A Phase 4, randomized, double-blind, placebo-controlled, multicenter, parallel-group study of the effect of dupilumab on sleep disturbance in patients with uncontrolled persistent asthma

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To assess the effect of dupilumab on sleep, to evaluate the effect of dupilumab on additional patient reported sleep outcomes, on objective sleep assessment, asthma symptoms, long function and the safety of dupilumab.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON52410

Source
ToetsingOnline

Brief title
LPS16677 Morpheo

Condition

- Allergic conditions
- Congenital respiratory tract disorders

Synonym
asthma, sleep disturbance

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Asthma, Dupilumab, Sleep disturbance

Outcome measures

Primary outcome

- Change in sleep disturbance score in Asthma Sleep Disturbance Questionnaire

Secondary outcome

- Change in the number of nocturnal awakenings in Sleep Diary

- Change in PROMIS sleep-related impairment assessment

- Change in sleep quality in Sleep Diary

- Change in restorative sleep in Sleep Diary

- Change in WASO in Sleep Diary

- Change in WASO (actigraphy data)

- Change in daytime and nighttime asthma symptoms in Asthma Daytime Symptom

Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD)

- Change in pre-bronchodilator (BD) FEV1

- Incidence of Adverse events

Study description

Background summary

Many patients with asthma experience sleep disturbances. Since sleep disturbances negatively affect overall patient quality of life, accurate detection and monitoring of sleep disturbances is important to the management

of asthma. Therefore, one of the asthma treatment goals is to eliminate asthma symptoms at night and decrease awakenings due to asthma symptoms. Better control of nocturnal asthma symptoms could lead to improved sleep quality and a decrease in daytime sleep-related symptoms.

In order to evaluate the effect of dupilumab on sleep quality in asthma patients, this study uses many assessments/questionnaires/diaries, including questions about asthma, sleep and quality of life. In addition this study requires the patients to wear a wrist watch called Actiwatch, 24 hours/per day.

Study objective

To assess the effect of dupilumab on sleep, to evaluate the effect of dupilumab on additional patient reported sleep outcomes, on objective sleep assessment, asthma symptoms, long function and the safety of dupilumab.

Study design

Phase 4, double blind, randomized, parallel

Intervention

- 2 subcutaneous injections with dupilumab 200 mg as starting dose on Day 1, followed by maintenance dose of 1 subcutaneous injection with dupilumab 200 mg every 2 weeks during 12 weeks
- 2 subcutaneous injections with placebo on Day 1, followed by 1 subcutaneous injection with placebo every 2 weeks during 12 weeks

Study burden and risks

- Burden and risks are related to the blood sampling, ECG, FeNO and Spirometry, 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

-Physician diagnosis of asthma based on the Global Initiative for Asthma (GINA) 2020 Guidelines
for >=12 months treated with medium to high dose inhaled corticosteroid (ICS) and a second
controller (ie, long-acting beta agonist, leukotriene receptor antagonist). A third controller is allowed
but not mandatory. The dose regimen should be stable for at least 1 month before the study and
during the screening period
-History of at least one severe asthma exacerbation within 1 year prior to screening. Severe exacerbation is
defined as deterioration of asthma that results in emergency treatment, hospitalization due to
asthma, or treatment with systemic steroids (oral or injectable)
-Eosinophils >=150 cells/µL and fractional exhaled nitric oxide (FeNO) >=25 ppb during screening, prior to randomization
NOTES:
* Historical values of blood eosinophil count meeting the eligibility criterion measured
within 6 months prior to screening Visit 1 in the absence of oral corticosteroid (OCS)
treatment are allowed.
* FeNO value to be checked for eligibility at Visit 2 as well.
-Asthma control questionnaire (ACQ)-5 >=2.5 at screening Visit 1 and Visit 2,

prior to randomization
-Pre-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) <= 80% of predicted normal
during screening, and at Visit 2, prior to randomization
-Exhibit bronchodilator reversibility (>=12% and 200 mL improvement in FEV1 post short-acting beta
agonist administration) during screening period, prior to randomization, unless reversibility test
meeting the inclusion criteria was done within 6 months prior to screening
Visit 1
-Weekly average nocturnal awakenings due to asthma symptoms in the week prior to screening
Visit 1 is >=1

Exclusion criteria

-Current smoker
-Former smoker for 10 years with a smoking history of >10 pack-years
-Severe asthma exacerbation during screening, prior to randomization
-History or clinical evidence of chronic obstructive pulmonary disease (COPD) including Asthma-
COPD Overlap Syndrome (ACOS) or any other significant lung disease (eg, lung fibrosis,
sarcoidosis, interstitial lung disease, pulmonary hypertension, bronchiectasis, Churg-Strauss
Syndrome)
-History of or current evidence of clinically significant non-respiratory diseases that in the opinion of
the investigator may interfere with the aims of the study or put the participant at undue risk
-Active tuberculosis (TB) or non-tuberculous mycobacterial infection, or a history of incompletely
treated TB will be excluded unless it is well documented by a specialist that the participant has
been adequately treated and can now start treatment with a biologic agent, in the medical judgment
of the Investigator and/or infectious disease specialist. Tuberculosis testing would be performed on
a country by country basis, according to local guidelines if required by Regulatory Authorities or
ethics boards
-Diagnosed active endoparasitic infection; suspected or high risk of endoparasitic infection, unless
clinical and (if necessary) laboratory assessment have ruled out active infection before randomization

-History of human immunodeficiency (HIV) infection or positive HIV test at screening Visit 1
-Active chronic or acute infection requiring treatment with systemic antibiotics, antivirals,
antiprotozoals, or antifungals within 2 weeks before screening
-Known or suspected immunodeficiency including history of invasive opportunistic infections,
despite infection resolution
-Current evidence of clinically significant oncological disease
-History of systemic hypersensitivity or anaphylaxis to any biologic therapy
-Severe uncontrolled depression
-Sleep disturbances not related to asthma, including sleep apnea, hypersomnia, or insomnia
secondary to chronic pain, atopic dermatitis (AD), COPD or other conditions
-Participant who works night shift (ie, any work between 8 pm and 6 am)
-Erratic sleep habits, as determined by the Investigator
-Restless leg syndrome or periodic limb movement disorder
-Chronic treatment with OCS for more than 2 weeks before screening Visit 1
- Participant taking sedative, anxiolytic, or hypnotic treatments, including melatonin, within 3 months
before randomization
-Participant taking systemic sedative antihistamines (excluding newer generations of
antihistamines) or theophylline
-Current treatment with antidepressants, lipophilic beta blockers, clonidine, opioids, or other
medications known to interfere with sleep and may confound the study assessments, as determined
by the Investigator
-Participant who has taken biologic therapy (including dupilumab)/systemic immunosuppressant to treat inflammatory disease or autoimmune disease (eg, rheumatoid
arthritis, inflammatory bowel disease, primary biliary cirrhosis, systemic lupus erythematosus, multiple sclerosis, etc) within 2 months or 5 half-lives before screening
Visit 1, whichever is longer
-Treatment with live (attenuated) vaccine within 4 weeks before screening Visit 1
NOTE: For participants who have vaccination with live, attenuated vaccines planned
during the course of the study (based on national vaccination schedule/local guidelines), it
will be determined, after consultation with a physician, whether the administration of
vaccine can be postponed until after the end of the study, (i.e. after the 12 week follow-up
period off-treatment or until the participant switches to commercialized

dupilumab or other
biologic product, whichever comes first), or preponed to before the start of the study
without compromising the health of the participant:
* Participant for whom administration of live (attenuated) vaccine can be safely postponed would be eligible to enroll into the study.
* Participant who have their vaccination preponed can enroll in the study only after a gap
of 4 weeks following administration of the vaccine.

Study design

Design

Study phase:	4
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):	15-02-2021
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dupixent
Generic name:	Dupilumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-07-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-09-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-10-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-10-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-11-2022
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	2020-001217-20
EudraCT	EUCTR2020-001217-20-NL
CCMO	NL74426.091.20