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Double-blind randomised controlled trial of Lesogaberan in cough

Submission date
16/03/2015

Recruitment status
No longer recruiting

Registration date
30/04/2015

Overall study status
Completed

Last Edited
22/04/2021

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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 which can last anywhere from 8 weeks to several years. This is called chronic cough. People with chronic cough find the symptoms distressing due to the social implications of coughing, and it can have a major impact on their quality of life. There are currently no effective treatments for chronic cough. It is thought that oversensitive airway nerves might play an important role in why some people suffer with chronic cough, but currently it is not known why or how people develop sensitive airways. This study aims to test the effectiveness of a drug known as Lesogaberan.

Who can participate?
Patients aged over 18 with a chronic dry cough of at least 8 weeks duration

What does the study involve?
Participants attend University Hospital South Manchester over a period of 13 weeks. Lesogaberan and placebo (a dummy tablet with no active ingredient) are given to them over two treatment periods. During the study neither the participants nor the study doctor knows which treatment (active or dummy) is being taken during each treatment period. Each participant is asked to undergo a series of tests to ensure their safety throughout the study, including physical examinations, ECGs, blood and urine tests. Other study tests include completion of questionnaires, a cough challenge test, 24-hour cough monitoring and oesophageal studies.

What are the possible benefits and risks of participating?
There is no direct benefit of participating in the study to the patient. The findings will further improve the understanding of chronic cough and enable the development of effective treatments. Lesogaberan is an unlicensed study medication but it has already been tested in several studies involving both healthy volunteers and patients with heartburn 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’ in the fingers. The other known side effects are headache, feeling hot, diarrhoea, flatulence and dizziness. Should any new information about this drug become available, participants will be contacted to discuss this. 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 a medication to open up the airways. Participants may also experience a hot feeling or irritation at the back of the throat or flushing to the face if they reach the higher doses of capsaicin. These effects are temporary and will wear off after a short time. The oesophageal manometry tests and 24-hour impedance monitoring are safe procedures regularly carried out for other medical conditions. There is minimal risk involved. During the insertion of the tubes participants may experience mild gagging or coughing but most patients tolerate the procedure well. After the test participants may feel a temporary sore throat. Blood tests sometimes cause bruising at the site of needle puncture and some people can feel faint whilst blood is being withdrawn. Rarely a small blood clot or infection can occur. The electrodes and sticky pads placed on the skin during ECG tests and 24-hour cough monitoring can occasionally lead to skin irritation. Although breathing tests are not painful, they can be tiring to perform. Participants may experience shortness of breath, coughing or chest tightness. Some people can feel lightheaded or faint. The study team will monitor them closely in the research ward whilst taking part in this study. A doctor will be available at all times should they feel unwell.

Where is the study run from?
University Hospital South Manchester (UK)

When is the study starting and how long is it expected to run for?
April 2015 to April 2016

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

Who is the main contact?
Dr Huda Badri
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2014-005074-11

Protocol serial number
14/GAR/002

Study information

Scientific Title
The role of GABAb receptor mechanisms in cough: a double-blind, randomised controlled trial of Lesogaberan in chronic cough patients with positive and negative symptom association probabilities

Acronym
GARMIn2

Study objectives
This study is designed to assess the anti-tussive effect of Lesogaberan in patients with chronic cough. Our aim is to determine the effect of a peripherally acting GABAb agonist (Lesogaberan) over placebo on 24-hour cough frequency, and the relationship of this effect to changes in cough reflex sensitivity and presence/absence of temporal associations between reflux and cough.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Liverpool East, 09/01/2015, ref: 14/NW/1497

Study design
Randomised controlled double-blind cross-over trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Refractory chronic cough

Interventions
Participants attend University Hospital South Manchester over a period of 13 weeks. Lesogaberan and placebo are given to them over two treatment periods. During the study neither the participants nor the study doctor knows which treatment (active or dummy) is being taken during each treatment period. Each participant is asked to undergo a series of tests to

ensure their safety throughout the study, including physical examinations, ECGs, blood and urine tests. Other study tests include completion of questionnaires, a cough challenge test, 24-hour cough monitoring and oesophageal studies.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Lesogaberan

Primary outcome(s)
24-hour objective cough frequency following 2 weeks treatment

Key secondary outcome(s))
1. 24-hour objective cough frequency on first treatment day
2. Cough reflex sensitivity to capsaicin after 2 weeks treatment
3. Cough reflex sensitivity to capsaicin on first treatment day
4. 24-hour cough frequency for SAP-positive vs SAP-negative patients on first treatment day
5. 24-hour cough frequency for SAP-positive vs SAP-negative patients after 2 weeks treatment
6. Cough severity VAS and cough-specific quality of life

Completion date
01/09/2017

Eligibility

Key inclusion criteria
1. Provision of signed, written and dated informed consent, prior to any study-specific procedures
2. Age over 18 years old
3. Agreement to comply with contraception restrictions as outlined in the protocol
3. BMI of 19-35 kg/m2 (inclusive)
4. Normal spirometry
5. Chronic dry cough of at least 8 weeks duration
6. Normal chest X-ray
7. Patients with cough related to nasal disease, reflux and asthma will be included. These conditions will be investigated but they will still be included

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
22

Key exclusion criteria
1. History of cardiac disease, clinically significant orthostatic reactions or syncope, renal disease and hepatic disease
2. Prolonged QTcF >450 ms or family history of long QT syndrome at baseline (any prolongation of QTcF during the study will be classed as an AE unless >500 or deemed clinically significant by the research physician)
3. Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG at enrolment that may interfere with the interpretation of the QTc interval changes. This includes subjects with any of the following:
3.1. Clinically significant PR interval prolongation
3.2. Intermittent second or third degree AV block
3.3. Incomplete, full or intermittent bundle branch block (QRS <11 ms with normal QRS and T-wave morphology is acceptable if there is no evidence of left ventricular hypertrophy)
3.4. Abnormal T-wave morphology, particularly in the protocol defined primary lead
4. Any clinically significant illness, medical or surgical procedure or trauma within the 4 weeks preceding the first administration of study medication including upper respiratory tract infections
5. Any clinically significant abnormalities in clinical chemistry, haematology results as judged by the investigator
6. Abnormal screening clinical pathology values or other clinically significant, unexplained biochemical abnormality according to the investigator; in particular, liver function tests (LFTs) should be within normal limits at screening
7. Systolic blood pressure below 110 mmHg at screening
8. Current smoker or ex-smoker with >20 pack year history, and <6 months abstinence
9. History of severe allergy/hypersensitivity or ongoing allergy/hypersensitivity, as judged by the investigator, or history of hypersensitivity to drugs with a similar chemical structure or class as Lesogaberan
10. History of drug addiction and/or alcohol abuse or other circumstances which in the investigators judgement may compromise the subject’s ability to comply with the study requirements
11. Pregnancy or breastfeeding
12. Treatment with ACE inhibitors will be excluded. Patients taking centrally acting medications e.g. opiates, amitriptyline, gabapentin, pregabalin for the treatment of cough, will be excluded unless they are willing to stop these treatments. Patients can be included if they are willing to stop opiates for 1 week prior to baseline visit through to follow-up visit. Pregabalin, gabapentin, amitriptyline and ACEi will need to be stopped for 4 weeks prior to baseline visit and through to follow-up visit
13. Has received another new chemical entity (defined as a compound which has not been approved for marketing) or has participated in any other clinical study that included drug treatment within 3 months of anticipated first administration of therapy in this study

Date of first enrolment

16/04/2015

Date of final enrolment
16/03/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital South Manchester
Respiratory and Allergy Clinical Research Facility
North West Lung Centre
Southmoor Road
Wythenshawe
Manchester
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M23 9LT

Sponsor information

Organisation
University Hospital South Manchester

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Industry

Funder Name
Medical Research Council

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

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Huda Badri (huda.badri@manchester.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes