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GARMIn: The Role of GABAB Receptor Mechanisms in Cough

Submission date
25/02/2014

Recruitment status
No longer recruiting

Registration date
25/02/2014

Overall study status
Completed

Last Edited
07/03/2017

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
People cough in order to clear their airways. Most coughs are caused by viruses and settle down by themselves, but some people develop persistent coughing for no reason which can last for many years. This is called chronic cough which is very troublesome and it can have a major impact on the daily life of sufferers. There are very few effective medicines available to treat chronic cough because we dont fully understand how and why coughing happens. We are doing this research to understand what mechanisms in the body produce coughing and why some people are more prone to developing a chronic cough than others. We will investigate this in this study by testing two different medications. The first one is called Baclofen. Baclofen is a licensed drug which is already used to treat some medical conditions involving the muscles. We already know that Baclofen can also reduce a persons cough. In this study, we would like to find out if another drug similar to Baclofen can also reduce a persons cough. The other drug is called Lesogaberan. Lesogaberan is a test medication and is not currently licensed. However, it has already been tested in many trials involving healthy volunteers and patients.

Who can participate?
To improve knowledge of certain diseases, patients and the public are often asked if they would like to be involved in research studies. This study is open to healthy individuals aged 18 to 70 years.

What does the study involve?
Taking part involves five visits to the University Hospital of South Manchester NHS Foundation Trust. Participants will be required to perform a capsaicin challenge test (designed to make a person cough), and undergo safety tests which include blood tests, urine tests (women only) and electrocardiograms (ECGs). Participants will also be given tablets containing Baclofen and Lesogaberan on separate occasions. They will also be given a tablet called a placebo. A placebo is a substance that looks the same as the study medicine but it does not contain any active ingredients, it is a dummy drug. Neither the study participants nor the researcher will know which drug has been given at each treatment visit. The order of treatment will be allocated at random (like tossing a coin).

What are the possible benefits and risks of participating?
There will be no direct benefit to participants by taking part in this study. However, we hope that the information we get from this study will help to improve treatment of cough in the future. Baclofen is a licensed drug which is used widely. The most common side effects reported by people taking Baclofen are drowsiness, light-headedness and headache. Lesogaberan is an unlicensed study medication but it has already been tested in several studies involving both healthy volunteers and patients and has been found to be well tolerated. The main side effect experienced by some people is a short-lasting feeling of pins and needles. During the study participants will be asked to perform a cough challenge test which involves inhaling capsaicin, a component of chilli peppers. Capsaicin can cause tightening of the airways, although this is rare. Breathing tests are performed during and after the test to monitor any chest tightening, which is easily treated by inhaling salbutamol (a medication to open up the airways).

Where is the study run from?
This study is taking place at the University Hospital of South Manchester NHS Foundation Trust.

When is the study starting and how long is it expected to run for?
The study started in January 2014 and will run until April 2014.

Who is funding the study?
Medical Research Council (UK).

Who is the main contact?
Dr Demi Valdramidou
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Contact information

Type(s)
Scientific

Contact name
Ms Dimitra Valdramidou

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14999

Study information

Scientific Title
The Role of GABAB Receptor Mechanisms in Cough: Effect of Lesogaberan, Baclofen and Placebo on Experimentally Induced Cough Responses in Healthy Controls

Acronym
GARMIn

Study objectives
The aim of this study is to investigate the effects of lesogaberan and baclofen on chronic cough.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West Haydock, 22/10/2013, ref: 13/NW/0715

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Topic: Respiratory; Subtopic: Respiratory (all Subtopics); Disease: Respiratory

Interventions
Baclofen, central acting GABA-B receptor agonist (mechanistic use), 40 mg, oral tablet
Placebo, 40 mg, oral tablet

Lesogaberan, peripheral acting GABA-B receptor agonist (mechanistic use), 120 mg, oral tablet
Placebo, 120 mg, oral tablet

Each study treatment will be taken during the study visit and will consist of a single capsule (lesogaberan 120 mg or matched placebo) and a single tablet (baclofen or matched placebo).

Total duration of treatment is five visits (maximum 5 hours per visit) over a 4-week period.

There is no planned follow-up visit after the final study visit.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Baclofen, lesogaberan

Primary outcome measure
Emax of Lesogaberan V placebo; Timepoint(s): Change in the maximal number of coughs (Emax) evoked by inhaled capsaicin

Secondary outcome measures
1. ED50 of Lesogaberan V placebo; Timepoint(s): Dose of inhaled capsaicin inducing at least half of maximal cough frequency (ED50)
2. Emax of Lesogaberan V Baclofen; Timepoint(s): Change in the maximal number of coughs (Emax) evoked by inhaled capsaicin

Overall study start date
09/01/2014

Completion date
30/04/2014

Eligibility

Key inclusion criteria
1. Provision of signed, written and dated informed consent, prior to any study-specific procedures
2. Aged 18 to 70 years
3. Body mass index (BMI) of between 19 and 30 kg/m2 (inclusive) and weight between 50 kg and 100 kg
4. Normal spirometry
5. Clinically normal physical findings
6. Subjects with no concurrent diseases who do not require any medication
7. Female subjects with no childbearing potential or using highly effective method of contraception for at least the previous 3 months
Target Gender: Male & Female; Upper Age Limit 70 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 15; UK Sample Size: 15

Key exclusion criteria
1. History of any clinically significant disease or disorder, in particular no current or past history of chronic cough or respiratory disease.
2. History or presence of gastrointestinal, hepatic or renal disease
3. Any clinically significant illness, medical or surgical procedure or trauma within 4 weeks of the first administration of study medication
4. Any clinically significant abnormalities in clinical chemistry, haematology or urinalysis results Abnormal screening laboratory values in Liver Function tests
5. History of clinically significant orthostatic reaction or syncope
6. Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG according to the investigator
7. Prolonged QTcF>450ms or family history of long QT syndrome

Date of first enrolment
09/01/2014

Date of final enrolment
30/04/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Wythenshaw Hospital
Manchester
United Kingdom
M23 9LT

Sponsor information

Organisation
University Hospital of South Manchester NHS Foundation Trust (UK)

Sponsor details
Wythenshawe Hospital, Southmoor Road , Wythenshawe
Manchester
England
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) Grant Codes: MR/K015141/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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?
HRA research summary			28/06/2023	No	No