ISRCTN42179756 https://doi.org/10.1186/ISRCTN42179756

Low-dose intravenous immunoglobulin treatment for Complex Regional Pain Syndrome

Submission date
28/06/2013

Recruitment status
No longer recruiting

Registration date
28/06/2013

Overall study status
Completed

Last Edited
11/12/2018

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic pain is often defined as any pain lasting more than 12 weeks. Many patients with chronic pain do not experience satisfactory pain relief with currently available treatments. This may be related to the fact that the causes for chronic pain are often not fully understood. We have previously treated patients with intravenous immunoglobulin (IVIG), a mixture of antibodies delivered into a vein, and have reported encouraging results. It is now important to perform a larger study to explore this further.

Who can participate?
Patients aged over 18 with complex regional pain syndrome, a condition in which a person experiences persistent severe and debilitating pain.

What does the study involve?
Patients are randomly allocated to receive two infusions of either IVIG or placebo (dummy drug) 3 weeks apart and to complete detailed pain diaries. They also have the option to receive two further infusions of IVIG 3 weeks apart once the data for the study has been collected.

What are the possible benefits and risks of participating?
IVIG may provide pain relief in patients where classical treatments are not satisfactorily effective. If IVIG treatment proves to be effective, this study may also stimulate research on the use of IVIG in other chronic pain syndromes.

Where is the study run from?
King's College London (UK)

When is the study starting and how long is it expected to run for?
August 2013 to November 2015

Who is funding the study?
Biotest UK Ltd, NIHR and Pain Relief Foundation (UK)

Who is the main contact?
Caroline Murphy
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2012-000058-73

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
12715

Study information

Scientific Title
A multi-centre (UK) double-blind randomised parallel group placebo controlled trial to evaluate the efficacy, safety, and tolerability of Intravenous Immunoglobulin (IVIg) 0.5g/kg plus standard treatment, versus matched placebo plus standard treatment in patients with long standing Complex Regional Pain Syndrome

Acronym
LIPS

Study objectives
Main objective of the trial:
To gain, within 44 months, both definite proof of the clinical efficacy, and a more confident estimate of the effect size of low-dose IVIg treatment to reduce pain in patients with moderate or severe Complex Regional Pain Syndrome.

Secondary objectives of the trial:
To achieve better understanding of this technology, including:
1. Stability of effect with repeat administration
2. Factors predicting a beneficial response
3. Effects on additional outcome parameters including stimulus-evoked pain, pain interference, quality of life, and short-term risk profile
4. Health economics evaluation
5. Creation of a bank of biological samples for future CRPS research

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=12715

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England Hatfield REC (formerly known as NRES Committee East of England Welwyn), 06 /06/2013, ref:12/EE/0164

Study design
Double-blind randomised parallel placebo-controlled trial; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Generic Health Relevance and Cross Cutting Themes; Subtopic: Generic Health Relevance (all Subtopics); Disease: Anaesthetics, Complex Regional Pain Syndrome

Interventions
The experimental intervention is 0.5 g/kg IntratectTM IVIg infusion, in combination with ongoing normal standard treatment for Complex Regional Pain Syndrome.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Added 26/01/2016:
The average 24h pain intensity over 37 days, recorded in pain diary entries for the previous 24 hours collected on days 6 to 42 (day 1=day of first infusion)

Secondary outcome measures
Added 26/01/2016:
1. Pain interference measured using the interference subscale of the Brief Pain Inventory at days 22 and 43
2. Quality of life measured using the Euroqol EQ-5D-5L at days 22 and 43
All other outcomes are exploratory.

Overall study start date
01/08/2013

Completion date
30/11/2015

Eligibility

Key inclusion criteria
1. Diagnosis of CRPS I or II according to Budapest research criteria (appendix 3) (15).
2. Disease duration of 1-5 years and a mean pain intensity on an 11-point (0-10) Numeric Rating Scale (NRS) over the first seven daily entries after screening within a pre-defined range (see section 9 for details of pain thresholds for eligibility).
3. Failure to respond (poor efficacy or unacceptable side effects) to drugs recommended for the treatment of neuropathic pain (16), including pregabalin or gabapentin, a tricyclic antidepressant, and mild and strong opioids (where not contraindicated or refused by the patient).
4. Previous specialised pain physiotherapy (17), including desensitisation techniques, and either mirror therapy (18) or graded motor imagery treatment (19), or both (where not contraindicated or refused by the patient).
5. Willingness to confirm the use of adequate birth control while on the trial will be required in pre-menopausal women without evidence for an inability to become pregnant.
6. Willingness to not start any other treatment for CRPS during the parallel part of the trial.
7. Age 18 years and above; Target Gender: Male & Female

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 108; UK Sample Size: 108

Key exclusion criteria
1. Other significant chronic pains, which in the view of the study doctor may make assessment of the pain arising from CRPS difficult.
2. If the patient recently started a new therapy for CRPS, which in the view of the study doctor may change the patients pain level during the time of participation in the trial.
3. Unstable medical conditions.
4. Litigation. Patients in litigation will be excluded only if conclusion of that litigation is imminent during the course of the study.
5. Pregnant or breastfeeding patients.
6. Less than half of the lower limit of the normal serum IgA level given by the respective trials unit laboratory
7. Rare contraindications to IVIg therapy as per summary of product characteristics (SmPC)
8. Receiving IVIg for other reasons,
9. Patients previously enrolled in CRPS IVIg/SCIG trials
10. Drugs or alcohol abuse
11. Psychiatric or mental health disorder which could in the judgement of the site investigator interfere with successful study participation
12. Unwillingness or inability to complete daily diaries, or inability to understand the questionnaires being used.
13. Cancer other than basal cell carcinoma within the last 5 years. However, those patients who have received definitive treatment, such as curative surgery more than 6 months ago, with no known recurrence can be included.
14. A history of hypercoagulable or thrombophilic clotting abnormalities.
15. A history of thrombembolic events: ischaemic stroke, confirmed myocardial infarction, pulmonary embolism; deep venous thrombosis except where immobility related (e.g., after injury or operation).
16. Renal failure, or serum creatinine greater than 1.5 times the upper limit of normal at screening
17. Any medical condition which in the opinion of the investigator would make it unsafe for the patient to participate or which would interfere with assessment of the outcome measures.

Date of first enrolment
15/08/2013

Date of final enrolment
28/10/2015

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
The Walton Centre NHS Trust
Liverpool
United Kingdom
L9 7LJ

Study participating centre
Guy's and St Thomas' Hospital
London
United Kingdom
SE1 9RT

Study participating centre
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Norfolk and Norwich University Hospital
Norwich
United Kingdom
NR4 7UY

Study participating centre
Royal National Hospital for Rheumatic Diseases
Bath
United Kingdom
BA1 1RL

Study participating centre
Gartnavel General Hospital
Glasgow
United Kingdom
G12 0YN

Study participating centre
University Hospitals of Leicester
Leicester

United Kingdom
LE3 9QP

Sponsor information

Organisation
University of Liverpool (UK)

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Sponsor type
University/education

Website
http://www.liv.ac.uk/

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Industry

Funder Name
Biotest UK Ltd

Funder Name
NIHR (UK) - Efficacy and Mechanism Evaluation; Grant Codes: 11/14/33

Funder Name
Pain Relief Foundation (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	24/10/2014		Yes	No
Results article	results	03/10/2017		Yes	No
Results article	results	01/11/2017		Yes	No
HRA research summary			28/06/2023	No	No