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Phase I study to assess the safety and tolerability of inhaled interferon-beta (IFN-beta1a) in controlled asthmatic male and female subjects

Submission date
14/02/2008

Recruitment status
No longer recruiting

Registration date
27/02/2008

Overall study status
Completed

Last Edited
15/11/2016

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Asthma is a common lung condition that causes occasional breathing difficulties. Interferon-β is a protein that occurs naturally in the body. One of its functions is to combat viruses. Interferon-β has been given as an injection to thousands of patients for other diseases (such as multiple sclerosis). Recent research has suggested that interferon-β might prevent the spread of the common cold from the nose to the lungs of people who have asthma. The common cold virus is known to cause a worsening of asthma symptoms (known as an exacerbation) in some people. It is hoped that interferon-β will be given as a treatment to people with asthma to prevent an exacerbation of asthma symptoms during a cold. The aim of this study is to find out how safe doses of inhaled interferon-β1a are in patients with asthma.

Who can participate?
Patients aged 18 to 55 with asthma

What does the study involve?
Participants are randomly allocated into four groups of ten. In each group, eight participants receive the active treatment (interferon-β1a) and two receive a placebo (a dummy drug). Group 1 receive a low dose as a single dose only. Group 2 receive a mid dose as a single dose and if this is found to be safe they move on to multiple dosing once every 3 days for a 14-day period. Group 3 receive the highest proposed dose as a single dose and then if this is found to be safe they move on to multiple dosing once every 3 days for a 14-day period. Group 4 also receive the highest dose as a single dose and then if this is found to be safe they move on to multiple dosing once a day for 14 days. The study involves 13 visits to the research facility and four overnight stays. The medication is given in the research facility each time. A follow-up visit takes place 15 days after the last dose of medication. A number of tests (such as lung function tests and many others) are conducted to assess the effects of interferon-β1a. Samples of blood, urine and sputum (mucus from the lungs) are tested to further understand how interferon-β1a is absorbed, distributed around the body, broken down and excreted from the body. The samples

are also analysed to determine how interferon-β1a is affecting the natural anti-virus defence systems in the body, and to find out whether tests could be developed to see if some asthmatic people are more likely to respond to interferon-β1a therapy than others.

What are the possible benefits and risks of participating?
It is unlikely that participants will benefit from taking the study drug but the information from this study may help to improve the treatment of people with asthma. As extensive tests are performed which are not routinely carried out, participants will learn more about their asthma and how best to control it. There are unknown risks involved in taking part in the study. The risks of interferon-β when given via injection are known, but the full risks of inhaling interferon-β1a are not known. A similar inhalation study has been carried out using a different make of interferon-β1a. This was given via inhalation to people without asthma. The findings suggest that the transfer of gas in the small airways of the lungs (TLCO) was temporarily affected. The dose given in this study was 10 times higher than the dose to be given in this study. The device and formulation are also different. As a precaution, TLCO will be monitored throughout this study and treated will be stopped if necessary. As with other medications, people treated with interferon-β1a may be at risk of developing allergic reactions or anaphylaxis. Symptoms of an allergic reaction generally include overall body itching, hives (a sort of rash), skin flushing or rash. Anaphylaxis is a more serious allergic reaction that may involve dizziness, vomiting, low blood pressure and difficulty breathing. This requires prompt medical care and may be life-threatening. Administration of medications by nebuliser inhalation may cause local irritation such as voice alteration, laryngitis or pharyngitis (sore throat).

Where is the study run from?
Southampton General Hospital (UK)

When is the study starting and how long is it expected to run for?
July 2008 to September 2009

Who is funding the study?
Synairgen Research Limited (UK)

Who is the main contact?
Prof. Ratko Djukanovic

Contact information

Type(s)
Scientific

Contact name
Prof Ratko Djukanovic

Contact details
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Additional identifiers

Protocol serial number
SG004

Study information

Scientific Title
A double-blind, placebo-controlled, single and multiple, dose-escalating, phase I study to assess the safety and tolerability of inhaled interferon-beta (IFN-beta1a) in controlled asthmatic male and female subjects

Study objectives
To evaluate the safety and tolerability of both single and multiple doses of inhaled interferon-beta (IFN-beta1a), administered over a 14 day period to controlled asthmatic subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Berkshire Research Ethics Committee, 10/03/2008, ref: 08/H0505/17

Study design
Multicentre randomised double-blind placebo-controlled single and multiple dose-escalating study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Asthma

Interventions
There will be 4 cohorts with 10 subjects in each cohort. The study medication is IFN-beta1a (IFN-beta1a plus excipient) and the placebo is the same excipient only.
1. Cohort 1 will receive a low dose of either IFN-beta1a or placebo as a single dose only
2. Cohort 2 will receive a mid dose of either IFN-beta1a or placebo as a single dose and then if all safety parameters are within acceptable ranges they will move on to multiple dosing once every 3 days for a 14 day period (5 doses in total, excluding the single dose)
3. Cohort 3 will receive the highest proposed dose of either IFN-beta1a or placebo as a single dose and then if all safety parameters are within acceptable ranges they will move on to multiple dosing once every 3 days for a 14 day period (5 doses in total, excluding the single dose)
4. Cohort 4 will also receive the highest dose of either IFN-beta1a or placebo as a single dose and then if all safety parameters are within acceptable ranges they will move on to multiple dosing, once a day for 14 days (14 doses excluding the single dose)

Both the IFN-beta1a and the placebo will be administered via inhalation using the CE marked I-neb® device manufactured by Respironics Respiratory Drug Delivery (UK) Limited.

For all treatment arms, follow up is for 2 weeks post the last dose of study medication. However, there are also optional follow up visits, whereby subjects will be requested to repeat any measurements which are outside of the acceptable ranges until they either return to within the acceptable range or the Investigator is satisfied that the measurements should stop. Therefore follow up could be for longer then 2 weeks. However, if all measurements are within acceptable ranges and there are no ongoing adverse events, follow up will only be for 2 weeks post their last dose of study medication.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Interferon-beta (IFN-beta1a)

Primary outcome(s)
The primary endpoints will be the assessment of respiratory function:
1. FEV1, measured at V1, V3.2, V3.3 (at 20 and 40 minutes, 1, 2, 4, 8 and 12 hours), V3.4, V4, V7.2, V7.3 (at 20 and 40 minutes, 1, 2, 4, 8 and 12 hours), V7.4, V8, V9, V10, V11, V12 and V13
2. Forced vital capacity (FVC), measured at V1, V3.2, V3.3 (at 20 and 40 minutes, 1, 2, 4, 8 and 12 hours), V3.4, V4, V7.2, V7.3 (at 20 and 40 minutes, 1, 2, 4, 8 and 12 hours), V7.4, V8, V9, V10, V11, V12 and V13
3. TLCO, measured at V1, V3.2, V3.4, V4, V7.2, V7.4, V8, V9, V10, V11, V12 and V13
4. Fraction of exhaled nitric oxide (FENO) levels, measured at V1, V3.1. V3.2, V3.4, V4, V7.1, V7.2, V7.4, V8, V9, V10, V11 and V12
5. Significant changes in sputum eosinophils counts, measured at V2, V3.4, V7.4 and V12

Timepoints:
Single dose:
V1 (screen 1): day -14 to -5
V2 (screen 2): day -10 to -2
V3.1 (night before dosing): -1 day (- 12 hours)
V3.2 (dosing day pre-dose): Day 0A
V3.3 (dosing day post-dosing): Day 0A
V3.4 (24 hours post-dosing): Day 1A
V4 (follow-up): Day 3A
V5 (telephone follow-up): 15 +/- 1 day
V6 (follow up): subjects in cohort 2, 3 and 4 will continue into multiple dosing if they meet the criteria. If they do not meet the criteria then they will require follow up visit 6.

Multiple dose:
V7.1 (night before dosing): -1 day (-12 hours)
V7.2 (1st multiple dose day pre-dose): Day 0B
V7.3 (dosing day post-dose): Day 0B
V7.4 (24 hours post-dosing): Day 1B
V8/V9/V10/V11: Day 1B+3, 6, 9, 12 days

V12 (follow-up 1): 3 days post EOT
V13 (follow-up 2): 5 days post EOT
V14 (telephone follow-up +/-1 day): 15 days EOT
V15 (follow-up): optional

Key secondary outcome(s))
The clinical review and interpretation of general safety measurements including the investigation of pharmacokinetics over time will be secondary endpoints.

Completion date
01/09/2009

Eligibility

Key inclusion criteria
To be eligible for inclusion into this study, each subject must fulfil the following criteria:
1. Diagnosis of controlled asthma requiring regular inhaled corticosteroids (ICS). Subjects must have been taking the same dose of ICS regularly for six weeks prior to Screening Visit one.
2. Forced expiratory volume in one second (FEV1) is equal to or greater than 80% predicted and diffusing capacity of the lung for carbon monoxide (DLCO/TLCO) equal to or greater than 80% predicted (pre-bronchodilator)
3. Presence of bronchial hyperresponsiveness as measured by a methacholine challenge which results in a provocative concentration causing a 20% fall in FEV1 (PC20) equal to or less than 16 mg/ml
4. Stable asthma, indicated by asthma symptoms and bronchodilator usage equal to or less than three times a week when needed to relieve symptoms. In addition to this, bronchodilator usage equal to or less than once a day if taken as a preventative prior to exercise will be allowed.
5. Male or female aged 18 to 55 years
6. Non-smoker or an ex-smoker who has stopped smoking for more than one year and has a smoking history of less than 10 pack-years
7. Written informed consent
8. Vital signs in the following normal range:
8.1. Oral body temperature: 35.0 - 37.5°C
8.2. Blood pressure:
8.2.1. After at least 3 minutes of rest, measured in the supine position:
Systolic blood pressure: 90 - 140 mmHg
Diastolic blood pressure: 50 - 90 mmHg
8.2.2. Then, after 3 minutes standing:
Systolic blood pressure: no more than a 20 mmHg drop
Diastolic blood pressure: no more than 10 mmHg drop
8.3. Pulse rate: after at least 3 minutes of rest, measured in supine position: 40 - 90 beats per minute (bpm)
8.4. Pulse oximetry greater then or equal to 95%
9. Motivation to complete all study visits, the ability to communicate well with the Investigator and be capable of understanding the nature of the research and its treatment including its risks and benefits

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Any condition, including findings in the medical history or in the pre-study assessments that in the opinion of the Investigator, constitute a risk or a contraindication for the participation of the subject into the study or that could interfere with the study objectives, conduct or evaluation. In particular:
1. Use of long acting bronchodilators
2. A change in dose of asthma medication during the past six weeks
3. Any clinically significant abnormality in the results of the pre-study safety laboratory tests
4. History of any lung disease other than asthma
5. Current participation in another clinical trial or participation in a clinical trial where the subject has received a dose of the test product (investigational medicinal product [IMP]) within 12 weeks prior to entry into the study (for small molecules) and within 6 months prior to entry into the study (for biologicals)
6. Any clinically significant abnormality on the 12 lead resting electrocardiogram
7. History or presence of hypertension or other significant cardiovascular abnormality
8. Occurrence of any acute infection or disease within the last six weeks prior to screening
9. History of asthma exacerbation and/or upper/lower respiratory tract infection within six weeks prior to screening
10. History of hypersensitivity to natural or recombinant interferon-beta or to any of the drug preparation excipients
11. History of severe depressive disorders and/or suicidal ideation
12. History of liver disease or liver blood test abnormalities other than Gilbert's syndrome
13. History of epilepsy or seizures
14. Definite or suspected personal history of adverse drug reaction or hypersensitivity to drugs with a similar chemical structure to interferon
15. History or presence of drug or alcohol abuse
16. Loss or donation of more than 400 ml of blood within 12 weeks prior to entry into the study
17. Subjects who have taken any prescription drugs within 6 weeks, other than medication for the treatment of asthma and drugs used for the treatment of atopic dermatitis, atopic rhinitis and other allergic conditions. All other concomitant medications will be at the discretion of the Investigator.
18. Subjects who have taken over-the-counter medication, with the exception of multi-vitamins and paracetamol, within 1 week before drug administration. All other concomitant medications will be allowed at the discretion of the Investigator.
19. Subjects will undergo training during the screening phase to ensure their ability to use the I-neb® device. If subjects do not show sufficient proficiency in the use of the device, they will not be eligible for inclusion in the study.
20. Pregnancy either current or planned over the next 12 weeks. For those who are sexually active precautions are to be advised to both male and female subjects to avoid pregnancy during the trial and follow-up period. These precautions include pregnancy testing at screening,

baseline and follow up, as well as the use of a highly effective method of birth control (i.e. the oral contraceptive pill or IUD and the use of condoms) or after surgical sterilisation (i.e. hysterectomy). Continued testing and monitoring will take place during the trial if required.

Date of first enrolment
01/07/2008

Date of final enrolment
01/09/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
The Medicines Evaluation Unit
The Langley Building
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9QZ

Sponsor information

Organisation
Synairgen Research Limited (UK)

ROR
https://ror.org/04h6ep125

Funder(s)

Funder type
Industry

Funder Name
Synairgen Research Limited (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes