Randomized, double-blind, placebo-controlled, parallel-group Phase 3 study to evaluate the efficacy, safety, and tolerability of SAR440340/REGN3500/itepekimab (anti-IL-33 mAb) in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD)

Published: 05-01-2021
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This study has been transitioned to CTIS with ID 2024-512012-21-00 check the CTIS register for the current data. Primary objectivePrimary population (former smokers cohort):- Evaluate the efficacy of itepekimab compared with placebo on the...

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

Summary

ID

NL-OMON54121

Source
ToetsingOnline

Brief title
EFC16819 Aerify2

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Chronic bronchitis, Chronic Obstructive Pulmonary Disease, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi B.V.
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: COPD, itepekimab

Outcome measures

Primary outcome

- Annualized rate of moderate or severe acute exacerbation of COPD (AECOPD) in former smokers.

Secondary outcome

Cohort former smokers:

- Change in pre-bronchodilator (BD) forced expiratory volume in 1 second (FEV1) from baseline to week 24.

- Change in post-BD FEV1 from baseline to week 24 and week 52.

- Change in pre-BD FEV1 from baseline to week 52.

- Time to first moderate or severe AECOPD from baseline through EOT.

- Annualized rate of severe AECOPD from baseline up to EOT.

- Time to first severe AECOPD from baseline through EOT.

- Annualized rate of corticosteroid-treated AECOPD from baseline up to EOT.

- Change in Evaluating Respiratory Symptoms in COPD (E-RS:COPD) total score from baseline to week 24 and week 52.

- Rate of change in post-BD FEV1 (L) (post-BD FEV1 slope) from baseline up to EOT.

- Change in St. George*s Respiratory Questionnaire (SGRQ) total score from baseline to week 24 and week 52.

- Proportion of participants with a decrease of at least 4 points in SGRQ total score from baseline to week 24 and week 52.

- Incidence of treatment-emergent adverse events (TEAEs), adverse event of special interests (AESIs), serious adverse events (SAEs), and adverse events (AEs) leading to permanent treatment discontinuation in former smokers.

- Incidence of potentially clinically significant laboratory test, vital signs, and electrocardiogram (ECGs) abnormalities in former smokers.

- Functional itepekimab concentrations in serum in former smokers.

- Incidence of treatment-emergent anti-itepekimab antibodies responses in former smokers.

Cohort current smokers:

- Annualized rate of moderate or severe AECOPD from baseline up to week 52.

- Change in pre-BD FEV1 from baseline up to week 24 and week 52.

- Incidence of TEAEs, AESIs, SAEs, and AEs leading to permanent treatment discontinuation in current smokers.

- Incidence of potentially clinically significant laboratory, vital signs, and ECGs abnormalities in current smokers.

- Functional itepekimab concentrations in serum in current smokers.

- Incidence of treatment-emergent anti-itepekimab antibodies responses in

current smokers.

Study description

Background summary

Chronic obstructive pulmonary disease is a serious and life-threatening disease. It is the third leading cause of death worldwide and the fourth leading cause of death in the US, responsible for over 3 million deaths worldwide in 2016 and 160 000 deaths annually in the US. It is also the largest contributor to respiratory-related mortality. Chronic obstructive pulmonary disease is characterized by progressive decline in lung function and recurrent exacerbations of symptoms. The latter results in rapid disease progression and are associated with increased mortality, particularly following exacerbations that require hospitalization. Tobacco smoke is the major contributor to COPD. Although smoking cessation in patients with established COPD slows the rate of lung function decline and reduces the risk of hospitalization and mortality, former smokers with COPD are still at high risk for exacerbations and substantial morbidity and risk of mortality remain, particularly when compared to former smokers without COPD. Currently available therapies have modest efficacy and/or important safety concerns.Data from the PoC Study ACT15104 in which itepekimab was studied versus placebo on top of approved SoC as background therapy provided preliminary clinical evidence that itepekimab has the potential to confer significant benefit beyond that provided by currently available therapies to former smokers with moderate-to-severe COPD.

Study objective

This study has been transitioned to CTIS with ID 2024-512012-21-00 check the CTIS register for the current data.

Primary objective
Primary population (former smokers cohort):
- Evaluate the efficacy of itepekimab compared with placebo on the annualized rate of acute moderate-or-severe COPD exacerbations in former smokers with moderate-to-severe COPD.

Secondary objectives
Primary population (former smokers cohort):
- Evaluate the efficacy of itepekimab compared with placebo on pulmonary function in former smokers with moderate-to-severe COPD.
- Evaluate the efficacy of itepekimab compared with placebo on occurrence of acute exacerbation of COPD (AECOPD) in former smokers with moderate-to-severe COPD.

- Evaluate the efficacy of itepekimab compared with placebo on severe AECOPD in former
smokers with moderate-to-severe COPD.
- Evaluate the efficacy of itepekimab compared with placebo on corticosteroid-treated AECOPD in former smokers with moderate-to-severe COPD
- Evaluate the efficacy of itepekimab compared with placebo on respiratory symptoms in former smokers with moderate-to-severe COPD.
- Evaluate the efficacy of itepekimab compared with placebo on Forced Expiratory Volume in 1 second (FEV1) slope in former smokers with moderate-to-severe COPD.
- Evaluate the efficacy of itepekimab compared with placebo on health-related quality of life (HRQoL) as assessed by St. George*s Respiratory Questionnaire (SGRQ) in former smokers with moderate-to-severe COPD.
- Evaluate the safety and tolerability of itepekimab in former smokers with moderate-to-severe COPD
- Evaluate the pharmacokinetic (PK) profile of itepekimab in former smokers with moderate-to severe COPD.
- Evaluate immunogenicity to itepekimab in former smokers with moderate-to-severe COPD.

Secondary population (current smokers cohort):
- Estimate the efficacy of itepekimab compared with placebo on the annualized rate of acute
moderate or severe COPD exacerbations in current smokers with moderate-to-severe COPD
- Estimate the efficacy of itepekimab compared with placebo on pulmonary function in current
smokers with moderate-to-severe COPD
- Estimate the safety and tolerability of itepekimab in current smokers with moderate-to-severe
COPD
- Estimate the PK profile of itepekimab in current smokers with moderate to severe COPD
- Estimate immunogenicity to itepekimab in current smokers with moderate-to-severe COPD

Study design

- Phase 3, double blind, randomized, parallel

Intervention

- Compound: SAR440340 (REGN3500)
- Pharmaceutical form: solution for injection in pre-filled syringe
- Route of administration: subcutaneous

Study burden and risks

- Burden and risks are related to the blood sampling, chest X-ray, injections with study medication and possible side effects of the study medication.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Participant must be 40 to 85 years of age inclusive.
- Physician diagnosis of COPD for at least 1 year (based on Global Initiative for Chronic
Obstructive Lung Disease [GOLD] definition.
- Smoking history of >=10 pack-years:

-- For former smokers: participants who report that they are not currently smoking and
smoking cessation must have occurred >=6 months prior to Screening (Visit 1A) with an
intention to quit permanently.
-- For current smokers: participants who report that they are currently smoking tobacco
(participant smoked at least 1 cigarette per day on average during the past 7 days) at
Screening (Visit 1A) and who are not currently participating in or planning to initiate a
smoking cessation intervention at Screening (Visit 1A) or during Screening period.
- Participants with moderate-to-severe COPD
- Participant-reported history of signs and symptoms of chronic bronchitis (chronic
productive cough for at least 3 months in the year prior to Screening in a participant in
whom other causes of chronic cough [eg, inadequately treated gastroesophageal reflux or
chronic rhinosinusitis; or clinical diagnosis of bronchiectasis] has been excluded).
- Documented history of high exacerbation risk defined as having had >=2 moderate or >=1
severe exacerbations within the year prior to Screening (Visit 1A), with at least 1
exacerbation treated with systemic corticosteroids. At least one exacerbation must have
occurred while participants were on their current controller therapy:
-- Moderate exacerbations will be recorded by the Investigator and are defined as acute
worsening of respiratory symptoms that requires either systemic corticosteroids (IM, IV, or
oral) and/or antibiotics.
-- Severe exacerbations will be recorded by the Investigator and are defined as AECOPD
that require hospitalization or observation for >24 hours in emergency department/urgent
care facility.
- Participants with standard of care controller therapy, for >=3 months prior to Screening
(Visit 1A) and at a stable dose of controller therapy for at least 1 month prior to the
Screening, including either: inhaled corticosteroid (ICS) + long-acting beta-agonist
(LABA), long-acting muscarinic antagonist (LAMA) + LABA or LAMA + LABA + ICS.
- Body mass index (BMI) >=18.0 kg/m^2, or BMI >=16.0 kg/m2 for participants

enrolled in
East-Asian countries.
- Female participant is not pregnant, not breastfeeding, and at least one of the following
conditions applies:
-- not a women of child-bearing potential (WOCBP) OR
-- a WOCBP who agrees to follow the contraceptive guidance during the intervention
period and for at least 20 weeks after the last dose of study intervention.

Exclusion criteria

- Current diagnosis of asthma according to the Global Initiative for Asthma (GINA)
guidelines, or documented history of asthma unless asthma resolved before 18 years of
age and has not recurred.
- For former smokers: Active smoking or vaping of any products (eg, nicotine, tetrahydrocannabinol [THC]) within 6 months prior to Screening (Visit 1A).
For current smokers: vaping of any products (eg, nicotine, THC) within 6 months prior to
Screening (Visit 1A).
- Clinically significant new abnormal electrocardiogram (ECG) within 6 months prior to, or
at Screening (Visit 1A) that may affect the participant*s participation in the study.
- Clinically significant and current pulmonary disease other than COPD, eg, sarcoidosis,
interstitial lung disease, bronchiectasis (clinical diagnosis), diagnosis of α-1 anti-trypsin
deficiency, or another diagnosed pulmonary disease.
- Diagnosis of cor pulmonale, evidence of right cardiac failure, or moderate-to-severe
pulmonary hypertension.
- Hypercapnia requiring bilevel positive airway pressure (BiPAP).
- Moderate or severe exacerbation of COPD (AECOPD) within 4 weeks prior to Screening
(Visit 1A).
- Prior history of / planned: lung pneumonectomy for any reason, or lung volume reduction
procedures (including bronchoscopic volume reduction) for COPD. Note: Surgical biopsy,
or segmentectomy, or wedge resection, or lobectomy for other diseases would not be
excluded.

- Unstable ischemic heart disease, including acute myocardial infarction within the past 1
year prior to Screening, or unstable angina in the 6 months prior to Screening (Visit 1A).
- Cardiac arrhythmias including paroxysmal (eg, intermittent) atrial fibrillation.
- Uncontrolled hypertension (ie, systolic blood pressure [BP] >180 mm Hg or diastolic BP
>110 mm Hg with or without use of anti-hypertensive therapy).
- Participants with active tuberculosis (TB), latent TB, a history of incompletely treated TB,
suspected extrapulmonary TB infection (TBI), or who are at high risk of contracting TB
(such as close contact with individuals with active or latent TB) or received Bacillus
Calmette-Guérin (BCG)-vaccination within 12 weeks prior to Screening (Visit 1A).
- History of human immunodeficiency virus (HIV) infection or positive HIV 1/2 serology at
Screening (Visit 1A).
- Suspicion of, or confirmed, coronavirus disease 2019 (COVID-19) infection or in contact
with known exposure to COVID-19 at Screening (Visit 1A); known history of COVID-19
infection within 4 weeks prior to Screening (Visit 1A); history of requiring mechanical
ventilation or extracorporeal membrane oxygenation (ECMO) secondary to COVID-19
within 3 months prior to Screening (Visit 1A); participants who have had a COVID-19
infection prior Screening (Visit 1A) who have not yet sufficiently recovered to participate in
the procedures of a clinical trial.
- Evidence of acute or chronic infection requiring systemic treatment with anti bacterial,
antiviral, antifungal, antiparasitic, or antiprotozoal medications within 4 weeks before
Screening (Visit 1A), significant viral infections within 4 weeks before Screening (Visit 1A)
that may not have been treated with antiviral treatment (eg, influenza receiving only
symptomatic treatment).
- Participants with active autoimmune disease or participants using immunosuppressive
therapy for autoimmune disease (eg, rheumatoid arthritis, inflammatory bowel disease,
primary biliary cirrhosis, systemic lupus erythematosus, multiple sclerosis.
- History of malignancy within 5 years before Screening (Visit 1A), except completely

treated in situ carcinoma of the cervix, completely treated and resolved nonmetastatic
squamous or basal cell carcinoma of the skin.
- Previous use of itepekimab.

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:	Recruiting
Start date (anticipated):	20-09-2021
Enrollment:	10
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	nvt
Generic name:	itepekimab

Ethics review

Approved WMO

Date:	05-01-2021

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-12-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-03-2024

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	2020-001819-24
EU-CTR	CTIS2024-512012-21-00
EudraCT	EUCTR2020-001819-24-NL
CCMO	NL75763.091.20