ISRCTN14939460 https://doi.org/10.1186/ISRCTN14939460

Combination analgesic development for enhanced clinical efficacy

Submission date
03/03/2017

Recruitment status
No longer recruiting

Registration date
06/03/2017

Overall study status
Completed

Last Edited
09/08/2017

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Fibromyalgia is a long-term condition that causes pain all over the body. Chronic (long-term) pain, including fibromyalgia, affects 1 in 3 Canadians and costs around $650 billion/year in North America. Current therapies are not always effective and have a lot of side-effects at high doses. Rational combination therapy (treatment with several drugs) with different drugs to treat fibromyalgia has shown potential for measurable improvements in pain relief, quality of life and healthcare usage. Today, more than 50% of fibromyalgia patients are taking two or more pain-relieving medications at once but combination use is based on little evidence. Research is urgently needed to identify safer, more effective, combinations. The aim of this study is to test a promising combination of pregabalin, a sedating drug that is used to treat epilepsy and fibromyalgia pain, and alpha-lipoic acid, a non-sedating antioxidant that is effective for neuropathic (nerve) pain and currently being studied for efficacy in fibromyalgia.

Who can participate?
Patients aged 18 and older with fibromyalgia

What does the study involve?
Participants are allocated to be treated with pregabalin, alpha-lipoic acid, and a combination of both drugs over three treatment periods in a random order. All drugs are taken by mouth daily with an increasing dose over a 45-day period, followed by 11 days at a decreasing dose. After the three treatment periods there are two final telephone follow-ups 2 weeks and 3 months later.

What are the possible benefits and risks of participating?
The results of this study will help to improve the treatment of fibromyalgia, particularly if the combination of drugs is found to work better than either drug alone. The risks and benefits of this study are the same as the risks and benefits of each of the drugs, pregabalin and lipoic acid. The benefits of pregabalin are pain relief, improved sleep and reduced anxiety. The benefits of lipoic acid are pain relief. The most common risks of pregabalin are dizziness, drowsiness and slowed mental function. The risks of lipoic acid are nausea and vomiting (only at doses greater than 1200mg/day).

Where is the study run from?
Queen's University (Canada)

When is the study starting and how long is it expected to run for?
May 2017 to November 2020

Who is funding the study?
1. Canadian Institutes of Health Research (Canada)
2. Strategy for Patient-Oriented Research (Canada)
3. Chronic Pain Network (Canada)

Who is the main contact?
Dr Ian Gilron

Contact information

Type(s)
Scientific

Contact name
Dr Ian Gilron

Contact details
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Additional identifiers

Protocol serial number
ANAE-313-17

Study information

Scientific Title
Randomized controlled trial of a pregabalin-lipoic acid combination for the treatment of fibromyalgia

Acronym
CADENCE

Study objectives
The combination of pregabalin and alpha-lipoic acid has superior analgesic efficacy versus either single agent for fibromyalgia.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board, 03 /03/2017, ref: ANAE-313-17

Primary study design
Interventional

Study design
Double-blind randomised three-period crossover trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fibromyalgia

Interventions
There are three treatment arms that cross over as per a balanced Latin square design.

Group 1: Participants receive oral pregabalin, administered twice daily, starting at a dose of 75 mg once daily and titrated to individual maximally tolerated dose over 45 days and followed by an 11-day dose taper and washout period
Group 2: Participants receive oral alpha-lipoic acid, administered twice daily, starting at a dose of 300 mg once daily and titrated to individual maximally tolerated dose over 45 days and followed by an 11-day dose taper and washout period
Group 3: Participants receive oral pregabalin and alpha-lipoic acid administered at the above doses, titrated to individual maximally tolerated dose over 45 days and followed by an 11-day dose taper and washout period

Upon completion of the trial after the three treatment periods, there will be two final telephone follow-ups at 2 weeks and 3 months after trial completion.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Pregabalin, alpha-lipoic acid

Primary outcome(s)
Mean daily pain, measured using a 0-10 numerical rating scale with 0 = no pain, 10 = worst pain imaginable, averaged over the maximally tolerated dose fixed dose week (days 39-45) of each treatment period

Key secondary outcome(s)
1. Pain, measured by 0-10 numerical rating scale at baseline and daily throughout entire trial
2. Pain, measured by short-form McGill Pain Questionnaire at baseline and during maximal

tolerated dose of each of the three treatment periods
3. Drug doses, measured in milligrams over the 7-day maximal tolerated dose phases of each of the three treatment periods
4. Adverse events, measured in % frequency over the titration phases, maximal tolerated dose phases and dose taper/washout phases of each of the three treatment periods
5. Global relief, measured with the global relief category scale during the maximal tolerated dose phases of each of the three treatment periods
6. Pain interference, measured with the Brief Pain Inventory and the Fibromyalgia Impact Questionnaire at baseline and during the maximal tolerated dose phases of each of the three treatment periods
7. Mood, measured with the Beck Depression Inventory-2 at baseline and during the maximal tolerated dose phases of each of the three treatment periods
8. Anxiety, measured with the Beck Anxiety Inventory at baseline and during the maximal tolerated dose phases of each of the three treatment periods
9. Quality of life, measured with the SF-36 survey at baseline and during the maximal tolerated dose phases of each of the three treatment periods
10. Blinding, measured with a blinding questionnaire during the maximal tolerated dose phases of each of the three treatment periods
11. Acetaminophen consumption, measured in milligrams during the dose taper/washout phases of each of the three treatment periods

Completion date
01/11/2020

Eligibility

Key inclusion criteria
1. Fibromyalgia
2. Daily pain (≥3/10) for at least 3 months
3. AST/ALT ≤120% upper limit of normal
4. Creatinine clearance ≥60 ml/min
5. Necessary abilities, visual acuity, and language skills for questionnaire completion and phone communication with research personnel
6. Adults over the age of 18

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria

1. Patients with major organ system disease, moderate to severe sedation or ataxia due to other required drugs, hypersensitivity to study medications, seizure disorder, or other painful condition >50% as severe as their fibromyalgia pain
2. Patients with a major, poorly controlled, psychiatric disorder, severe depression or suicidal ideation, or active substance abuse disorder
3. Patients who live alone and cannot assure daily contact with a friend, family member, or caregiver
4. Women of childbearing potential will be required to receive a highly effective form of contraception and a negative pregnancy test at baseline
5. Allergy or hypersensitivity to any of the study medications
6. Seizure disorder

Date of first enrolment
01/07/2017

Date of final enrolment
01/11/2020

Locations

Countries of recruitment
Canada

Central African Republic

Study participating centre
Queen's University
Providence Care K7L2V7
99 University Ave
Kingston
Canada
K7L 2V7

Sponsor information

Organisation
Canadian Institutes of Health Research (Canada), Strategy for Patient-Oriented Research (SPOR), Chronic Pain Network

ROR
https://ror.org/01gavpb45

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
Strategy for Patient-Oriented Research

Funder Name
Chronic Pain Network

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Ian Gilron.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	04/08/2017		Yes	No