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# Combination drug therapy for fibromyalgia pain

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

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

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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

Phase IV

### 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
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**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, 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
Not provided at time of registration

### Study outputs

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