Combination drug therapy for fibromyalgia pain

[] Prospectively registered Submission date Recruitment status 12/01/2011 No longer recruiting [] Protocol [] Statistical analysis plan Registration date Overall study status 28/02/2011 Completed [X] Results [] Individual participant data Last Edited Condition category 14/03/2017 Musculoskeletal Diseases

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

ANAE-172-01

Study information

Scientific Title

Combination pharmacotherapy for the management of pain in fibromyalgia: a double-blind, randomised, placebo-controlled, four-period crossover trial

Study objectives

A combination of duloxetine and pregabalin has a superior therapeutic profile than that of either drug alone for reducing fibromyalgia pain.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Queen's University Research Ethics Board, 09/11/2010

Study design

Double-blind randomised placebo-controlled four-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

Fibromyalgia

Interventions

- 1. Pregabalin-duloxetion combination
- 2. Pregabalin
- 3. Duloxetine
- 4. Inert placebo

As per a double-dummy, balanced Latin Square design, trial treatments are administered orally in four different treatment periods. In each of the four periods, doses of study medication are gradually titrated - over 24 days - towards each individual maximal tolerated dose and continued at that dose for seven days followed by an 11 day taper-washout period. Ceiling doses are 450 mg daily for pregabalin and 120 mg daily for duloxetine. Total duration of follow-up is 9 months.

Intervention Type

Drug

Phase

Drug/device/biological/vaccine name(s)

Duloxetine, pregabalin

Primary outcome measure

Daily pain intensity, recorded at study baseline and during each treatment at maximal tolerated dose (MTD)

Secondary outcome measures

Recorded at baseline and during each treatment at maximal tolerated dose (MTD):

- 1. Fibromyalgia Impact Questionnaire
- 2. Number of tender points
- 3. Medical Outcomes Study Sleep Scale
- 4. Global pain relief
- 5. Brief Pain Inventory
- 6. Beck Depression Inventory 2
- 7. Beck Anxiety Inventory
- 8. Short form McGill Pain Questionnaire
- 9. 36-item short form (SF-36) quality of life survey
- 10. Maximal tolerated doses of of duloxetine and pregabalin
- 11. Frequency/severity of other treatment-emergent adverse effects
- 12. Blinding questionnaires
- 13. Acetaminophen consumption

Overall study start date

01/02/2011

Completion date

30/01/2014

Eligibility

Key inclusion criteria

- 1. Fibromyalgia according to American College of Rheumatology (ACR) criteria 1990
- 2. Experiencing daily moderate pain (greater than or equal to 4/10) for at least 3 months
- 3. Adults aged 18 to 70 years, either sex
- 4. Patients entering the study on duloxetine, gabapentinoids and other drugs which adversely interact with study drugs (e.g., selective serotonin receptor inhibitors [SSRIs], momanime oxidase inhibitors [MAOIs], tramadol etc.) must be weaned off. Participants taking less than 200 mg morphine equivalents/day are allowed to continue these medications at a steady dose.
- 5. Permitted analgesic medications are non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen (4 g/d) and aspirin (less than or equal to 325 mg/d for cardiac prophylaxis)
- 6. Serum laboratory results obtained at study entry:
- 6.1. Liver function tests: alanine aminotransferase (ALT)/aspartate aminotransferase (AST) less than 1.2 times upper limit of normal
- 6.2. Creatinine clearance less than 1.5 times upper limit of normal
- 6.3. Negative serum betaHCG for women of childbearing potential
- 7. Adequate birth control for all women of child-bearing potential
- 8. Sufficient cognitive function and English language skills to complete questionnaires and communicate verbally with the nursing staff to permit titration of the study drugs

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

69

Key exclusion criteria

- 1. Presence of a painful condition, including inflammatory rheumatic disease, as severe as (or worse than), but distinct from, their fibromyalgia
- 2. Pregnancy or lactation
- 3. Women of child-bearing potential not using adequate contraceptives
- 4. End-stage kidney or liver disease
- 5. Unstable cardiovascular disease (myocardial infarction [MI] within preceding year, unstable angina or congestive heart failure) or clinically relevant abnormal 12-lead electrocardiogram
- 6. Signs or symptoms of any central neurologic disorder (including seizures)
- 7. Untreated endocrine disorder
- 8. A severe mood disorder as diagnosed by a psychiatrist and/or active suicidal ideation
- 9. Hypersensitivity to any of the study medications
- 10. History of significant abuse of illicit drugs, prescription drugs or alcohol as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV R)
- 11. Patients requiring continued treatment with drugs which adversely interact with study medication (e.g. quinolone antibiotics, warfarin, SSRIs etc.)
- 12. Patients taking more than 200 mg morphine equivalents/day
- 13. Uncontrolled diabetes mellitus
- 14. Uncontrolled hypertension
- 15. Documented human immunodeficiency virus (HIV), hepatitis and other clinically relevant liver dysfunction
- 16. Malignant diseases (including brain tumours)
- 17. Subjects under other investigational studies
- 18. Hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrose isomaltase insufficiency
- 19. Uncontrolled narrow-angle glaucoma
- 20. Continued use of MAOIs, fluvoxamine, selective serotonin reuptake inhibitors (SSRIs) and anticoagulants

Date of first enrolment

01/02/2011

Date of final enrolment

30/01/2014

Locations

Countries of recruitment

Canada

Study participating centre Kingston General Hospital

Kingston Canada K7L2V7

Sponsor information

Organisation

Queen's University (Canada)

Sponsor details

Department of Anesthesiology 99 University Avenue Kingston Canada K7L 3N6

Sponsor type

University/education

Website

http://www.queensu.ca/

ROR

https://ror.org/02y72wh86

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 - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Canada

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2016		Yes	No