised to skin, and not associated with generalised side effects. The active ingredient capsaicin is the substance in chilli peppers that gives their hot pungency. The patch has been shown to produce pain relief and nerve regeneration over 3 months in NFCI. There is evidence that 2-3 monthly repeated Capsaicin 8% patch applications over a year may produce progressive pain relief in painful diabetic neuropathy. Hence, this study aims to investigate, for the first time, the effect of repeated Capsaicin 8% patch treatment in subjects with NFCI, applied as licensed, 3-monthly over 1 year.

Who can participate?
Patients aged 18 – 60 years old who have NFCI

What does the study involve?
The participants will be randomised 1:1 to receive either the Capsaicin 8% patch or placebo patches ("dummy" patches, containing no drug).

What are the possible benefits and risks of participating?
Repeated applications of the Qutenza patch over 1 year are expected to provide progressive pain relief, and also nerve regeneration, to restore the nerve fibres.

The most common side effects are expected to include transient redness, pain and itchiness at the patch application site during patch application, which is prevented or reduced by cooling

packs. A 4-mm skin punch biopsy will be collected after local anaesthetic is injected into the skin to minimise any pain from the procedure. There is a chance that the skin wound may become infected, however this is very unlikely.

Where is the study run from?
Hammersmith Hospital, Imperial College London and Imperial College Healthcare NHS Trust.

When is the study starting and how long is it expected to run for?
August 2023 to August 2027

Who is funding the study?
The Ministry of Defence (UK)

Who is the main contact?
Prof Praveen Anand, p.anand@imperial.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Praveen Anand

Contact details
Imperial College London, Du Cane Rd.
London
United Kingdom
W12 0NN
+44 (0)20 3313 1000
p.anand@imperial.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-001212-26

Integrated Research Application System (IRAS)
313094

Protocol serial number
22IC7533

Study information

Scientific Title
Capsaicin 8% patch Qutenza treatment in non-freezing cold injury (NFCI): a clinical trial of repeated patch applications for pain relief and nerve regeneration

Acronym

CANREGRO

Study objectives
Capsaicin 8% patch applications, but not placebo patches, repeated every 3 months over a year as licensed, will show progressive improvement in pain relief, and restoration of nerve fibres, in non-freezing cold injury (NFCI).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/12/2023, Ministry of Defence Research Ethics Committee (Defence Science and Technology Laboratory, Portsdown West, Portsdown Hill Rd, Fareham, PO17 6AD, United Kingdom; +44 (0)300 153 5372; DST-MODRECTeam@mod.gov.uk), ref: 2114/MODREC/22

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled clinical trial (RCT)

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-freezing cold injury, NFCI (Trench Foot).

Interventions
This study is a randomized, double-blind, placebo-controlled clinical trial (RCT) with baseline and post-treatment sensory tests and skin biopsy after repeated treatments with a Capsaicin 8% patch (Qutenza). Participants will be randomly allocated with a 1 to 1 ratio to either receive a 30-minute capsaicin 8% patch (Qutenza) application to both feet up to the distal calf (Capsaicin treatment group, number of subjects = 27) while continuing to take their usual medications as part of their Standard of Care (SOC) or to receive placebo patches (with no capsaicin) plus SOC (Placebo group, number of subjects = 27) every 3 months for 1 year.

Randomization will be performed via OpenClinica, an electronic platform, by the Imperial Clinical Trials Unit. The Pharmacy will be informed of the randomisation treatment code allocation by the Imperial Clinical Trials Unit. Neither the researchers nor the participants in the study will know whether the patch applied is the Capsaicin 8% patch or the placebo patch.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Capsaicin 8% patch (Qutenza 179 mg cutaneous patch), inert placebo patch

Primary outcome(s)

Pain measured using a visual analogue score (VAS) at baseline (pre-treatment visit) and 3, 6, 9, and 12 months after the baseline visit (post-treatment follow-up visits)

Key secondary outcome(s)
Changes in nerve markers showing nerve fibre density (with marker PGP9.5) and regeneration (with marker GAP-43) after application of Capsaicin 8% patch in skin biopsies at the site of the treatment measured using immunohistology at baseline (pre-treatment visit) and 3, 6, 9, 12 months after the initial baseline visit (post-treatment follow-up visits).

Completion date
10/08/2027

Eligibility

Key inclusion criteria
1. Military service personnel aged 18-60 years with non-freezing cold injury (NFCI) resulting in painful neuropathy
2. History of distal symmetric sensory polyneuropathy affecting feet for at least 8 weeks, confirmed on clinical examination and/or sensory testing and assessed on the 11-point pain intensity numerical pain rating scale (NPRS).
3. Patients with a history of pain intensity equal to or greater than 4 NPRS points are eligible to participate.
4. The use of systemic analgesics to relieve pain including anti-depressants, anticonvulsants, opioids, salicylates, paracetamol, and non-steroidal anti-inflammatory drugs (NSAIDs) will be permitted, providing any changes are recorded for the entire duration of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Participating in another clinical trial or who has done so within 30 days before screening
2. Additional medical condition or illness that, in the opinion of the Investigator, would interfere

with study compliance and/or impair the patient's alcohol or drug abuse) within the previous six months before enrolment
3. A history of severe allergies or multiple drug allergies and/or reported hypersensitivity to capsaicin
4. Other conditions that may lead to neuropathic pain or hypersensitivity e.g. diabetes, and HIV
5. Topical anaesthetic or capsaicin applications, or history of previous treatment with the Capsaicin 8% patch (to minimise unblinding)
6. Pregnant or nursing mothers will not be included in this study; relevant history will be taken. A pregnancy test will be performed and patients who are pregnant will be excluded from the study.

Date of first enrolment
01/02/2024

Date of final enrolment
10/08/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Peripheral Neuropathy Unit, Imperial College London
Hammersmith Hospital, Du Cane Road
London
England
W12 0NN

Study participating centre
Richmond Pharmacology
1a Newcomen Street, London Bridge
London
England
SE1 1YR

Sponsor information

Organisation
Imperial College London

ROR

https://ror.org/041kmwe10

Funder(s)

Funder type
Not defined

Funder Name
Ministry of Defence

Alternative Name(s)
MOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Pseudonymised data will be stored within the department on a secure University computer in accordance with Imperial College policy. Only researchers involved in the study will have access to these data. During the overall duration of the study medical records and the data collected for the study may also be looked at by authorised people from the Sponsor or NHS Trust, to check that the study is being carried out correctly. All will have a duty of confidentiality to the research participant and will do their best to meet this duty. By signing the consent form, patients authorise the release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

IPD sharing plan summary
Stored in non-publicly available repository