Randomised, double-blind, chronic dosing (56 week) placebo-controlled, parallel group, multicentre, phase 3 study to evaluate the efficacy and safety of 2 doses of benralizumab (MEDI-563) in patients with moderate to very severe Chronic Ostructive Pulmonary Disease (COPD) with a history of COPD exacerbations (GALATHEA)

Published: 04-06-2014
Last updated: 20-04-2024

Primary Objective:To evaluate the efficacy and safety of 2 doses of benralizumab in patients with moderate to very severe Chronic Pulmonary Disease (COPD).Secondary Objectives:To evaluate the effect of two doses of benralizumab on:* health status/...

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

Summary

ID

NL-OMON41749

Source
ToetsingOnline

Brief title
Galathea

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Chronic Obstructive Pulmonary Disease, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca BV.

Intervention

Keyword: anti-IL-5 receptor mAb, blood eosinophils, COPD, exacerbations

Outcome measures

Primary outcome

Primary outcome measure:

Annual COPD exacerbation rate, where a COPD exacerbation is defined by

symptomatic worsening of COPD requiring:

- Use of systemic corticosteroids for at least 3 days. A single depot

injectable dose of corticosteroids will be considered equivalent to a 3- day

course of systemic corticosteroids; and /or

- Use of antibiotics; and/or

- an inpatient hospitalization due to COPD.

Secondary outcome

1.To evaluate the effect of two doses of benralizumab on health

status/health-related quality of life

- St. George`s Respiratory Questionnaire: SGRQ,

- COPD assessment tool. CAT

2. To evaluate the effect of two doses of benralizumab on pulmonary function

- pre-dose/pre-bronchodilator Forced expiratory volume in one second (FEV1) at study center.

3. To evaluate the effect of two doses of benralizumab on respiratory symptoms

- Baseline/Transitional Dyspnea index (BDI/TDI)

- exacerbationsof chronic Pulmonary disease tool- respiratory symptoms (E-RS)

4. To evaluate the effect of two doses of benralizumab on rescue medication use.

- Total rescue medication use (average puffs/day)

5. To evaluate the effect of two doses of benralizumab on nocturnal awakenings.

- Number of nights with awakening due to COPD.

6. To evaluate the effect of two doses of benralizumab on the severity, frequency and duration of EXACT-PRO defined events.

- Exacerbations of Chronic Pulmonary Disease tool- Patient reported outcome (EXACT-PRO)

7. To evaluate the effect of two doses of benralizumab on other parameters associated with COPD exacerbations.

- Time to first COPD exacerbation and proportion of subject with 1 or more exacerbation.

8. To evaluate the effect of two doses of benralizumab on emergency room visits and hospitalizations due to COPD.

- Annual rate of COPD exacerbations that are associated with an emergency room visit or a hospitalization.

9. To evaluate the effect of two doses of benralizumab on healthcare resource utilization due to COPD.

- COPD specific resource utilization (e.g. unscheduled physician visits, unscheduled phone calls to physicians, use of other COPD medications)

10. To evaluate the pharmacokinetics and immunogenicity of two doses benralizumab.

- Pharmacokinetic (PK) parameters

- Anti-drug antibodies (ADA)

Safety objective: To evaluate the safety and tolerability of two doses of benralizumab

- Adverse events/serious adverse events (AE/SAE)

- laboratory variables

- 12 lead ecg

- Physical Examination

- Vital signs

Study description

Background summary

Chronic obstructive pulmonry disease (COPD) is a significant cause of morbidity and mortality worldwide. In contrast to other chronic diseases , COPD is increasing in prevalence and is projected to be the third-leading cause of death and disability worldwide by 2020.

Acute exacerbations of COPD are defined as a sustained worsening of the patient`s condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular

medication in a patient with underlying COPD. (Rodriquez-Roisin R2000)
While airway inflammation in COPD has been traditionally described as being predominately neutrophili, elevated blood and sputum eosinophils have been reported in a subset of COPD patients (SAHA and Brightling 2006;Bafadhel et al 2011). The prevalence of elevated blood eosinophils in COPD has been less well catharacterized;however, blood eosiniphils have been reported to be an accurate predictor of >3% sputum eosiniphils in COPD. (Bafadhel et al 2011).

Treatment options are limited in severe exacerbations of COPD and by depleting eosiniophils in the periphery and sputum; benralizumab may be an alternative treatment option for this high unmet need in COPD associated with elevated blood and/or sputum eosinophils.

Interleukin-5 is a cytokine secreted predominantly by T-Lymphocytes, mast cells, and eosinophils and is involved in regulating the differentiation, proliferation and activation of eosiniphils via the human IL-5 Receptor (IL-5R; Kouro and Takatsu 2009).
Benralizumab (MEDI 563) is a humanized, afucosylated, monoclonal antibody that binds specifically to the human IL-5 receptor alpha subunit (IL-5R)on the target cell. Benralizumab is being developed for the treatment of both chronic obstructive pulmonary disease (COPD) and persistent asthma associated with elevated eosinophils.

Study objective

Primary Objective:
To evaluate the efficacy and safety of 2 doses of benralizumab in patients with moderate to very severe Chronic Pulmonary Disease (COPD).

Secondary Objectives:
To evaluate the effect of two doses of benralizumab on:
* health status/ health-related quality of life
* on pulmonary function
* on respiratory symptoms
* on rescue medication use
* on nocturnal awakenings
* on the severity, frequency and duration of EXACT-PRO defined events.
* on other parameters associated with COPD exacerbations
* on emergency room visits and hospitalizations due to COPD
* on healthcare resource utilization due to COPD
To evaluate the pharmacokinetics and immunogenicity of two doses of benralizumab

Safety objective:
To evaluate the safety and tolerability of two doses of benralizumab

In addtion, several exploratory objectives will be studied (CSP section 2.4).

Study design

A randomised, double-blind, chronic dosing (56 week), placebo controlled, parallel group, multicentre, Phase III study to evaluate the efficacy and safety of benralizumab, 30 mg, 100 mg in patients with moderate to very severe COPD receiving standard maintanence therapy (inhaled ICS/LABA, ICS/LABA/LAMA or LABA/LAMA) with a history of COPD exacerbations.

Intervention

Patient will receive benralizumab 30 mg, 100 mg or placeo subcutaneously every 4 weeks for the first 3 doses and then every 8 weeks thereafter till week 48. Subject will be randomised 1:1:1 and stratified by country and eosinophil count. Groups will be stratified to "high" blood eosinophil counts (>220/uL) and "low" blood eosinophil counts (<220/uL) in a ratio 2:1.

Study burden and risks

The subject is asked to visit the site at least 13 times. The visit time will last maximally 6 hours.
The subject will be contacted by telehone at least 7 times. These telephone contacts will last maximally 15 minutes each.

Blood samples will be taken in this study. The total volume of blood that will be collected is approximately 170 ml.
The subject will undergo physical examinations at every hospital visit.
The subject will undergo a spirometry test at least 10 times during the study.
One X-ray of the thorax will be done.

The subject will be asked to fill out 3 questionnaires at all hospital visits with a maximum of 10 times.
Women of child bearing potential have to provide a urine sample to test for pregnancy at screening and each time before administration of studymedication (8 times).

The subject has to fill out questionnaires every day (in the morning and evening) in an eDiary. This takes approximately 10 minutes a day. Once a week, a weekly questionnaire has to be completed in the eDiary.

The subject will receive the stduymedication at least 8 times. The studymedication may cause allergic reactions that can be life threatening. A study physician will supervise the administration of the study drug and will observe the subjectat the study centre for at least 2 hours after each injection; treatment will be immediately available if a subject has symptoms

related to study drug administration.There is a possibility of a allergic reaction of the studymedication. Therefore the subject must be in observation at the hospital.

The taking of bloodsamples and subcutaneous injection may cause some discomfort.
The studymedication may cause some side effects. There is a theoratical risk that prolonged eosinophil depletion may diminish the ability to defend against helminthic parasites, or negatively impact the natural history of certain malignant tumors.

Contacts

Public
Astra Zeneca

Louis Pasteurlaan 5
Zoetermeer 2719 EE
NL
Scientific
Astra Zeneca

Louis Pasteurlaan 5
Zoetermeer 2719 EE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Informed consent. ;2.Subjects 40-85 y.o. ;3.Moderate to very severe COPD with post-BD FEV1>20% and *65% . ;4.*2 moderate or *1 severe COPD exacerbation(s) required treatment or hospitalization within 2-52 weeks prior to Visit1. ;5.mMRC score *1 at Visit 1. ;6.Treatment with double or triple therapy throughout the year prior to Visit 1, constant 2 weeks prior to Visit 1. ;7.Tobacco history of *10 pack-years. ;8.Women of childbearing potential must use a highly effective form of birth control from Visit 1 until 16 weeks after their last dose, and negative serum pregnancy test result at Visit 1. ;9.Male subjects who are sexually active must be surgically sterile one year prior to Visit 1 or use an adequate method of contraception from the first IP dose until 16 weeks after their last dose. ;10.Compliance with maintenance therapy during run-in *70% from visit 2 to visit 4.

Exclusion criteria

1. Clinically important pulmonary disease other than COPD or another diagnosed pulmonary or systemic disease associated with elevated peripheral eosinophil counts.;2. Any disorder or major physical impairment that is not stable by Investigator opinion and/or could affect: - subject safety*study findings or their interpretation or subject*s ability to complete the entire study duration.;3. Unstable ischemic heart disease, arrhythmia, cardiomyopathy, or other relevant cardiovascular disorder that in Investigator*s judgment may put the patient at risk or negatively affect the study outcome.;4. Treatment with systemic corticosteroids and/or antibiotics, and/or hospitalization for a COPD exacerbation within 2 weeks prior to Visit1 or during the enrolment and screening/run-in period.;5. Acute upper or lower respiratory infection requiring antibiotics or antiviral medication within 2 weeks prior to Visit1 or during the enrolment and screening/run-in period.;6. Pneumonia within 8 weeks prior to Visit1 or during the enrolment and screening/run-in period.;7. Pregnant, breastfeeding, or lactating women.;8. Risk factors for pneumonia (including but not limited to: immunosuppression, neurological disorder with increased risk of aspiration).;9. History of anaphylaxis to any other biologic therapy. ;10. Long term oxygen therapy with signs and/or symptoms of cor pulmonale, right ventricular failure. ;11. Use of immunosuppressive medication , including rectal corticosteroids and systemic steroids within 2 weeks prior to enrolment (visit1) and/or during the enrolment/screening/run-in period. ;12. Receipt of any investigational non-biologic product within 30 days or 5 half-lives prior to Visit 1. ;13. Subjects who in the opinion of the investigator or qualified designee have evidence of active tuberculosis (TB). Subjects with a recent (within 2 years) first-time or newly positive purified protein derivative (PPD) test or Quantiferon test need to complete an appropriate course of treatment before being considered for enrolment.;14. Lung volume reduction surgery within the 6 months prior to Visit 1. History of partial or total lung resection (single lobe or segmentectomy is acceptable). ;15. Asthma as a primary or main diagnosis according to the GINA guidelines or other accepted guidelines. ;16. Previous treatment with benralizumab.;17. Helminth parasitic infection diagnosed within 24 weeks prior to Visit 1.

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):	07-08-2014
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Benralizumab
Generic name:	Benralizumab

Ethics review

Approved WMO Date:	04-06-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-07-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	08-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-03-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-03-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2015

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2019
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
EudraCT	EUCTR2013-004590-27-NL
ClinicalTrials.gov	NCT02138916
CCMO	NL48303.060.14