ISRCTN16682024 https://doi.org/10.1186/ISRCTN16682024

Assessing the efficacy of Ibudilast as an adjuvant treatment to decompressive surgery for degenerative cervical myelopathy

Submission date
27/08/2020

Recruitment status
Recruiting

Registration date
03/09/2020

Overall study status
Ongoing

Last Edited
06/06/2025

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
Degenerative cervical myelopathy (DCM), wear and tear arthritis of the spine, specifically the neck, resulting in injury to the spinal cord, is the most common spinal cord disorder of adulthood. In DCM, arthritis of the spine causes compression of the spinal cord.
The symptoms of DCM are often mistaken for the natural consequences of aging, including numb and clumsy hands, loss of coordination, imbalance, and bladder and bowel problems. The weakness can progress to severe paralysis. Every year approximately 4 individuals in 100,000 undergo surgery for DCM, however, many more individuals are thought to suffer from DCM.
The main treatment for DCM is surgery. The aim of surgery is to create space and remove the compression of the spinal cord. This is known to prevent further injury. Unfortunately, the post-operative improvements are often incomplete and many patients remain severely disabled. Improving outcomes after surgery represents an important unmet clinical need.
Clinical and preclinical findings indicate that the drug Ibudilast can stimulate repair by stem cells and nerve cells in the spinal cord. Ibudilast is well-tolerated and used to treat asthma and post-stroke dizziness in Japan and is currently being investigated for use in treating other neurological diseases.
This study will investigate whether daily administration of Ibudilast by mouth for a maximum of 34 weeks can improve hand function, strength, balance, and urinary problems, and reduce pain.

Who can participate?
Individuals between 18-80 years old, diagnosed with DCM and scheduled for an operation for the first time will be invited to participate in the trial.

What does the study involve?
The study will entail patient questionnaires and clinical assessments before surgery, shortly after surgery and 3, 6, and 12 months after surgery. Moreover, patients will undergo MRI scans pre-operatively and at 6-months post-operatively to determine whether the treatment was successful.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
The study will initially be conducted at 6 sites in the UK, with more sites added as necessary.

When is the study starting and how long is it expected to run for?
September 2020 to March 2029

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Paula Turnbull, paula.turnbull@nhs.net

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-004856-41

Integrated Research Application System (IRAS)
213009

ClinicalTrials.gov (NCT)
NCT04631471

Protocol serial number
CPMS 44808, IRAS 213009

Study information

Scientific Title
REgeneration in CErvical DEgenerative myelopathy (RECEDE): a multi-centre, double-blind, randomised, placebo controlled trial assessing the efficacy of Ibudilast as an adjuvant treatment to decompressive surgery for degenerative cervical myelopathy

Acronym
RECEDE

Study objectives
Ibudilast improves recovery following surgical decompression of degenerative cervical myelopathy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/06/2020, London - Central Research Ethics Committee (The Association of Anaesthetists, 21 Portland Pl, Marylebone, London, UK W1B 1PY; +44 (0)207 104 8208; londoncentral.rec@hra.nhs.uk), ref: 20/LO/0185

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Degenerative cervical myelopathy

Interventions

Participants in the trial will be randomly allocated to one of two groups by their unique trial ID number. One group will be given Ibudilast, the test drug, while the other group will receive a placebo that will appear the same as the Ibudilast. Neither participants nor their doctors will know which group they have been allocated to. By comparing the outcomes between the two groups, we will be able to see whether giving Ibudilast provides a benefit to patients. This study includes a placebo arm since it is not known whether Ibudilast provides benefit and hence a position of equipoise exists.

Each participant will be on trial for approximately 15 months (±21 days). Ibudilast treatment will start within 10 weeks prior to surgery and will continue for up to 24 weeks after surgery. Treatment will be halted 5 days prior to surgery and resumed at the previous maximum dose right after operation. Patients will be taking Ibudilast for a maximum of 34 weeks. Participants will be followed up for 12 months after surgery.

The majority of participants will be identified from participating neurosurgical centres, typically via outpatient clinics. After being told about the study and given the participant information sheet, potential participants will have time to think about participating, and they will have the opportunity to ask a member of the research team any questions they might have. If potential participants decide to take part, they will be asked to sign a consent form and will be given a copy of the participant information sheet and informed consent form to keep. Then they will be given a unique trial ID number that, along with their date of birth, will be used to identify them during their involvement in the trial.

Screening procedures to establish eligibility include a review of participant medical history, age, DCM characteristics, and medications. Clinicians will also perform the following assessments: neurological examination, mJOA assessment, laboratory tests (Full Blood Count, Liver Function Test, Urea and Electrolytes, and urine analysis), an Electrocardiogram, and a serum pregnancy test for women, as we are not including pregnant women in this trial.

Initial assessments following confirmation of eligibility include demographics (weight, gender, ethnicity, date of birth) and review of potential adverse events (starting from point of giving informed consent). Clinicians will also perform the following assessments: 30 metres walk test, VAS pain, SF-36 and EQ-5D/Health Resource usage. Optional additional assessments include: GRASSP-Cervical Myelopathy, SCIMv3, NDI, Quick-DASH and Carer QoL (for sub-study). Dosing diary will be issued during this visit and patients will be instructed on how to fulfill it. A serum sample will be taken for PK studies.

Pre-operatively, following the start of treatment, adverse events will be reviewed by phone call, and Ibudilast or placebo will be delivered by courier or collected from the site by the participant. Additionally, study drug compliance will be assessed, and any changes to medical or drug history will be reviewed. Clinicians will also perform the following assessments: Laboratory Tests (FBC, LFT and U&Es), WHO performance status, Neurological examination, mJOA, 30m walk test, Respiratory Physiology, MRI and a serum sample for PK studies will be taken. Participants will be asked to complete the following questionnaires: VAS pain, SF-36, and EQ-5D/Health Resource usage. The following optional assessments will be conducted for sub-studies: Carer QoL, and Gait Lab (sub-study for Addenbrooke's only). The following assessments are optional: GRASSP-Cervical Myelopathy, SCIMv3, NDI and Quick-DASH.

An optional CSF sample will be taken intra-operatively, if possible but not limited to, and a paired serum sample for PK studies will be taken.

Post-operative procedures on discharge will include: adverse events will be reviewed (including operative complications), drug compliance assessed, and further IMP dispensed. Clinicians will also perform a neurological examination. Participants will be asked to complete the VAS Pain questionnaire. The NDI questionnaire is optional.

Follow-up assessments at 3 months post-surgery (±21 days) include a review of medication and adverse events, study drug compliance assessment, and further IMP dispensed. Clinicians will also perform the following assessments: Laboratory Tests (FBC, LFT and U&Es), neurological examination, mJOA, 30m walk test and a serum sample for PK studies will be taken. Participants will be asked to complete the following questionnaires: VAS pain and SF-36. The following optional assessments will be conducted for sub-studies: Carer QoL and Gait Lab (sub-study for Addenbrooke's only). The following assessments are optional: GRASSP-Cervical Myelopathy, NDI, EQ-5D/Health Resource usage and Quick-DASH.

SImilarly at 6 months post-surgery (±21 days), medication will be reviewed, adverse events reviewed, and study drug compliance assessed. Clinicians will also perform the following assessments: Laboratory Tests (FBC, LFT and U&Es), neurological examination, mJOA, 30m walk test, Respiratory physiology, MRI and a serum sample for PK studies will be taken. Participants will be asked to complete the following questionnaires: VAS pain, SF-36, and EQ-5D/Health Resource usage. The following optional assessments will be conducted for sub-studies: Carer QoL and Gait lab (sub-study at Addenbrooke's only). The following assessments are optional: GRASSP-Cervical Myelopathy, SCIMv3, NDI and Quick-DASH.

At the end of the trial, at 12 months post-surgery (±21 days), adverse events will be reviewed. Clinicians will perform the following assessments: Laboratory Tests (FBC, LFT and U&Es), neurological examination, mJOA, 30m walk test and a serum sample for PK studies will be taken. Participants will be asked to complete the following questionnaires: VAS pain, SF-36 and EQ-5D /Health Resource usage. The following optional assessment will be conducted for sub-study: Carer QoL. The following assessments are optional: GRASSP-Cervical Myelopathy, NDI and Quick-DASH.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ibudilast

Primary outcome(s)
1. Motor dysfunction in upper and lower extremities, loss of sensation, and sphincter dysfunction measured by change in the modified Japanese Orthopaedic Association Score (mJOA), an18-point clinician-administered scale, between screening and 6 months post-operatively
2. Neck pain measured bychange in Visual Analogue Scale (VAS) neck pain between screening and 6 months post-operatively

Key secondary outcome(s))
Health-related quality of life measured using the Physical Component Summary (PCS) and the Mental Component Summary (MCS) from the Short Form 36 (SF-36) v2 questionnaire between screening and 6 months post-operatively

Completion date
31/03/2029

Eligibility

Key inclusion criteria
1. Aged 18 to 80 years
2. Informed consent to participate given
3. Degenerative cervical myelopathy
4. Preoperative mJOA score ≥8 and ≤14
5. Scheduled for first surgical decompression as part of usual clinical practice

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Previous surgery for degenerative cervical myelopathy
2. Degenerative cervical myelopathy symptoms due to cervical trauma, determined at the discretion of the investigator
3. Hypersensitivity to Ibudilast or any of the formulation components
4. Evidence of acute hepatitis, clinically significant chronic hepatitis, or evidence of clinically significant impaired hepatic function through clinical and laboratory evaluation (including ALP >1.5x ULN; ALT or AST >2x ULN; GGT >3x ULN)
5. Evidence of thrombocytopenia at screening through laboratory evaluation including platelet count <5000
6. Active malignancy defined as a history of invasive malignancy, except if the patient has received treatment and displayed no clinical signs and symptoms for ≥5 years
7. Recent history (≤3 years) of chemical substance dependency or significant psychosocial disturbance that may impact the outcome or trial participation
8. Female patients with child bearing potential who are unwilling or unable to use reliable

methods of contraception
9. Female patients who are pregnant, lactating or planning pregnancy during the course of the trial
10. Inability to comply with trial procedures or follow-up schedule including IMP regime
11. Unable to take gelatin-based product
12. Participation in another CTIMP or device trial ≤30 days before the time of recruitment
13. Functional disability from a concomitant neurological disease that would mask the symptoms of degenerative cervical myelopathy, determined at the discretion of the investigator. Including but not limited to stroke with a residual disability, cerebellar ataxia, Parkinson's disease, symptomatic lumbar stenosis, and multiple sclerosis.
14. Resting pulse < 50 bpm, sinoatrial or atrioventricular block, uncontrolled hypertension, or corrected QT interval (QTcF) >450 ms
15. History of stomach or intestinal surgery or any other condition that could interfere with, or is judged by the investigator to interfere, with absorption, distribution, metabolism, or excretion of IMP
16. Unable to converse, read, or write English

Date of first enrolment
28/09/2020

Date of final enrolment
28/02/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Hills Road
Cambridge
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CB2 0QQ

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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NW1 2PG

Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
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Study participating centre
Kings College Hospital NHS Foundation Trust
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: CS-2015-15-023

Funder Name
National Institute for Health Research (NIHR) (UK)

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 and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	07/03/2023	08/03/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes