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Pain improvement with novel combination analgesic regimens

Submission date 31/10/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 06/01/2017	**Overall study status** Completed	
Last Edited 12/06/2017	**Condition category** Signs and Symptoms	

Plain English summary of protocol

Background and study aims
Chronic (long-term) pain, including neuropathic pain caused by problems with signals from the nerves, affects 20-30% of Canadians and costs about $650 billion/year in North America alone. For many patients the currently available treatments do not work and are also often limited by their side effects. Combining two or more medications for neuropathic pain can provide additional benefits, and the use of combination treatment is quite common even though there is little evidence to show us which specific combinations are most helpful and safe. 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 neuropathic pain, and alpha-lipoic acid, a non-sedating antioxidant that is also effective for neuropathic pain.

Who can participate?
Patients aged 18 to 89 with neuropathic pain

What does the study involve?
Participants are treated with pregabalin, alpha-lipoic acid, and a combination of both drugs over three treatment periods. All drugs are taken orally 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 neuropathic pain, 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 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?
March 2017 to February 2021

Who is funding the study?
Canadian Institutes of Health Research (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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PJT-148654

Study information

Scientific Title
Randomized controlled trial of a pregabalin-lipoic acid combination for the treatment of chronic neuropathic pain

Acronym
PAIN-CARE

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

Ethics approval required

Old ethics approval format

Ethics approval(s)
Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board, 15 /12/2016, ref: ANAE-305-16

Study design
Double-blind randomised three-period crossover trial

Primary study design
Interventional

Secondary study design
Randomised cross over 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
Neuropathic pain

Interventions
There are three treatment arms that cross over as per a balanced Latin square design.
1. 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
2. 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
3. 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 measure
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

Secondary outcome measures
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 and Neuropathic Pain Symptom Inventory 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 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

Overall study start date
01/03/2017

Completion date
28/02/2021

Eligibility

Key inclusion criteria
1. Neuropathic pain
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. Glycosylated hemoglobin ≤9.5%
6. Necessary abilities, visual acuity, and language skills for questionnaire completion and phone communication with research personnel
7. Adults between the ages of 18 to 89

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
84

Key exclusion criteria
1. Patients with major organ system disease, cardiovascular autonomic neuropathy, 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 neuropathic 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

Date of first enrolment
01/03/2017

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
Canada

Study participating centre
Queen's University
Providence Care
Kingston
Canada
K7L2V7

Sponsor information

Organisation
Canadian Institutes of Health Research

Sponsor details
160 Elgin Street
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Sponsor type
Government

Website
http://www.cihr-irsc.gc.ca/

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, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal.

Intention to publish date
28/02/2022

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	08/06/2017		Yes	No