

Better treatments for refractory breathlessness

Submission date 31/05/2016	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 13/06/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/12/2022	Condition category Respiratory	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Breathlessness is a common symptom affecting 50-70% of people with cancer and over 90% of people with non-cancer lung disease. In some cases, even when the underlying causes are treated, the breathlessness itself continues (refractory breathlessness). This can be very distressing, causing fear and panic; reduced quality of life, including social life; and can result in emergency hospital admissions. At the moment, there is no standard treatment for refractory breathlessness. This study is looking at a commonly used antidepressant drug called mirtazapine, which is used to treat depression and anxiety. This drug affects a brain chemical called serotonin, which is active when people are breathless. Reports involving small numbers of patients suggest that mirtazapine may be an effective treatment for breathlessness, possibly because it also reduces feelings of panic. The aim of this study is to find out whether conducting a small trial looking at the effectiveness of mirtazapine in the treatment of refractory breathlessness is feasible and whether enough patients can be recruited to take part.

Who can participate?

Adult patients with cancer or non-cancer lung disease experiencing refractory breathlessness.

What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group take 15mg tablets of mirtazapine every day for 28 days. Half way through the study (day 14) participants have their breathlessness assessed on a numbered scale to find out if it has improved. If there is no improvement and the drug is not causing any side effects, then the dose is doubled for the remaining 14 days of the study. Those in the second group take a placebo (dummy pill) every day for 28 days. Participants are then followed up for seven days following completion of the study to find out if their breathlessness has improved. After 12 months, the number of participants recruited to the study are recorded in order to find out if enough patients could be recruited.

What are the possible benefits and risks of participating?

Not provided at time of registration.

Where is the study run from?

1. Kings College Hospital (UK)
2. Castle Hill Hospital (UK)
3. Hull Royal Infirmary (UK)

4. Nottingham City Hospital Campus (UK)

5. Queens Medical Centre Campus (UK)

When is the study starting and how long is it expected to run for?

November 2015 to January 2018

Who is funding the study?

Marie Curie Cancer Care (UK)

Who is the main contact?

Dr Heather Cook

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Contact information

Type(s)

Public

Contact name

Dr Heather Cook

Contact details

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Additional identifiers

EudraCT/CTIS number

2015-004064-11

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

30471

Study information

Scientific Title

BETter TreatmEnts for Refractory Breathlessness: A feasibility study of the use of mirtazapine for refractory breathlessness

Acronym

BETTER-B (Feasibility)

Study objectives

The aim of this study is to determine the feasibility of conducting a large-scale randomised, double-blind, placebo-controlled study of mirtazapine for refractory breathlessness.

Ethics approval required

Old ethics approval format

Ethics approval(s)

London - Central Research Ethics Committee, 29/01/2016, ref: 16/LO/0091

Study design

Randomised; Interventional; Design type: Treatment, Drug

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Specialty: Respiratory disorders, Primary sub-specialty: Respiratory disorders; UKCRC code/
Disease: Respiratory/ Other diseases of the respiratory system

Interventions

Participants will be randomised via minimisation on a 1:1 ratio to receive either oral mirtazapine (15mg/day) or placebo medication for 28 days. At day 14 of treatment breathlessness intensity ("at worst" over the previous 24 hours) will be assessed using the numerical rating scale (NRS). If there is no improvement in NRS (i.e. NRS does not increase by 1 point or more compared to baseline NRS) and the drug has been well tolerated, the daily dose of treatment will be doubled.

Participants will be followed up by phone 7 days after the end of trial treatment to assess whether any adverse events or reactions have occurred.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Mirtazapine

Primary outcome measure

Recruitment rate is measured by the number of patients recruited across three hospitals over 12 months.

Secondary outcome measures

Feasibility:

1. Number of patients screened for eligibility and reasons for non-eligibility
2. Proportion of eligible patients randomised and reasons for non-randomisation
3. Proportion of patients for which blinding is maintained
4. Proportion of research assessors for which blinding is maintained
5. Proportion of patients remaining on study for 28 days
6. Proportion of and reasons for patients with missing data for trial outcomes
7. Proportion of patients who would be eligible for dose escalation at 28 days
8. Treatment compliance over the period

Activity, symptoms and quality of life:

1. Breathlessness mastery is assessed using the Chronic Respiratory Questionnaire (CRQ) and modified Medical Research Council (mMRC) dyspnoea scale on day 14 and day 28
2. Lower extremity functioning is measured using the Short Physical Performance Battery (SPPB) on day 28
3. Coping self-belief is measured using the Generalized Self-Efficacy Scale (GSES) on day 28
4. Palliative symptoms is measured using the Integrated Palliative care Outcome Scale (IPOS) on day 14 and day 28
5. Anxiety and depression are measured using the Hospital Anxiety and Depression Scale (HADS) on day 14 and day 28
6. Quality of life is measured using the EQ-5D-5L on day 28 and Australian-modified Karnofsky Performance Scale (AKPS) on day 14 and day 28
7. Health Economics are assessed using the Client Services Receipt Inventory (CSRI) on day 28

Safety and toxicity:

1. Adverse reactions are assessed using the Common Terminology Criteria for Adverse Events (CTCAE) categorisation on days 7, 14, 21 and 28
2. Occurrence of SAEs, SARs and SUSARs
3. Opioid medication is assessed on days 7, 14, 21 and 28

Overall study start date

01/11/2015

Completion date

26/12/2018

Eligibility

Key inclusion criteria

1. Male or female aged ≥ 18 years old
2. Modified MRC dyspnoea scale grade 3 or 4
3. Diagnosis of either:
 - 3.1. Cancer
 - 3.2. Chronic obstructive pulmonary disease (COPD)

- 3.3. Interstitial lung disease (ILD)
- 3.4. Chronic heart failure (New York Heart Association class III or IV)
4. On optimal treatment of the underlying condition in the opinion of the identifying clinician
5. Management of the underlying condition unchanged for the previous 1 week
6. Reversible causes of breathlessness optimally treated in the opinion of the identifying clinician
7. Expected prognosis of ≥ 2 months
8. If female and of child-bearing potential, must agree to use adequate contraception
9. Able to complete questionnaires and trial assessments
10. Able to provide written informed consent

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 60; UK Sample Size: 60

Total final enrolment

64

Key exclusion criteria

1. Existing antidepressant use
2. Known contraindication to mirtazapine
3. Hypersensitivity to the active substance or to any of the components of the mirtazapine or placebo (e.g. lactose intolerance)
4. Australia modified Karnofsky Performance Scale ≤ 40
5. Pregnant or breast-feeding women
6. Patients with acute cardiac events within 3 months of randomisation (myocardial infarction, unstable angina pectoris, or significant cardiac conduction disturbance)
7. Patients with known hepatic impairment
8. Patients with known renal impairment
9. Patients with uncontrolled blood pressure
10. Patients with uncontrolled diabetes mellitus
11. Patients with uncontrolled seizures, epilepsy or organic brain syndrome
12. Patients with severe depression or suicidal thoughts
13. Patients with a history of psychotic illness (schizophrenia, bipolar disorder, mania or hypomania, or other psychotic disturbances)

Date of first enrolment

01/08/2016

Date of final enrolment

31/07/2017

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Kings College Hospital

Denmark Hill

London

United Kingdom

SE5 9RS

Study participating centre

Castle Hill Hospital

Castle Road

Cottingham

United Kingdom

HU16 5JQ

Study participating centre

Hull Royal Infirmary

Anlaby Road

Hull

United Kingdom

HU3 2JZ

Study participating centre

Nottingham City Hospital Campus

Hucknall Road

Nottingham

United Kingdom

NG5 1PB

Study participating centre

Queens Medical Centre Campus

Lister Road

Nottingham
United Kingdom
NG7 2RT

Sponsor information

Organisation

Kings College Hospital NHS Foundation Trust

Sponsor details

161 Denmark Hill
London
England
United Kingdom
SE5 8EF

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/01n0k5m85>

Funder(s)

Funder type

Charity

Funder Name

Marie Curie Cancer Care

Alternative Name(s)

Marie Curie Cancer Care

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Results of the study are intended to be reported in a peer reviewed scientific journal once data collection and data analysis is completed.

Intention to publish date

31/01/2019

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2020	10/01/2020	Yes	No
Results article	qualitative results	22/02/2020	24/02/2020	Yes	No
Protocol file	version 2.0	11/02/2016	15/12/2022	No	No
HRA research summary			28/06/2023	No	No