A randomised, double-blind, placebo-controlled, parallel-group, multi-centre 24-week study to evaluate the efficacy and safety of mepolizumab adjunctive therapy in subjects with severe eosinophilic asthma on markers of asthma control (study 200862, MUSCA)

Published: 05-11-2014
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Primary: To evaluate the efficacy of mepolizumab 100 mg subcutaneous (SC) every 4 weeks versus placebo on health-related quality of life (HR-QoL) in adult and adolescent subjects with severe eosinophilic asthma. Secondary: To assess the effects of...

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

Summary

ID

NL-OMON44402

Source
ToetsingOnline

Brief title
study 200862 MUSCA

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 BV

Intervention

Keyword: add-on, mepolizumab, placebo, severe asthma

Outcome measures

Primary outcome

Mean change from baseline in St. George*s Respiratory Questionnaire (SGRQ)

score at Week 24

Secondary outcome

Mean change from baseline in clinic prebronchodilator FEV1 at Week 24,

percentage of subjects achieving a *4 point reduction from baseline in SGRQ

score at Week 24, mean change from baseline in Asthma Control Questionnaire

(ACQ-5) score at Week 24, adverse events.

Study description

Background summary

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.
Mepolizumab is being developed for the treatment of a.o. severe astma.
The targeted population in this study will be severe refractory asthmatics with evidence of eosinophilic airway inflammation as assessed by blood eosinophil levels. This severe, refractory, eosinophilic asthma population, is the subset

of asthmatics most likely to benefit from treatment with mepolizumab.
There are currently no approved therapies for severe eosinophilic asthma and, therefore, the comparator arm will be standard of care treatment. Standard of care will consist of high dose ICS and another controller, e.g. LABA, with or without maintenance oral corticosteroids (OCS).
The primary efficacy endpoint will be improvement in HR-QoL as measured by SGRQ. Other assessments of asthma control will include lung function and the asthma control questionnaire. The treatment duration will be 24 weeks. The optimal duration for HR-QoL assessment is uncertain, but based on the responses seen in two recently completed trials in the population of interest, the study duration of 24 weeks will enable an adequate time to assess the impact of mepolizumab on SGRQ and other study endpoints.

Study objective

Primary: To evaluate the efficacy of mepolizumab 100 mg subcutaneous (SC) every 4 weeks versus placebo on health-related quality of life (HR-QoL) in adult and adolescent subjects with severe eosinophilic asthma.
Secondary: To assess the effects of mepolizumab compared to placebo on lung function, asthma control, tolerability and safety.

Study design

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 astma.
Salbutamol rescue medication.
Screening 1-4 weeks. Treatment period 24 weeks. Follow-up period 4 weeks.
Dutch centres will not participate in substudies.
Approx. 544 patients.

Intervention

Treatment with mepolizumab or placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: 8 visits in approx. 6 months. Duration 1-3 h.
6 times 1 s.c. injection (1 ml)
Physical examination 2 times.
Blood draws 6 times (approx. 3-14 ml/occasion). At screening testing for op hepatitis B-C.
Pregnancy test 8 times.

Pulmonary function test 7 times. At screening incl. reversibility.
ECG 3 times.
Peak expiratory flow daily (1-2 times).
7 times completion of questionnaires (1-5 per visit).
Assessment of (change in) performance 5 times, efficacy of study medication 3 times.
Paper and electronic diary. Asthmatic complaints, rescue medication, other complaints and medication and level of exercise.
Optional pharmacogenetic testing (1x 6 ml blood)

Contacts

Public
GlaxoSmithKline

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NL
Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Prior documentation of eosinophilic asthma or high likelihood of eosinophilic asthma as per

randomization criteria 1 and 2 (see protocol section 5.3).
* 12 (in NL: 18) years of age and above.
* A well-documented requirement for regular treatment with high dose inhaled corticosteroid (ICS) in the 12 months prior to Visit 1 with or without maintenance oral corticosteroids (OCS), see protocol page 29 for details.
* Current treatment with an additional controller medication, besides ICS, for at least 3 months or a documented failure in the past 12 months of an additional controller medication for at least 3 successive months.
* For subjects *18 years at visit 1, a pre-bronchodilator FEV1 <80%. For subjects 12-17 years <90% or FEV1/FVC ratio < 0.8.
* Previously confirmed history of *2 exacerbations in the past 12 months. See protocol page 30 for details.
* Adequate contraception for females of childbearing potential.

Exclusion criteria

* Current smokers or former smokers with a smoking history of *10 pack years.
* Lung conditions other than asthma, malignancies, liver diseases, cardiovascular diseases. See protocol page 31 for details.
* Other conditions that could lead to elevated eosinophils. See protocol page 32 for details.
* Xolair within 130 days of Visit 1. Other Monoclonal Antibodies to treat inflammatory disease within 5 half-lives of Visit 1.
* 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):	28-01-2015
Enrollment:	25
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	05-11-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-12-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2015
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:	18-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	22-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-01-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-01-2016
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; registratienummer n.n.b.
EudraCT	EUCTR2014-002513-27-NL
CCMO	NL50555.060.14