A randomized multi-center, double-blind, placebo-controlled, parallel-group trial to explore the effects of 78 week omalizumab treatment given as add on therapy on markers of airway inflammation and remodeling in patients with moderate to severe persistent allergic asthma receiving inhaled corticosteroids and long acting beta-agonists.

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* Primary objective: To determine the effect of 78-weeks therapy with omalizumab compared to placebo on the number of sub-epithelial eosinophils, a marker of airway inflammation, in patients with persistent moderate to severe allergic asthma. *...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Observational invasive

Summary

ID

NL-OMON32348

Source
ToetsingOnline

Brief title
Xolair 2432

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
airway inflammation, asthma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: airway inflammation, asthma, omalizumab

Outcome measures

Primary outcome

* To evaluate the effect of 78-weeks therapy with omalizumab compared to placebo on additional markers of airway inflammation, including the number of interleukin-13+ or -4+ cells, and other markers as appropriate, assessed in bronchial biopsies.

* To evaluate the clinical efficacy of 78-weeks therapy with omalizumab compared to placebo in patients with moderate to severe asthma, based on the number of clinically significant asthma exacerbations, spirometry, GETE (global evaluation of treatment effectiveness) after 16 weeks treatment, FENO (fractional exhaled nitric oxide) and asthma control as measured by the Asthma Control Questionnaire (ACQ).

* To evaluate the effect of 52 and 76-weeks therapy with omalizumab compared to placebo on markers of airway inflammation such as eosinophils and chemokines

and cytokines, in induced sputum.

* To evaluate the correlation of the bronchial biopsy parameters with clinical efficacy and markers of systemic inflammation (such as the number of circulating eosinophils and free IgE) after 78-weeks therapy with omalizumab compared to placebo.

* To conduct exploratory pharmacogenomic studies to identify gene expression patterns, proteins, and metabolites of blood that are associated with treatment response to omalizumab, or that possibly correlate with the severity or progression of asthma.

* To conduct exploratory analyses of serum cytokines and markers of systemic inflammation that are associated with treatment response to omalizumab or that possibly correlate with the severity or progression of asthma.

Secondary outcome

see above

Study description

Background summary

Xolair is a medication called a monoclonal antibody. It works by blocking one of the body*s chemicals involved in lung inflammation in patients with allergic asthma. Xolair has been shown to reduce asthma symptoms and to decrease the incidence of asthma exacerbations.
The main reason for this study is to find out if Xolair works by reducing inflammation of the airways that causes your asthma to get worse.
This study aims to investigate the effect of omalizumab on the number of tissue eosinophils and other markers of airway inflammation and remodeling, including thickness of the lamina reticularis, in moderate to severe asthmatics with persistent symptoms and evidence of airway inflammation despite treatment with inhaled corticosteroids and long acting beta-agonists. This study will also investigate the correlation between systemic and pulmonary inflammation, and

the correlation between clinical outcomes and changes within the tissue, to assist in the future identification of patients with tissue eosinophilia and their response to treatment, without the need for invasive bronchoscopy.

Study objective

* Primary objective: To determine the effect of 78-weeks therapy with omalizumab compared to placebo on the number of sub-epithelial eosinophils, a marker of airway inflammation, in patients with persistent moderate to severe allergic asthma.

* Secondary objectives: To evaluate the effect of 78-weeks therapy with omalizumab compared to placebo on sub-epithelial mast cells and CD4+ T-lymphocytes, as markers of airway inflammation and the thickness of the reticular basement membrane, as a marker of airway remodeling, assessed in bronchial biopsies.
To evaluate the safety and tolerability of 78-weeks therapy with omalizumab compared to placebo.

Study design

This is an international, multi-center, randomized, double-blind, placebo-controlled, parallel group study to explore the effects of 78-weeks omalizumab therapy on markers of airway inflammation and remodeling in patients with persistent moderate to severe asthma. Patients entered into this study are 18-60 years old diagnosed with moderate to severe allergic asthma with persistent airway inflammation and persistent symptoms, despite treatment with high doses of inhaled corticosteroid (>= 800 µg per day beclomethasone diproprionate [BDP] or equivalent total ex-valve dose) and long acting β-2 agonists [LABA] (as either fixed or separate combination treatment).

Study burden and risks

Skin prick testing results in very few allergic reactions involving the entire body and is generally considered to be the most convenient method for detecting allergies.
The blood test is a routine procedure which may cause temporary discomfort or slight bruising at the site of blood drawing or fainting. During collection of blood samples, patients may experience pain and/or bruising at the site on your arm where blood is taken. Localized blood clotting and infections may occur, but this is rare.
When patients are given a dose of study medication they may experience temporary discomfort or bruising at some or all of the places where you receive the injections in your arm.
On rare occasions it is possible that a bronchoscopy procedure causes bronchospasm (tightening in your lung passages), hypoxaemia (a fall in the

amount of oxygen in your blood), fever, allergic reactions to local anaesthetics and bleeding. Complications can be cough, hoarseness, collapsed lung, and bleeding from the sample site.
It is possible that an induced sputum collection procedure causes bronchospasm (tightening in your lung passages).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. patients who are 18 - 60 years of age
2. with a body weight >= 20 kg and <= 150 kg and with a serum total IgE level >= 30 to <= 700 IU/ml. The combination of body weight and serum total IgE level must fall within the dosing cells of the approved European dosing table
3. patients with moderate to severe allergic asthma, with persistent symptoms despite

receiving an inhaled corticosteroid and long acting beta-agonist (i.e. Step 4 or 5 treatment as per 2006 GINA guidelines - Appendix 3)
4. with >= 2% eosinophilia in induced sputum at visits 1 and 2
5. with a positive skin prick test (diameter of wheal * 3 mm) or RAST test to at least one perennial aero-allergen (eg. dust mite, cat/dog dander, cockroaches), documented within the past 2 years or demonstrated at Visit 1, to which the patient will be exposed on a regular basis (most days) for the duration of the study. In addition a RAST test may be performed for patients with a borderline skin prick test result. Patients with a total IgE level of <= 76 IU require an unequivocal positive RAST test (>=71 IU/mL) to be eligible. Skin prick test procedures can be found in Appendix 7
6. with FEV1 *60% of the predicted normal value for the patient (demonstrable at least 6 hours after last short acting β-2 agonist use and 12 hours after last long β-2 acting agonist use) at Visit 1. FEV1 % predicted must be stable at the second screening visit (Visit 2) and the randomization visit (Visit 3) (within 10%)
7. receiving high dose inhaled corticosteroid >= 800µg per day BDP or equivalent, as monotherapy or fixed dose combination, and a regular inhaled long acting β-2 agonist at stable doses for at least 3 months prior to screening

Exclusion criteria

1. Other therapies/medication:
• who are receiving:
• ß adrenergic antagonist medication (e.g.: propranolol) or anticipate use during the study
• methotrexate, gold salts, cyclosporin or troleandomycin within 3 months of Visit 1 or anticipate their use during the study
• desensitization therapy with less than 3 months of stable maintenance doses prior to the screening visit (Visit 1)
• maintenance systemic corticosteroids
• leukotriene receptor antagonists, theophylline or oral or inhaled anticholinergics
• who have received omalizumab previously
2. Concurrent diseases/conditions and history of other diseases/conditions:
• who have been treated for an asthma exacerbation during the 4 weeks prior to randomization
• who are current smokers, or have a smoking history > 10 pack years
• with elevated serum IgE levels for reasons other than allergy (e.g.: parasite infections, hyperimmunoglobulin E syndrome, Wiskott-Aldrich Syndrome or clinical allergic bronchopulmonary aspergillosis)
3. Ingredient hypersensitivity:
• with known hypersensitivity to any ingredients, including excipients (sucrose, histidine, polysorbate 20) of the study medication or drugs related to omalizumab (e.g.: monoclonal antibodies, polyclonal gamma globulin)
4. Exclusion criteria for flexible fiberoptic bronchoscopy:
• history of allergic reactions to local anesthetics to be used in the procedure
• any clotting abnormality (e.g. abnormal platelet count)
• recent acute myocardial infarction, unstable angina and other relevant medical conditions

deemed appropriate by the investigator
• history of chronic CO2 retention
• a patient is considered to be unsuitable for bronchoscopy, according to the judgment of the investigator
• a patient who has been intubated because of their asthma

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-05-2009
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Omalizumab
Generic name:	Xolair
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	26-02-2008

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-004653-29-NL
CCMO	NL21894.058.08