A Randomized, Double-blind, Placebo-controlled, Parallel Group, Multicenter, Phase 2a Study to Explore the Efficacy and Safety of Tezepelumab in Patients with Moderate to Very Severe Chronic Obstructive Pulmonary Disease (COPD) (COURSE)

Published: 03-07-2019
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To evaluate the effect of tezepelumab as compared with placebo on COPD exacerbations in subjects with moderate to very severe COPD

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON52380

Source
ToetsingOnline

Brief title
COURSE

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
Chronic Obstructive Pulmoray Disease, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: opdrachtgever/sponsor AstraZeneca

Intervention

Keyword: Exacerbations, moderate to severe COPD, tezepelumab

Outcome measures

Primary outcome

Primary endpoint: Rate of moderate or severe COPD exacerbations

Primary outcome measure: Moderate or severe COPD exacerbation rate ratio (tezepelumab vs placebo)

Supportive endpoint: Rate of moderate (excluding exacerbations treated only with antibiotics) or severe COPD exacerbations

Supportive Measure: Moderate (excluding exacerbations treated only with antibiotics) or severe COPD exacerbation rate ratio (tezepelumab vs placebo)

Secondary outcome

To evaluate the effect of tezepelumab compared with placebo on time to first moderate/severe exacerbation

-Time to first moderate or severe COPD exacerbation

To evaluate the effect of tezepelumab as compared with placebo on severe COPD exacerbations

-Rate of severe COPD excerbations

Secondary Objectives

- To evaluate the effect of tezepelumab compared with placebo on time to first exacerbation

- To evaluate the effect of tezepelumab as compared with placebo on severe COPD exacerbations

- To evaluate the effect of tezepelumab as compared with placebo on prebronchodilator (BD) lung function

- To evaluate the effect of tezepelumab as compared with placebo on respiratory health status/health-related quality of life

- To evaluate the pharmacokinetics (PK) and immunogenicity of tezepelumab

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is a progressive disease and 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 (AECOPD) are responsible for a large portion of the economic burden of COPD. In addition to a substantial economic burden, AECOPDs are also responsible for much of the morbidity and mortality from COPD. Patients with frequent AECOPD show associated increased airway inflammation and accelerated decline in lung function compared with patients with infrequent exacerbations.

Tezepelumab is a fully human immunoglobulin G (IgG) monoclonal antibody (mAb) directed against thymic stromal lymphoprotein (TSLP). Tezepelumab binds to human TSLP and prevents its interaction with the TSLP receptor (TSLPR). The hypothesis for the mechanism of action of tezepelumab in COPD is two-fold. First, because TSLP is one of the earliest responses to airway damage caused by a range of stimuli, inhibition of TSLP is expected to prevent the acute response to epithelial
damage and prevent COPD exacerbations. Secondly, given that TSLP is an upstream

and pleiotropic cytokine, the blockade of TSLP is anticipated to have broad impact on the spectrum of acute and chronic airway inflammatory responses seen in COPD. Both effects are expected to reduce COPD exacerbations and improve COPD symptoms

It is hypothesized that inhibition of upstream TSLP by tezepelumab will be effective in reducing airway inflammation in patients with COPD and reducing annualized COPD exacerbation rates. The purpose of the present study is to investigate the ability of tezepelumab versus placebo to enable reduction of the annualized COPD exacerbation rate in subjects with moderate to very severe COPD receiving standard maintenance therapy.

Study objective

To evaluate the effect of tezepelumab as compared with placebo on COPD exacerbations in subjects with moderate to very severe COPD

Study design

This is a Phase 2a, multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of tezepelumab 420 mg administered by SC injection Q4W in subjects with moderate to very severe COPD receiving triple inhaled maintenance therapy (ICS, LABA and LAMA), and having had >=2 documented COPD exacerbations in the 12 months prior to visit 1. Approximately 30% of subjects will have had at least 1 severe exacerbation (an exacerbation resulting in hospitalization) within the 12 months prior to Visit 1. Approximately 40% of subjects will have had >=3 exacerbations within the 12 months prior to Visit 1.

The study will randomize approximately 338 subjects 1:1 to the treatment arms, stratified by region, and number of prior exacerbations. Approximately 60% of the subjects will be targeted to have >=150 eosinophils/µL at enrolment, with a maximum of approximately 40% below this threshold.

Induced sputum analysis will be performed in a subset of subjects and in a limited number of sites globally. The aim of the induced sputum subset analysis is to explore the mechanisms by which tezepelumab might reduce COPD excerbations. In these same selected subjects, analysis of nasal lining fluid and epithelial transcriptomics will also be performed.

Intervention

Subjects will be randomized in a 1:1 ratio to either 420 mg of tezepelumab or matching placebo both administered Q4W SC. During treatment period, IP will be administered from day 0 until week 48.

Study burden and risks

The subject is asked to visit the site at least 18 times. The visit time will last maximal 4 hours.
The subject will be contacted by telephone at least 1 time at the end of the study. This telephone call will last maximally 15 minutes

Blood samples will be taken in this study. The total volume of blood that will be collected is approximately 285-450 ml.
The subject will undergo physical examinations at every hospital visit.
The subject will undergo a spirometry test at least 8 times during the study
The subject will undergo a FeNo test at least 8 times during the study
The subject (only in the substudy) will undergo a sputum test at least 2 times during the study
The subject (only in the substudy) will undergo a nasal lining fluid test at least 6 times during the study.
One X-ray of the thorax will be done

The subject will be asked to fill out questionnaires at all hospital visits with a maximum of 8 times.
Woman of child bearing potential have to provide a urine sample to test for pregnancy at screening and each time before administration of studymedication (14 times)

The subject must fill out questionnaires every day (in the morning and evening) in an e-Diary. This takes approximately 10 minutes a day.

The subject will receive the study medication at least 13 times. The study medication may cause allergic reactions. A study physician will supervise the administration of the study drug and will observe the subject at the study center 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 an allergic reaction of study medication. Therefore, the subject must be in observation at the hospital.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1.Female or Male subjects between 40-80 years
2.History of moderate to severe physician-diagnosed COPD for at least 12 months prior to enrollment with a post-bronchodilator FEV1 > 20% and < 80% of predicted normal value
3.History of at least 2 documented moderate to severe COPD exacerbation's, within 2-52 weeks prior to enrollment
4.CAT score of > 15 at Visit 1
5.Subjects should have evidence of having been treated with triple (medium or high dose ICS/LABA/LAMA) therapy for COPD throughout the year prior to enrollment, the dose should be stable for 3 months prior to screening visit.
6.Current smoker or ex-smoker with a tobacco history of > 10 pack years
7.If on allergen-specific immunotherapy, subjects must be on a maintenance dose and schedule for at least 2 months prior to screening visit.
8.If on theophylline or roflumilast, subjects must be on maintenance treatment for at least 12 months prior to screening visit and on stable dose 3 months prior to screening visit.

Exclusion criteria

1) Clinically important pulmonary disease other than COPD, as judged by Investigator.
2) Current or previous asthma diagnosis

3) Any disorder, including, but not limited to, cardiovascular, gastrointestinal, hepatic, renal, neurological, musculoskeletal, infectious (including risk factors for pneumonia), endocrine, metabolic, haematological, immune, psychiatric, or major physical impairment that is not stable
4) Treatment with systemic corticosteroids and/or antibiotics, and/or hospitalization for a COPD exacerbation within 14 days prior to enrollment (Visit 1) based on last dose of corticosteroids or last date of hospitalization, whichever occurred later.
5) History of clinically significant infection (excluding pneumonia), acute upper or lower respiratory infection, requiring antibiotics or antiviral medication within 14 days prior to enrollment (Visit 1) or during the screening period.
6) History of pneumonia requiring antibiotics or antiviral medication within 28 days prior to enrollment (Visit 1) or during the screening period.
7) History of allergy or reaction to any component of tezepelumab.
8) History of anaphylaxis to any other biologic therapy.
9) History of alcohol or drug abuse within the past year.
10) History of cancer:
11) Subjects with tuberculosis (TB).
12) Major surgery within 8 weeks prior to Visit 1 or planned surgical procedures requiring general anaesthesia
13) Pregnant, breastfeeding, or lactating women.
14) The chest/lungs with pathology that precludes the patient*s ability to complete the study.
15) The patient has active Covid 19 infection during the screening period.
16) Receipt of any COVID-19 vaccine 28 days prior to date of randomization

Study design

Design

Study phase:	2
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):	15-10-2019
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	tezepelumab

Ethics review

Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-09-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-11-2019

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-04-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-06-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-05-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2022
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2022
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	04039113
EudraCT	EUCTR2019-001363-67-NL
CCMO	NL70257.100.19