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A randomised trial to see if an oral cannabis-based medicine (CBD) can help to treat chemotherapy related nerve pain

Submission date
15/10/2025

Recruitment status
Recruiting

Registration date
03/12/2025

Overall study status
Ongoing

Last Edited
15/05/2026

Condition category
Nervous System Diseases

[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
One in 3 people will have cancer in their lifetime and many will be treated using treatments such as Chemotherapy. One harmful side effect of these treatments is that they can damage the nerves in the body. This is called Chemotherapy Induced Peripheral Neuropathy (CIPN). CIPN is very common, can affect up to 90% of patients and causes long-term pain in up to half of patients. This leads to problems carrying out normal day to day activities and affects their quality of life. CIPN is hard to treat with current medicines.
We want to improve pain levels in CIPN patients. Laboratory work and early studies in patients has shown that substances found in the Cannabis sativa plant called cannabinoids (CBDs) can help with nerve pain like that seen in CIPN. As there hasn't been much research using CBDs in CIPN, our study will test CBD. We also want to include in our study tests which look at what happens in the pain and mood systems in the brain when you take CBD. We can measure the different CBDs in the blood before and after treatment and look at the effects on the patient's own natural CBD system.

Who can participate?
Patients aged 18 years or over with at least 3 months post neurotoxic chemotherapy and stable CIPN over at least 6 weeks

What does the study involve?
Patients will answer questions that measure their CIPN symptoms, questions about their quality of life, and ask if they are worried and depressed. We will take blood samples to measure the body's natural CBD levels and perform a brain scan in patients using a machine called an MRI scanner. Patients will be split into one of two groups, taking either drug or placebo for 5 weeks, then switching to the other treatment for another 5 weeks. After 5 weeks, the study tests will be repeated and the patient will not take treatment for 2 weeks (a 'washout' period). At the end of the study, we will look at the effects of the treatment on pain relief, quality of life, physical function, the brain and mood. This work is important as it will tell us if a larger study is needed to show that CBDs are an effective treatment for CIPN, and how the study should be done.

What are the possible benefits and risks of participating?
You may or may not get a direct personal benefit from using the study medication. If you do not, the information you give and the results from this study may help to improve the healthcare of patients in the future.
The results of this study may be used for the future commercial development of a new medicinal product, treatment or test. Your participation in this study will not entitle you to benefit financially from the commercial development of the product, treatment or test.
Possible sides effects of CBD are weight changes, diarrhoea, nausea, urine infections, increased liver tests, fever, cough, a rash, irritability, depression or thoughts of suicide. This is not common and the nurses will ensure that participants are safe throughout the trial. While enrolled in this study, participants will be unable to take part in any other drug trial. If any unexpected abnormalities show up on routine blood tests or on MRI scans, these will be followed up by the team and appropriate others clinically and communicated to the participant and their GP. Some people may find the extra visits to the clinic, the number of assessments, telephone calls and questionnaires tiring. These are kept to a minimum and collect only the information required for the study. These may be inconvenient however participants will be guided through this process by a member of the research team. There may be some discomfort or bruising after blood is taken. Participants having the MRI scans will have to attend the Royal Infirmary of Edinburgh for two MRI scans (before treatment begins and after 5 weeks of treatment). Some people may feel uncomfortable in the MRI scanner.
Safety: The research team will record adverse events that they become aware of, and promptly report SARs and SUSARs to the study Sponsor. The trial will have a Data Monitoring Committee that will monitor safety throughout the study.

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

When is the study starting and how long is it expected to run for?
May 2026 to January 2027

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

Who is the main contact?
action.trial@ed.ac.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1012593

Protocol serial number
AC25008

Study information

Scientific Title
A Phase II randomised cross-over trial of orAl Cannabinoid versus placebo in the Treatment of chemotherapy Induced peripheral neurOpathic paiN (ACTION)

Acronym
ACTION

Study objectives
Main clinical objective: To determine if taking an oral CBD solution for 5 weeks provides effective pain relief for chemotherapy induced peripheral nerve pain, assessed using the EORTC CIPN20 (sensory subscale) questionnaire.

Main mechanistic objective: To determine whether there are pre/post-treatment changes in key pain brain regions (linked with pain and mood) in participants taking a CBD oral solution by performing an MRI brain scan, and whether this can be linked to changes in clinical pain/well-being scores.

Clinical: To determine whether 5 weeks of a CBD solution (MRX1) affects:
• Side effects
• Severity of the different components of nerve pain
• Overall pain
• Mood
• Cognition
• Sleep
• Quality of life

• Specific bedside examination for nerve pain
• Patient's own impression of effectiveness of treatment

Health economic:
• Potential impact of CBD treatment on health care costs and carer costs

Mechanistic:
• Whether wider brain changes on MRI scans, which are associated with inflammation change after 5 weeks of CBD treatment
• Is there a relationship between pain relief from CBD and the patient's background cannabinoid levels, known as the endocannabinoid system

Exploratory:
• To understand questionnaire responses at specific time points in relation to patient diaries, evaluating pain, sleep, mood, function and general well-being

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 26/11/2025, East of Scotland Research Ethics Service (EoSRES) (Tayside medical Science Centre, Residency Block Level 3, George Pirie Way, Ninewells Hospital and Medical School, Dundee, DD1 9SY, United Kingdom; -; tay.eosres@nhs.scot), ref: 25/ES/0092

Primary study design
Interventional

Study design
Interventional double blind randomized cross over placebo controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Chemotherapy induced peripheral neuropathy

Interventions
A clinical efficacy and mechanistic phase 2 RCT, of MRX1 versus matched placebo oral solution, using a randomised, double-blind, placebo-controlled, cross-over design. Participants will be randomised 1:1 to one of two treatment sequences (placebo, IMP or IMP, placebo) using a web-based randomisation service. Participants will receive each of the treatment sequences in a period lasting 5 weeks (10 weeks in total for both), separated by a wash-out period of 2 weeks (no study drug medication), meaning that it takes 12 weeks for each patient to get through the 2 treatment sequences. During each sequence the patient will follow a pre-determined dosing regimen, with the possibility of escalating the dose after clinical assessment each 6-8 days. The assessment is either phone or face to face to coincide with collecting more IMP from pharmacy. The decision by the clinician to escalate dose, remain on a stable dose, reduce dose or even stop IMP depends on clinical assessment of wanted effects (pain relief) versus unwanted effects (side effects). The decision will be made in conversation with the patient during the consult each week. Trial assessments will include structured validated questionnaires to assess CIPN and associated symptom clusters and QoL, as well as 6 blood samples in total for cytokines and

endocannabinoid levels along with 2 MRI scans for mechanistic endpoints. We will only do the MRI scans in the first treatment sequence-at baseline and at end of week 5, to minimise what we ask of patients.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
MRX1 [Cannabidiol]

Primary outcome(s)
1. Sensory peripheral neuropathy is measured using the EORTC QLQ-CIPN20 sensory scale at weeks 5 and 12
2. Resting-state functional connectivity of the anterior cingulate cortex is measured using rsfMRI at baseline and week 5

Key secondary outcome(s)
Clinical:
1. Adverse events and side effects are measured using participant self-report and clinical records at weeks 5 and 12
2. Chemotherapy-induced peripheral neuropathy is measured using total EORTC CIPN 20 scores and EORTC QLQc30 scores at week 5 and 12
3. CIPN pain severity is measured using the Brief Pain Inventory short form (BPI sf) at weeks 5 and 12
4. Mood is measured using Generalised Anxiety Disorder-7 questionnaire (GAD7) and (Patient Health Questionnaire-9) PHQ9 total scores at week 5 and 12
5. Perceived cognitive function is measured using the FACT-Cog Version 3 total score at weeks 5 and 12
6. Sleep quality is measured using the Pittsburgh Sleep Quality Index at weeks 5 and 12
7. Health-related quality of life is measured using total EORTC QLQ-C30 scores at weeks 5 and 12
8. Somatosensory function is measured using quantitative sensory testing (QST) at weeks 5 and 12
9. Patient Global Impression of Change (PGIC) is measured using standardised questions at weeks 5 and 12

Health economic:
10. Health status is measured using the EQ-5D-5L at weeks 5, 8 and 12
11. Health care utilisation is measured using participant self-report and clinical records at weeks 5, 8 and 12
12. Cost-effectiveness is measured using modelled cost per QALY at weeks 5, 8 and 12

Mechanistic:
13. Resting-state functional connectivity and white matter microstructural integrity are measured using rsfMRI and diffusion MRI at week 5
14. Brain metabolite concentrations are measured using magnetic resonance spectroscopy at week 5
15. Endocannabinoid levels are measured using blood samples at baseline, weeks 5, 8 and 12
16. Inflammatory markers are measured using blood samples at weeks 5 and 12

Exploratory:
17. Period-dependent fluctuations in clinical outcomes including chemotherapy-induced peripheral neuropathy, quality of life, depression, anxiety and pain are measured using EORTC QLQ-CIPN20, EORTC QLQ-C30, PHQ-9, GAD-7 and BPI-SF at baseline, weeks 5, 8 and 12
18. Temporal fluctuations in pain, sleep, mood, function and general well-being are measured using participant daily diary entries during the 1-week pre-randomisation period, and at weeks 5 and 12

Completion date
31/10/2027

Eligibility

Key inclusion criteria
1. 18 years or over
2. At least 3 months post neurotoxic chemotherapy
3. Stable CIPN over at least 6 weeks
4. EORTC CIPN20 sensory scale > 10
5. 0-10 VAS (Visual Analogue Scale) PAIN ≥ 3
6. Willing and able to give written consent
7. Willing not to take additional cannabinoids during the trial period
8. Willing to use effective contraception throughout the trial (A woman is considered of childbearing potential (WOCBP), i.e., fertile, following menarche and until becoming post-menopausal unless permanently sterile. See below for accepted effective contraception1.
9. Willing to continue effective contraception for 30 days after completion of trial for woman participants and for 90 days for male participants
10. No contraindications to MRI scan
1Methods considered to be effective contraceptives:
- Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal or transdermal)
- Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable or implantable)
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomised partner (provided that partner is the sole sexual partner of the WOCBP trial participant and that the vasectomised partner has received medical assessment of the surgical success)
- Sexual abstinence, defined as refraining from heterosexual intercourse during the entire trial period and for 90 days post study completion. The reliability of sexual abstinence will be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject. Periodic abstinence (calendar, symptothermal, post-ovulation methods) is not an acceptable method of contraception.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
99 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Patients who have had any changes to analgesia in last 30 days
2. Patients who have had any intervention which may result in a change to CIPN during the course of the study *2
3. Patients currently taking any of the following medication; opioids, erythromycin, clarithromycin, fluconazole, itraconazole, sulfamethoxazole, clopidogrel, rifampicin, warfarin, selected antiepileptic agents (including phenytoin, carbamazepine, sodium valproate) clobazam, stiripentol, Everolimus *3
4. Patients currently taking any antidepressants and anticonvulsants if used as adjuvant analgesics
5. Routine use of cannabis products for medicinal or recreational purposes (at any time in the last 4 weeks) or of any illicit drug precludes inclusion in the study (CBD at Baseline) *4
6. Patients with severe pain due to CIPN on VAS;>8/10
7. Female patients who are not post-menopausal and not using highly effective contraception (as detailed at end of this section)
8. Male patients who are not using highly effective contraception with female partner (as detailed at the end of this section)
9. Patients who are pregnant or breastfeeding
10. Chronic alcohol use
11. Any liver disease with abnormal bilirubin, AST or ALT: History of severe liver disease (Alanine transaminase (ALT) and/or aspartate aminotransferase (AST) more than 3-times the upper limit of normal (ULN)) and bilirubin greater than 2 times the ULN OR moderate to severe hepatic impairment (Child–Pugh class B or C).
12. Current or recent (≤12 months) substance use disorder or misuse of prescription medicines; positive drugs of abuse (DoA) screen when performed at investigator's discretion.
13. Patients with hypersensitivity to any of constituents of IMP in the IB
14. Any hospital admission for mental ill health in last 5 years
15. Suicidal thoughts or severe depression within the past year
16. Any live vaccines within 14 days before study entry

*2 Any treatment, oncological or non-oncological, which could change CIPN during the course of the study (including changes to hormone treatment in the 30 days prior to recruitment, patients who start neurotoxic chemotherapy during the study, patients who start any drug which can cause CIPN during the study). These are the most likely scenarios in our patient group which we are therefore giving as examples but this is not an exhaustive list.
*3 All concomitant medication will be reviewed as part of the screening process. Relevant

Cannabidiol–Psychoactive Drug Interactions, as listed in Appendix 1, will be considered.
*4 Urine samples will be collected at baseline and week 8 (pre-dose) and analysed via a dipstick at time of collection. We can detect any THC taken in the previous 35-40 days with the dipstick which means in practical terms we will capture any illicit THC use. This is to measure any cannabis /cannabinoid use out with the IMP. If the test results are positive for THC the participant will be withdrawn.

Date of first enrolment
18/05/2026

Date of final enrolment
31/01/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
Western General Hospital
Crewe Road South
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Study participating centre
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Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request. De-identified data will be shared with approved researchers and research projects post data analysis via the Edinburgh Clinical Trials Unit Data Sharing Committee.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.0	19/03/2026	15/05/2026	No	No