

Combination drug therapy for fibromyalgia pain

Submission date 12/01/2011	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 28/02/2011	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 14/03/2017	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Ian Gilron

Contact details
Department of Anesthesiology
Victory 2 Pavillion
Kingston General Hospital
76 Stuart Street
Kingston
Canada
K7L2V7

Additional identifiers

Protocol serial number
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

Primary study design

Interventional

Study design

Double-blind randomised placebo-controlled four-period crossover trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Fibromyalgia

Interventions

1. Pregabalin-duloxetine 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

Phase IV

Drug/device/biological/vaccine name(s)

Duloxetine, pregabalin

Primary outcome(s)

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

Key secondary outcome(s)

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 duloxetine and pregabalin
11. Frequency/severity of other treatment-emergent adverse effects
12. Blinding questionnaires
13. Acetaminophen consumption

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], monoamine 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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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)

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, 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

Results and Publications

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