Study 117113: Mepolizumab vs. Placebo as add-on treatment for frequently exacerbating COPD patients characterized by eosinophil level

Published: 11-03-2014
Last updated: 20-04-2024

Primary: To evaluate the efficacy and safety of mepolizumab 100 mg and 300 mg subcutaneous given every 4 weeks compared to placebo on the frequency of moderate and severe exacerbations in COPD subjects at high risk of exacerbations despite the use...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON44215

Source
ToetsingOnline

Brief title
MEA117113

Condition

- Respiratory disorders NEC

Synonym
COPD; chronic obstructive pulmonary disease

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline

Source(s) of monetary or material Support: GlaxoSmithKline

Intervention

Keyword: COPD, exacerbations, mepolizumab, severe

Outcome measures

Primary outcome

Frequency of moderate to severe exacerbations.

Secondary outcome

Time to first moderate/severe exacerbation. Frequency of COPD exacerbations

requiring emergency department visits and/or hospitalizations. Change from

baseline mean total St. George*s Respiratory Questionnaire-COPD (SGRQ-C) score.

Change from baseline COPD assessment test (CAT) score.

Study description

Background summary

While COPD is generally viewed as a disease driven by neutrophilic inflammation up to 40% of COPD patients have an inflammatory pattern that includes elevated sputum eosinophils. Recent studies identified that increased eosinophilic airway inflammation occurs during COPD exacerbations and that peripheral eosinophils levels were used successfully as a surrogate to predict response to corticosteroid therapy.
Mepolizumab is a fully humanized IgG antibody (IgG1, kappa) which binds to and inhibits the ability of IL-5 to bind to the IL-5 receptor. IL-5 receptors are primarily expressed on eosinophils. IL-5, through binding to the IL-5 receptor is a major regulator of eosinophils resulting in accumulation in tissues and modulation of eosinophil behavior at every stage from maturation to survival. Mepolizumab reduces eosinophils in the periphery and in tissues.
There is reason to believe that mepolizumab will reduce IL-5 and eosinophils in a well-defined COPD population. The study target population consists of a population who despite a history of use of optimal standard of care therapy continue to be at risk for future exacerbation. Based on extrapolation of the efficacy findings in severe asthma and the similarities between the severe asthma and severe COPD patients in terms of eosinophils and IL-5 levels it is

hypothesized that the reduction of eosinophils with mepolizumab in COPD patients would translate into a reduction of COPD exacerbations.

Study objective

Primary: To evaluate the efficacy and safety of mepolizumab 100 mg and 300 mg subcutaneous given every 4 weeks compared to placebo on the frequency of moderate and severe exacerbations in COPD subjects at high risk of exacerbations despite the use of optimized standard of care background therapy.
Secondary: Quality of life, health care utilization, and symptoms.

Study design

Randomised, double-blind, placebo-controlled, parallel-group phase III study.
Randomisation (1:1:1) to
* Mepolizumab 100 mg s.c. every 4 weeks
* Mepolizumab 300 mg s.c. every 4 weeks
* Placebo every 4 weeks.
Continuation of standard treatment for COPD.
Salbutamol rescue medication.
Treatment phase 52 weeks. Follow-up period 8 weeks.
Approx. 660 patients.
Independent data monitoring committee.

Intervention

Treatment with mepolizumab or placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: 16 visits in approx. 14 months. Duration 1-3 h.
13 times 3 s.c. injections (1 ml per injection)
Physical examination 6 times.
Blood draws 16 times (approx. 5-50 ml/occasion, approx. 280 ml in total). At screening testing for op hepatitis B-C.
Pregnancy test 15 times.
Pulmonary function test 9 times. At screening incl. reversibility.
Chest X-ray once (if not performed in the past 3 months).
ECG 6 times.
Questionnaire COPD symptoms (CAT) 14 times.
Other questionnaires 3-5 times.
Paper and electronic diary. Hospital visits, adverse effects, use of medication (paper) and symptoms, rescue medication and level of exercise (electronic).
Counseling for cessation of smoking, 2 times.

Optional pharmacogenetic testing (1x 6 ml blood)

Contacts

Public
GlaxoSmithKline

Huis ter Heideweg 62
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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

* Clinically documented history of COPD for at least 1 year in accordance with the definition by the American Thoracic Society/European Respiratory Society.
* Pre and post-salbutamol FEV1/FVC ratio of <0.70 at visit 1 and post-salbutamol FEV1> 20% and *80% of predicted.
* At least two moderate COPD exacerbations or at least one severe COPD exacerbation in the 12 months prior to visit 1. See protocol page 27-28 for details.
* A well documented requirement for optimized standard of care background therapy that includes ICS plus 2 additional COPD medications (i.e., triple therapy) for the 12 months prior to visit 1. See protocol page 28 for details.

* Males and females 40 years and above.
* Current smoger, ex-smoker or never smoker. See protocol page 28-29 for details.

Exclusion criteria

* Asthma and other respiratory disorders. See protocol page 29 for details.
* Pneumonia, exacerbation, lower respiratory infection within the 4 weeks prior to visit 1.
* Participation in the acute phase of a pulmonary rehabilitation program within 4 weeks prior to visit 1.
* Other conditions that could lead to elevated eosinophils.
* Known, pre-existing parasitic infestation within 6 months prior to 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):	29-10-2014
Enrollment:	38
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	mepolizumab

Generic name:	mepolizumab

Ethics review

Approved WMO Date:	11-03-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-02-2015
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	16-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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; registatienummer n.n.b.
EudraCT	EUCTR2013-004297-98-NL
CCMO	NL48043.060.14