The efficacy of mepolizumab treatment on rhinovirus induced asthma exacerbations

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With this project we aim to determine the efficacy of anti-IL-5 treatment (mepolizumab) on virus-induced exacerbations in allergic asthma patients.Specific research questionsDoes IL-5 neutralisation:1) reduce the inflammatory response (T cell...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON36480

Source
ToetsingOnline

Brief title
Mepolizumab and virus-induced asthma exacerbations

Condition

- Allergic conditions
- Viral infectious disorders
- Bronchial disorders (excl neoplasms)

Synonym
asthma, virus-induced asthma exacerbation

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: GlaxoSmithKline,GSK en astmafonds

Intervention

Keyword: asthma, inflammation, interleukin-5, virus

Outcome measures

Primary outcome

Lungfunction, determined by the difference in pre-bronchodilator FEV1 between day 70 and 77 (1 day prior and 6 days after inoculation with RV16).

Secondary outcome

Symptom scores for common cold and asthma will be recorded, as well as additional lungfunction parameters (PEF and FVC). The viral load in the nasal swabs and bronchial brushes will be determined by PCR. Additionally we will determine cell counts and phenotype of inflammatory cells in BALF and blood and the production of inflammatory mediators in BALF and blood.

Study description

Background summary

Virus-induced exacerbations represent the major clinical manifestation of asthma, but the underlying mechanisms are poorly understood. It has recently been shown that neutralisation of interleukin-5 (IL-5) reduces the exacerbation rate in severe asthmatics with eosinophilic inflammation, whereas anti-IL-5 treatment does not affect asthma symptoms in stable asthmatics. Since virus-induced asthma exacerbations are associated with reduced Th1- and enhanced Th2 cytokine production, we hypothesise that the Th2 cytokine IL-5 critically impairs the host response to viral airway infections in allergic asthma patients leading to an exaggerated inflammatory response.

Study objective

With this project we aim to determine the efficacy of anti-IL-5 treatment (mepolizumab) on virus-induced exacerbations in allergic asthma patients.

Specific research questions

Does IL-5 neutralisation:
1) reduce the inflammatory response (T cell responses, eosinophil and neutrophil numbers and production of inflammatory mediators) to viral airway infections in allergic asthma patients?
2) prevent or reduce asthma symptoms during virus-induced asthma exacerbations?

Study design

To determine whether mepolizumab has a direct impact on viral-induced asthma exacerbations, we will perform a double-blind placebo-controlled trial. Mild to moderate allergic asthma patients are treated thrice with either mepolizumab or placebo (day 0, 28 and 56). Two weeks after the last infusion both groups (14 per group) are inoculated with rhinovirus type 16 (RV16). One day before and 6 days after the inoculation the volunteers will undergo a bronchoscopy to obtain bronchoalveolar lavage fluid (BALF) and 4 epithelial brushes. In addition, lungfunction tests (FEV1 and PC20histamin) will be performed 4 days after RV16 exposure. Approximately 6 weeks after RV16 exposure blood will be drawn to confirm infection based on neutralising antibodies.

Intervention

Patients will receive three times an infusion with either mepolizumab or placebo (on day 0, 28 and 56). Two weeks after the last infusion, all patients will be infected with RV16.

Study burden and risks

After anamnesis and a physical examination, individuals will be subjected to a lungfunction test. Also blood will be drawn and all patients will receive three infusions with mepolizumab or placebo. These are all considered to be a mild burden. Bronchoscopy, used to obtain BAL fluid and epithelial brushes, is an invasive technique that, despite the use of the anaesthetic lidocain, inflicts an unpleasant feeling and thus a considerable burden to the individual. A bronchscopy may give rise to a dry cough and some distress of the nose, where the bronchocsope is inserted. During brushing a superficial bleeding may develop which normally stops rapidly. The bronchoscopy will take 15 minutes to complete.

Experimental RV16 infections will cause mild common cold symptoms. RV16 infection will evoke a transient exacerbation of asthma symptoms. The RV16 infection protocol is a standard procedure to challenge healthy individuals, asthmatics and COPD patients. The rationale for using RV16 is that this rhinovirus strain causes mild common cold symptoms as compared to other rhinovirus strains. In addition, rhinoviruses are endemic, causing common colds

in the general population. No adverse events of using RV16 inoculation in healthy individuals and asthma and COPD patients have been reported. Exposure to RV16 will cause a considerable burden that will last for several days (up to a week).

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

Age between 18 * 50 years
Intermittent or mild persistent asthma according to the criteria by the Global Initiative for Asthma
Non-smoking or stopped smoking more than 12 months ago and * 5 pack years
Clinically stable, no history of exacerbations within the last 6 weeks prior to the study
Steroid-naïve or those patients who are currently not on corticosteroids and have not taken

any corticosteroids by any dosing-routes within 2 weeks prior to the study
Baseline FEV1 at least 80% of predicted
PC20histamine < 9.8 mg/ml
Positive skin prick test to one or more of the 12 common aeroallergen extracts

Exclusion criteria

Moderate to severe asthma patients (according to the GINA guidelines)
Patients who have had an exacerbation during the past 6 months, as indicated by a course of systemic steroids or antibiotics
Presence of antibodies directed against rhinovirus type 16 (titer > 4)
Smokers or ex-smokers (< 12 months or > 6 pack years)
Women who are pregnant, lactating or who have a positive urine pregnancy test at visit 1
Patients who are in close contact with young children (< 2 years), either professional or family related
Participation in any clinical investigational drug treatment protocol within the preceding 3 months

Study design

Design

Study type:	Interventional
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):	24-02-2012
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mepolizumab
Generic name:	Mepolizumab

Ethics review

Approved WMO Date:	21-04-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2011-000586-12-NL

Register	ID
CCMO	NL35271.018.11
Other	NTR in aanvraag