ISRCTN15124178 https://doi.org/10.1186/ISRCTN15124178

SoMOSA: Study of mechanisms of action of omalizumab in severe asthma

Submission date 10/12/2015	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 06/09/2016	**Overall study status** Completed	
Last Edited 31/01/2018	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Asthma is a long-term condition which affects the airways. It can affect people of any age, however in usually is first spotted during childhood. When a person is suffering from asthma, the bronchi (tubes which carry air in and out of the lungs) can become narrowed or swollen (inflammation). This causes the sufferer to feel tightness in the chest as the airways become inflamed, causing coughing and difficulty breathing. Most patients with asthma are able to control their condition using medication, however for some patients it is much harder to treat (severe uncontrolled asthma). Xolair is currently licensed in the UK to treat patients with severe asthma but it is clear that not everyone with severe asthma will benefit from treatment. The aim of this study is to investigate the effects of Xolair treatment on the body's immune system in patients with severe asthma.

Who can participate?
Adults with severe uncontrolled asthma who have had at least two serious attacks in the last year

What does the study involve?
All participants are treated with injections under the skin (subcutaneous injections of Xolair at a dose between 75mg and 600mg, based on their weight, for 52 weeks (standard length of treatment). Participants will stay on their standard, pre-study treatments throughout the 52 weeks. Participants are assessed 16 weeks after starting treatment by their physician to find out how well they are responding to treatment. At the same time, participants provide a urine sample so that it can be tested for levels of a chemical called PGD2 which is produced by certain cells in the immune system in asthma.

What are the possible benefits and risks of participating?
There is a chance that some patients may benefit from better controlled asthma as a result of taking Xolair. There are no notable risks associated with participating.

Where is the study run from?
Southampton General Hospital (lead centre) and 17 other NHS hospitals in the UK.

When is the study starting and how long is it expected to run for?
September 2015 to November 2018

Who is funding the study?
Novartis Pharma AG (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
19765

Study information

Scientific Title
A study identifying which biomarkers are predictive of a good clinical response following treatment with Xolair in patients with severe asthma

Study objectives
Primary hypothesis:
Xolair treatment results in significant reduction in the concentrations of 2,3-dinor-11-β-PGF2α in urine after 16 weeks of treatment in patients who respond with a clinical improvement (as judged by GETE evaluation), and in those with long-term clinical benefit (as judged by reduced exacerbations and reduced dose of oral corticosteroids in patients on maintenance oral corticosteroids during 1 year of treatment).

Secondary hypothesis:
The concentration of 2,3-dinor-11-β-PGF2α in urine at baseline is predictive of a good clinical response to Xolair (judged by GETE evaluation and reduced exacerbations during 1 year

treatment). Similarly, a change in 2,3-dinor-11-β-PGF2α in urine between baseline and 16 weeks of Xolair treatment is predictive of a good clinical response.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 5, 24/08/2015, ref: 15/WA/0302

Primary study design
Interventional

Study design
Interventional non-randomised study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Respiratory disorders; Subtopic: Respiratory (all Subtopics); Disease: Respiratory

Interventions
All participants will be treated with Xolair 75mg – 600mg as a subcutaneous injection (as per the SmPC guidelines) for a treatment period of 52 weeks. Dosing will be in line with the approved dosing table within the SmPC and will be based on weight and serum IgE.

Participants will stay on their standard, prestudy treatment with inhaled corticosteroids and long acting inhaled steroids. The same will apply to participants who additionally are on maintenance oral corticosteroids. Participants will be assessed 16 weeks after starting treatment with Xolair by their physician using standard evaluation (GETE) and will be defined as “responders” or “non-responders”. The dose of Xolair will only be modified (according to SmPC) if there are significant changes in the patient’s body weight.

Intervention Type
Other

Primary outcome(s)
Concentration of (PGD2) 2,3-dinor-11-β-PGF2α in urine is measured at baseline and 16 weeks.

Key secondary outcome(s)
Clinical response to Xolair assessed by GETE at 16 weeks.

Completion date
31/08/2019

Eligibility

Key inclusion criteria
1. Aged 18-70 years
2. Severe uncontrolled asthma (GINA step 4 and 5) despite daily treatment with high-dose

inhaled corticosteroids (ICS) and long-acting beta agonists (LABA). (High-dose ICS will be a minimum twice daily dose of 800 mcg of beclomethasone dipropionate equivalent inhaler for at least 8 weeks before screening). Potential participants will need to fulfil the criteria for uncontrolled asthma as judged by their Asthma Control Questionnaire (ACQ) score =1.5 during the screening period.
3. Participants on maintenance treatment with oral corticosteroids will also be included and will also have to meet the same ACQ inclusion criterion (ACQ=1.5)
4. Atopic, as identified by positive skin prick test or in vitro reactivity to a perennial aeroallergen
5. Two or more documented severe asthma exacerbations within the previous 12 months that require courses of prednisolone, defined as increased asthma symptoms requiring treatment in the community or in hospital with systemic corticosteroid rescue therapy or an increase in daily oral corticosteroids for participants already on maintenance oral corticosteroids for >2 months
6. Frequent daytime symptoms or night-time awakenings
7. Reduced lung function (FEV1 <80%) recorded anytime within the past 2 years
8. IgE level of 30 to 1500 IU/mL
9. Body weight less than 150 kg
10. Able to give written informed consent prior to participation in the study, which includes ability to comply with the requirements and restrictions listed in the consent form
11. Able to read, comprehend, and write at a sufficient level to complete study related materials

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Key exclusion criteria
1.An exacerbation requiring treatment with systemic corticosteroids (or an increase in the baseline dose of OCS) within the 30 days before screening
2. Active lung disease other than asthma
3. Treatment with Xolair or another biologic in the 12 months before screening
4. Elevated serum IgE levels for reasons other than allergy (for example, parasite infections, the hyperimmunoglobulin E syndrome, the Wiskott–Aldrich syndrome, or bronchopulmonary aspergillosis)
5. The following medication is not allowed during the run-in and treatment period and should not have been taken for at least 3 months prior to screening: methotrexate, cyclosporine, intravenous immunoglobulin or immunosuppressant’s
6. Current smokeror having smoked in the past year. Ex-smokers will have to be confirmed by a negative cotinine test. If there is a history of smoking for >10 pack years, then asthma diagnosis

should have been made before the age of 40 and objective evidence of reversibility of FEV1>12% and 200ml should be available [either previously recorded or done as part of screening for this study]. Potential participants where an asthma/COPD overlap is suspected should not be included.
7. The participant has a history of current recreational drug use or other allergy, which, in the opinion of the responsible physician, contra-indicates their participation
8. Female patient who is pregnant or lactating or up to 6 weeks post partum or 6 weeks cessation of breast feeding
9. Those participants who, in the opinion of the investigator, have a risk of non-compliance with study procedures
10. The participant has a recent history of incapacitating psychiatric disorders
11. History or current evidence of an upper or lower respiratory infection or symptoms (including common cold) within 4 weeks of baseline assessments (in such participant assessments should be deferred until after 4 weeks have lapsed from the cold)

Date of first enrolment
01/10/2015

Date of final enrolment
28/02/2018

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
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SO16 6YD

Study participating centre
Belfast City Hospital
Lisburn Road
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BT9 7AB

Study participating centre
Churchill Hospital
Old Road
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OX3 7LE

Study participating centre
Glenfield Hospital
Groby Road
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LE3 9QP

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NG5 1PB
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Gartnavel Hospital
1053 Great Western Road
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G12 0YN

Study participating centre
Royal Hallamshire Hospital
Glossop Road
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S10 2JF

Study participating centre
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M23 9LT

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Study participating centre
Royal Brompton Hospital
Sydney Street
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Guy's Hospital
Great Maze Pond
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SE1 9RT

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Bordesley Green East
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B9 5SS

Study participating centre
Bradford Teaching Hospital
Duckworth Lane
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United Kingdom
BD9 6RJ

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
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CB2 0QQ

Study participating centre
Derriford Hospital Plymouth
Derriford Road
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Study participating centre
Royal Liverpool Hospital
Prescot Street
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United Kingdom
L7 8XP

Study participating centre
St James Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
Southampton University Hospitals NHS Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name
Novartis Pharma AG

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?
HRA research summary			28/06/2023	No	No