MEA115575: A Randomised, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of Mepolizumab Adjunctive Therapy to Reduce Steroid Use in Subjects with Severe Refractory Asthma (MEA115575)

Published: 23-07-2012
Last updated: 26-04-2024

Primary: To compare the effects of mepolizumab adjunctive therapy with placebo on reducing the use of maintenance oral corticosteroids (OCS).Secondary: Safety, tolerability, other efficacy parameters, quality of life.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON37249

Source
ToetsingOnline

Brief title
MEA115575

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma; bronchial asthma

Research involving

Human

Sponsors and support

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

Intervention

Keyword: asthma, mepolizumab, placebo, severe

Outcome measures

Primary outcome

% reduction of OCS dose at week 24 compared to the baseline.

Secondary outcome

Proportion of subjects who achieve a reduction of 50% or greater in their daily OCS dose, proportion of subjects who achieve a reduction of OCS dose to less than or equal to 5.0mg, proportion of subjects who achieve a total reduction of OCS dose, median percentage reduction from baseline in daily OCS dose at week 24, proportion of eligible subject who achieve complete reduction of OCS, clinically significant exacerbations, idem requiring hospitalization, idem requiring ED visits, change in St. George*s Respiratory Questionnaire, FEV1.

Study description

Background summary

Mepolizumab is currently under clinical development for severe asthma. Mepolizumab is a humanized antiinterleukin 5 (anti-IL5) antibody (IgG Kappa) that binds to and inactivates IL-5. IL-5 is the principle eosinophilic regulatory cytokine. It is critical for the development and release of eosinophils from the bone marrow, enhances adhesion to endothelial cells, and promotes the persistence and activation of eosinophils. Eosinophils are thought to play a major role in maintaining airway inflammation. Mepolizumab binds with

high affinity to human interleukin-5 and blocks its binding to and the activation of the IL-5 receptor (CD125). It is hypothesized that blocking IL-5 with mepolizumab will have a positive effect in reducing eosinophilic inflammation in patients with severe refractory asthma who are dependent on maintenance steroid to treat their asthma. This concept has been previously investigated in a small study (N= 20) of asthmatics with persistent sputum eosinophils. The results of this study demonstrated that mepolizumab was well tolerated and effective in reducing the dose of prednisone while preventing exacerbations, decreasing blood and sputum eosinophil numbers, and improving lung function and quality of life.
Recently a study of IV mepolizumab of over 600 subjects with severe refractory uncontrolled asthma has been completed. All 3 doses investigated (75mg, 250 mg and 750mg) resulted in a clinically significant reduction in the frequency of severe exacerbations when compared to placebo and produced a marked and sustained suppression of blood eosinophils. The safety profile was similar across all treatment arms and was similar to placebo.
A PK/PD model has been developed for mepolizumab with data obtained from prior studies. Two of these 5 studies administered mepolizumab via the subcutaneous (SC) route. The model well describes the relationship between plasma mepolizumab concentration and eosinophil counts (irrespective of the route of administration. Based on prior PK studies, the bioavailability of mepolizumab administered SC is approximately 75% and therefore a dose of 100mg SC is anticipated to provide similar exposure to the 75mg IV effective dose. A SC route of administration has been chosen for the current study as it is generally preferred by patients and is easy to administer.
The purpose of this study is to investigate the efficacy of adjunctive mepolizumab therapy, in comparison to standard of care, to reduce the use of oral corticosteroids while maintaining asthma control in subjects with severe refractory asthma.
In NL no minors will be included.

Study objective

Primary: To compare the effects of mepolizumab adjunctive therapy with placebo on reducing the use of maintenance oral corticosteroids (OCS).
Secondary: Safety, tolerability, other efficacy parameters, quality of life.

Study design

Studieopzet:
Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Phase III study.
Randomisation (1:1) to
* Mepolizumab 100 mg s.c. every 4 weeks
* Placebo every 4 weeks.
Continuation of standard treatment for asthma.
Salbutamol rescue medication.

Run-in period for determination of lowest effective oral prednis(ol)on dose (3-8 weeks).
Treatment phase 24 weeks. Week 4-20: dose reduction of oral steroids.
Possibility to participate in open-label extension study.
Follow-up phase 8 weeks (for those not participating in extension study).
Approx. 120 patients.
Independent DSMB.

Intervention

Treatment with mepolizumab or placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: 10 visits in approx. 6 months. Duration 1-3h.
6 s.c. injections (1 ml)
Blood draws 9x (total approx. 125 ml)
Physical examination 2x
Pulmonary function test 9x
ECG 6x
Daily peakflow measurements
Diary steoid use, rescue medication, symptoms, sleep quality, peak flow, concomitant illnesses, new medications
Questionnaires (symptoms, sleep, depression, daily activities) 1x 6, 3x 5, 1x 2, 2x 1
Optinal pharmacogenetic testing (1x 6 ml blood)

Contacts

Public
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* At least 12 years of age at Visit 1 and a minimum weight of 45kg (in NL at least 18 years).
* Severe asthma and a well-documented requirement for regular treatment with maintenance systemic corticosteroids in the 6 months prior to Visit 1 and using a stable oral corticosteroid dose for 4 weeks prior to Visit 1. See protocol page 23 for details.
* A documented requirement for regular treatment with high dose inhaled corticosteroid in the 6 months prior to Visit 1. See protocol page 23 for details.
* Current treatment with an additional controller medication for at least 3 months OR documentation of having used and failed an additional controller medication for at least 3 successive months during the prior 12 months.
* Prior documentation of eosinophilic asthma or high likelihood of eosinophilic asthma. See protocol page 23 for details.

Exclusion criteria

* Current smokers or former smokers with a smoking history of *10 pack years.
* Clinically important lung condition other than asthma.
* Other conditions that could lead to elevated eosinophils.
* Omalizumab [Xolair] within 130 days of Visit 1.
* Any biological (other than Xolair) to treat inflammatory disease within 5 half-lives of Visit 1.
* Previous participation in any study of mepolizumab and received Investigational Product.
* Pregnancy or breastfeeding

Study design

Design

Study phase:	3
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):	29-10-2012
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	mepolizumab
Generic name:	mepolizumab

Ethics review

Approved WMO Date:	23-07-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2012
Application type:	First submission

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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-001497-29-NL
CCMO	NL41502.018.12