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Neurostimulation for nociceptive pain

Submission date 08/05/2025	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 09/05/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 27/01/2026	**Condition category** Signs and Symptoms	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
In this study, we are collecting information to try to understand the effects of stimulating the lumbar sympathetic chain in patients with either osteoarthritis in one knee or endometriosis. It is thought that pain relief by stimulating this nerve may be achieved by altering the pain-signalling processes to the brain.
A commercially available peripheral nerve stimulation system will be used in this study. This device is CE marked in the UK, meaning it has been assessed by the manufacturer and deemed to meet EU safety, health and environmental protection requirements. It is covered by the NHS. Although used to treat a number of different types of pain, previous research has shown that peripheral nerve stimulation devices improved pain and showed a benefit for up to 12 months for conditions other than those being studied here.

Who can participate?
This therapy may be considered as an option if the following describes your situation:
1. You have had knee pain due to osteoarthritis or pelvic pain due to endometriosis for more than 6 months and it is affecting your ability to function.
2. You have previously tried and failed at least one conservative treatment for chronic pain, including but not limited to pharmacological therapy, physical therapy and interventional pain procedures for persistent pain.
3. You still have persistent pain in your knee or pelvic pain.
4. You are motivated to explore a new option.

What does the study involve?
Once deemed suitable, you will be asked to take part in the study at the screening visit. Once accepted and study consent is signed, a commercially available implantable neurostimulator will be implanted through a minimally invasive procedure done under X-ray guidance.
These commercially available devices directly activate the peripheral nerves using mild electrical stimulation that is generated by a battery (called a pulse generator) and delivered by two leads. In the study, the leads will be placed near the intended nerve target. The leads deliver the mild electrical stimulation to the nerve and the pulse generator provides the energy. The battery and leads have been deemed suitable for evaluating whether stimulation of the lumbar sympathetic chain works for your condition. Many studies have shown that people with pain conditions who have these commercially available neurostimulators have meaningful reductions in pain and disability.

What are the possible benefits and risks of participating?
If you decide to take part in this research study, there is a potential opportunity to temporarily reduce your long-standing chronic pain. The information gathered in this study will add to the understanding of treatment options for patients suffering from similar chronic pain in the future. The sponsor is undertaking this research to ensure the future device is much smaller and easier to use. So your participation in this study will also help with optimising this future device, which in turn will improve outcomes for many others living with your type of pain in the future.
If you take part in this trial, you will have implantation of an existing FDA-approved and CE-marked device used for peripheral nerve stimulation with the goal of lowering/reducing your pain.
There are risks associated with the implant procedure and might involve:
1. Bleeding, which may lead to bruising and in rare cases may require further surgery (1 in 300 cases).
2. The electrode near your spine may move or not work and so you may need further surgery over the life of the device, which is expected to be between 30 and 35 years. Whilst our experience of using the device for this length of time is very low, the best estimate is that 1 in 10 cases will require further surgery.
3. You may develop an infection and most of these are not dangerous. Your doctor might have to remove the system to prevent the spread of infection, even if the system was helping your pain (3 in 100 cases).
4. There is a risk of allergy to the implant material. If you are allergic to metals such as nickel, let the doctor know (1 in 1000 cases).
5. Risk of nerve damage, and we normally look out for this in the first few hours after operation (1 in 3000 cases).
6. Hardware malfunction/battery failure of the system (3 in 100 cases).
7. Potential inability to undergo an MRI scan due to the implantable pulse generator
At the end of the study, you will be given the option of explant or to continue with the therapy. If you opt to continue with the therapy, you will transfer over to standard peripheral nerve stimulator after-care and follow-up as per standard NHS guidelines. If the therapy does not help with your pain condition, the device can be safely removed through a minor surgical procedure and the treatment will no longer be ongoing with a return to standard of care.
If you take part in this study you will have a peripheral nerve stimulator inserted using x-ray guidance. X-rays are a type of ionising radiation which are used to form images of your body and to guide your doctor during the insertion of the peripheral nerve stimulator. You may also have some X-rays after the procedure to check that the peripheral nerve stimulator is in the right place.
Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during their lifetime. Taking part in this study may increase the chances of this happening to you to 50.02%.

Where is the study run from?
Leeds Teaching Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
September 2023 to December 2026

Who is funding the study?
ABVF BV. (Netherlands)

Who is the main contact?
Arun Sridhar, Arun.sridhar@abvf.bio

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Ganesan Baranidharan

Contact details
Leeds Teaching Hospital NHS Trust
Brotherton Wing
Leeds
United Kingdom
LS1 3EX
+44 (0)113 3926234
g.baranidharan@nhs.net

Type(s)
Public, Scientific

Contact name
Dr Arun Sridhar

Contact details
ABVF B.V. Stationsplein 45, A4.004
Rotterdam
Netherlands
3013AK
+44 (0)7542927522
arun.sridhar@abvf.bio

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
327347

Protocol serial number
56471

Study information

Scientific Title

Prospective, open-label trial to assess the tolerability of lumbar sympathetic chain stimulation in patients with nociceptive pain due to knee osteoarthritis or endometriosis

Acronym
LSyNC

Study objectives
Stimulation of a novel nerve target will alleviate pain and provide analgesia for patients with knee pain due to knee osteoarthritis (OA) and endometriosis-induced pelvic pain

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/09/2023, South East Scotland REC 01 (The North of Scotland Research Ethics Service, Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, United Kingdom; +44 (0)1224 558458; gram.nosres@nhs.scot), ref: 23/NS/0089

Study design
Open-label early feasibility study

Primary study design
Observational

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Analgesic treatment of knee osteoarthritis and endometriosis

Interventions
Neurostimulation of a novel nerve target

Patients with knee pain due to knee OA and patients with pelvic pain due to endometriosis will have insertion of a commercially available stimulation device on the lumbar sympathetic chain (LSC). To monitor the safety and tolerability of the LSC stimulation, patients will be followed up at:
1. 21 days after insertion of the device where the wound will be examined and the device will be activated
2. Have a video check-in every week for 3 weeks
3. Return to the pain clinic for a face-to-face appointment at 30, 60, 90 and 180 days after the device has been activated
4. Have video check-ins at 120 and 150 days after the device has been activated

Intervention Type
Device

Phase
Phase I

Drug/device/biological/vaccine name(s)

Implantable peripheral nerve stimulation device

Primary outcome(s)

Patients with knee OA:
1. Change from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale at 30, 60, 90 and 180 days. The WOMAC is a self-administered, disease-specific questionnaire which assesses clinically important, participant-relevant symptoms for pain, stiffness, and physical function in participants with OA. The WOMAC pain subscale is a 5-item questionnaire that assesses the amount of pain experienced due to OA of an index joint (knee or hip) during the past 48 hours. It is calculated as the mean of scores from 5 questions, which may not be a whole (integer) number. Scores for each question on the WOMAC Pain subscale are scored on a five-point scale ranging from 0 (no pain) to 4 (extreme pain), where higher scores indicate higher pain.
2. Change from baseline in WOMAC Physical Function Subscale at 30, 60, 90 and 180 days. Physical function refers to the patient's ability to move around and perform usual activities of daily living. The WOMAC physical function subscale is a 17-item questionnaire used to assess the degree of difficulty experienced due to OA in an index joint (knee or hip) during the past 48 hours. It is calculated as a mean of the scores from 17 individual questions, which may not be a whole (integer) number. Scores for each question on the WOMAC physical function subscale are scored on a five-point scale ranging from 0 (no difficulty) to 4 (extreme difficulty), where higher scores indicate extreme difficulty/worse physical function.
3. Change from baseline in Knee Injury and OsteoArthritis Outcome Score (KOOS) at 30, 60, 90 and 180 days.
4. Change from baseline in the following tests: knee range of motion (ROM), knee swelling, and ambulation ability at 30, 60, 90 and 180 days. (These outcomes may be captured retroactively if the referring physician has captured these data as part of their standard of care).

Patients with pelvic pain secondary to endometriosis:
1. Change from baseline in the Endopain 4D Questionnaire 52 at 30, 60, 90 and 180 days. The Endopain 4D Questionnaire comprises 20 items that assess patient reported pain symptoms in women treated for endometriosis including dysmenorrhoea, non- menstrual pelvic pain, intense pain, worsening pain, pain before period, stabbing pain, lower back pain, leg/hip pain, disabling pain, pain affecting mobility, dyspareunia, interruption of sexual intercourse, painful bowel movements, bowel spasms, diarrhoea/constipation, pain when urinating, bladder pain, sciatica and right shoulder pain.

All patients:
1. Change from baseline in pain at 30, 60, 90 and 180 days measured using NRS
2. Change from baseline in health-related quality of life (HRQoL) at 30, 60, 90 and 180 days measured using the EQ-5D-5L
3. Proportion of participants reporting an improvement in EQ-5D-5L index score (≥0.200) at 30, 60, 90 and 180 days using the EQ-5D-5L Health questionnaire
4. Change in baseline in autonomic function as assessed with heart rate variability (HRV), baroreflex sensitivity (BRS) and skin sympathetic nerve activity (SKNA) at 30, 60, 90 and 180 days
5. Change in blood draw measures to assess cortisol, metanephrine levels and c-reactive protein (CRP) at 30, 60, 90 and 180 days
6. Patient and Clinician Global Impression of Change (PGIC, CGIC) at 30, 60, 90 and 180 days
7. Change in medication at 30, 60, 90 and 180 days

Key secondary outcome(s))

There are no secondary outcome measures

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Inclusion criteria for both knee and pelvic pain:
1. Agree to maintain a stable dose of analgesics 30 days prior to enrolment.
2. Willing to hold their usual analgesic medication constant throughout the study.
3. Able and willing to comply with the follow-up schedule and protocol.
4. Previously tried and failed at least one conservative treatment for chronic pain, including but not limited to pharmacological therapy, physical therapy and interventional pain procedures for persistent pain.
5. Been deemed suitable for the study by the pain MDT.
6. Willing to provide informed consent.
7. Maximum daily dose of 90 mg morphine equivalents. If the patients are taking more than this dose, they will be offered a referral to an opioid reduction clinic to achieve the target opioid dose, and the baseline opioid will be taken as the dose on referral.
8. In the investigator's opinion, the patient is a suitable candidate for LSC stimulation.
9. Participants diagnosed with persistent refractory pelvic pain secondary to endometriosis for at least 6 months OR knee pain secondary to OA for at least 6 months.
10. Subject is able to distinguish between primary pain (knee or pelvis) from other sources of pain.

Inclusion criteria for knee pain secondary to osteoarthritis:
1. Male or non-pregnant female aged 30-75 years with chronic moderate to severe knee pain due to OA (baseline pain diary scores of ≥ 6 of 10 on NRS for knee pain).
2. If female and of child-bearing age, willing to use contraception throughout the trial.

Inclusion criteria for pelvic pain secondary to endometriosis:
1. Pre-menopausal women aged 18 to 50 years old.
2. If of childbearing age, willing to use contraception throughout the trial.
3. Recurrent symptoms suggestive of superficial peritoneal endometriosis (ASRM stage 1 or 2) identified during laparoscopy, confirmed via biopsy and performed within the last 5 years, who prefer not to undergo repeat surgery. OR Symptoms suggestive of ovarian endometrioma seen on ultrasound or MRI with cyst ≤3 cm in diameter.
4. If on hormonal therapies, they must be on a stable dose for at least 90 days prior to implant and agree to maintain a stable dose throughout the study.
5. Baseline pain diary scores of ≥6 of 10 on NRS for pelvic pain.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Exclusion criteria for both knee and pelvic pain:
1. Female participants of childbearing potential who are pregnant/nursing or plan to become pregnant during the course of the trial.
2. Escalating or changing pain condition within the past month as evidenced by investigator examination.
3. Has a psychiatric or psychological condition that would interfere with participation in the study.
4. Have a history of major depression, severe anxiety or post-traumatic stress disorder within 2 years of screening or a history of other major psychiatric disorders.
5. Chemical sympathectomy treatment within the past 6 months.
6. Currently has an active implantable device such as a pacemaker, spinal cord stimulator or intrathecal drug delivery system.
7. In the investigator's opinion has an active infection.
8. Participated in another clinical investigation within 30 days.
9. Medical co-morbidities that preclude surgical intervention.
10. Patient is incapable of understanding or responding to the study questionnaires.
11. Patient is incapable of understanding or operating the patient programmer handset.
12. Patient has a BMI > 45kg/m2 with obesity related comorbidity.
13. Participant has a current or previous condition, which will probably require MRI investigation sometime in the following 2 years.
14. Participant has another predominant persistent painful condition other than persistent refractory pelvic pain or knee pain.
15. History of alcohol/IV drug abuse in the last 3 years.
16. History or symptoms of autoimmune disorders, cancer within the last 5 years except for cutaneous basal cell or squamous cell cancer resolved by excision, allergic reaction to monoclonal antibodies or IgG-fusion proteins, Hepatitis B, C or HIV, drug abuse, fibromyalgia, clinically significant cardiac disease, diabetes mellitus requiring oral treatment or insulin, clinically significant neurological disease or clinically significant psychiatric disorders.
17. Any anxiolytic beta blocker dosage exceeding 40 mg/day. Dosage must be stable for at least 3 months prior to enrolment.
18. Known postural hypotension, bradycardia or cardiac arrhythmia.
19. History of refractory hypotension or vasovagal syncope.
20. Severe DASS-21 scores of ≥21 for depression, ≥15 for anxiety or ≥26 for stress.
21. Within the past 6 months have tried interventional pain procedures for persistent pain.

Exclusion criteria for pelvic pain secondary to endometriosis:
1. Diagnosis of Irritable Bowel Syndrome (IBS) diagnosed by a qualified physician using the ROME 4 criteria, with the IBS identified as a predominant pain generator.
2. Diagnosis of Painful Bladder Syndrome as determined by O'Leary-Sant questionnaire with combined symptom and problem scores (symptoms + problem index) of ≥12.

Exclusion criteria for knee pain:
1. Hip pain is greater than or equal to knee pain.
2. Previous joint replacement of the target knee(s) for this study.

Date of first enrolment
15/03/2024

Date of final enrolment
28/02/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Sponsor information

Organisation
ABVF B.V.

Funder(s)

Funder type
Industry

Funder Name
ABVF B.V

Results and Publications

Individual participant data (IPD) sharing plan

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

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.5	21/05/2025	27/01/2026	No	No