A 2-treatment period, randomized, placebo-controlled, multicenter parallel-group study to assess the safety of QAW039 when added to existing asthma therapy in GINA steps 3, 4 and 5 patients with uncontrolled asthma

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The overall purpose of this study is to provide long-term safety data for fevipiprant (QAW039) (150 mg once daily and 450 mg once daily),compared with placebo, when added to the Global Initiative for Asthma (GINA) steps 3, 4, and 5 standard-of-care...

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

Summary

ID

NL-OMON48545

Source
ToetsingOnline

Brief title
CQAW039A2315

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma, N/A

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor / verrichter van het onderzoek)

Intervention

Keyword: asthma, CRHT2, QAW039, safety

Outcome measures

Primary outcome

Treatment Period 1 (double-blind, 52-week treatment period):

In patients with moderate-to-severe asthma receiving SoC asthma therapy, to evaluate the long-term safety of QAW039 (150 mg once daily and 450 mg once daily), compared with placebo, as assessed by:

- treatment emergent adverse events (AEs);

- treatment emergent serious adverse events (SAEs); and

- study treatment discontinuations due to treatment emergent AEs.

Treatment Period 1 and Treatment Period 2 combined:

In patients with moderate-to-severe-asthma receiving SoC asthma therapy, to evaluate the long-term safety of QAW039 (150 mg once daily and 450 mg once daily), compared with placebo, as assessed by:

- treatment emergent AEs

- treatment emergent SAEs; and

- study treatment discontinuations due to treatment emergent AEs.

Secondary outcome

Treatment Period 1 (double-blind, 52-week treatment period):

In patients with moderate-to-severe asthma receiving SoC asthma therapy, to evaluate the long-term safety of QAW039 (150 mg once daily and 450 mg once daily), compared with placebo, as assessed by:

- the rate of patients with at least 1 treatment emergent AE by primary system organ class; and.
- the rate of treatment emergent patient deaths and patient hospitalizations (any visit to the hospital requiring an overnight stay or an emergency room visit greater than 24 hours) due to an asthma exacerbation.

Treatment Period 1 and Treatment Period 2 combined:

In patients with moderate-to-severe-asthma receiving SoC asthma therapy, to evaluate the long-term safety of QAW039 (150 mg once daily and 450 mg once daily), compared with placebo, as assessed by:

• the rate of patients with at least 1 treatment emergent AE by primary system organ class; and

• the rate of treatment emergent patient deaths and patient hospitalizations (any visit to the hospital requiring an overnight stay or an emergency room visit greater than 24 hours) due to an asthma exacerbation.

Study description

Background summary

Despite existing therapies, there is still significant unmet medical need in asthma.
Severe asthma is defined as asthma that requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic

corticosteroids. Severe asthma is a heterogeneous condition consisting of phenotypes such as eosinophilic asthma.This subgroup has also been defined as "refractory" asthma.
Recurrent exacerbations are a major problem in some patients with severe asthma. It seems inhalation therapy, and oral cortico-steroids are not as effective for this sub-group as in the milder forms of asthma.Therefore, there remains a need for therapy, which is well tolerated, is easy to administrate, and anti-inflammatory works, in which it suppresses the sputum eosinophils and thereby reduces the asthma exacerbations.
QAW039 is a CRTh2 antagonist expected to provide benefit in asthma by binding to CRTh2 receptors on eosinophils, basophils, and T lymphocytes in the blood and tissues; thus, inhibiting migration and activation of these cells into the airway tissues and blocking the PGD2-driven release of Th2 cytokines (Chevalier, et al 2005). Since these are the major effector cells and soluble factors driving airway inflammation in asthma, treatment with QAW039 should result in a decrease in these parameters of airway inflammation as well as a clinical improvement in asthma.

The overall purpose of this study is to provide long-term safety data for fevipiprant (QAW039) (150 mg once daily and 450 mg once daily), compared with placebo, when added to the Global Initiative for Asthma (GINA) steps 3, 4, and 5 standard-of-care (SoC) asthma therapy (GINA 2016), in adult and adolescent (>=12 years) patients with moderate-tosevere asthma.

Study objective

The overall purpose of this study is to provide long-term safety data for fevipiprant (QAW039) (150 mg once daily and 450 mg once daily), compared with placebo, when added to the Global Initiative for Asthma (GINA) steps 3, 4, and 5 standard-of-care (SoC) asthma therapy (GINA 2016), in adult and adolescent (>=12 years) patients with moderate-tosevere asthma.

Study design

This study is a 2-treatment period, randomized, multicenter parallel-group safety study. Treatment Period 1 is a 52-week, double-blind treatment period in which QAW039 or placebo is added to GINA steps 3, 4 and 5 SoC asthma therapy. Treatment Period 2 is an optional 104-week, single-blind treatment period in which patients will receive QAW039 or placebo added to GINA steps 3, 4 and 5 SoC asthma therapy.
The study will include the following:
- Screening Period of up to 2 weeks to assess eligibility of new patients.
- Treatment Period 1*double-blind period of 52 weeks.
- Treatment Period 2*single-blind period of 104 weeks.

- Follow-up Period of 4 weeks, investigational and drug-free, following the last dose of study drug.

Intervention

Treatment with 150 mg or 450 mg QAW039 or placebo once daily.

Study burden and risks

The study consists of 2 periods.

Burden:
Period 1:
Physical examination: 7x
ECG: 7x
Females of childbearing potential: Pregnancy test: 1x in serum, 7x in urine
Blood collection: 7x
Reversibility test: 1x in case not participated previously in another QAW039 trial.
Spirometry: 12x
Completion Questionnaire: 1x in case not participated previously in another QAW039 trial.

Period 2:
Physical examination:97x
ECG: 9x
Females of childbearing potential: Pregnancy test: 10x in urine
Blood collection: 9x
Urine collection: 9x

Risks:
Side effects QAW0139 and risks of study procedures.

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

Patients completing a prior Phase 3 study of QAW039 (NLD: CQAW039A2314):
- Written Informed consent
- Completion of the Treatment Period (on blinded study drug) of a prior Phase 3 study of QAW039.
- Patient is able to safely continue into the study as judged by the investigator., Patients who have not previously participated in a study of QAW039:
- Written informed consent.
- Male and female patients aged >=12 years (NLD: >=18 years).
- A diagnosis of asthma, uncontrolled on GINA 3/4/5 asthma medication.
- Evidence of airway reversibility or airway hyper- reactivity.
- FEV1 of <=85% of the predicted normal value.
- An ACQ score >=1.5 prior to entering the study.

Exclusion criteria

Patients completing a prior phase 3 study of QAW039:
- Pregnant or nursing (lactating) women.
- Women of child-bearing potential unless they are using basic methods of contraception during dosing of study drug.
- Patients who did not complete the Treatment Period on blinded study drug of the prior QAW039 study they participated in.
- Inability to comply with all study requirements.

- Patient who experienced a serious and drug-related AE in the prior QAW039 study they participated in., Patients who have not previously participated in a study of QAW039:
- Use of other investigational drugs within 5 half-lives of study entry, or within 30 days, whichever is longer.
- Subjects who have participated in another trial of QAW039.
- A QTcF (Fridericia) >=450 msec (male) or >=460 msec (female) at Visit 1 or Visit 201 on the ECG Analysis Report provided by the ECG core laboratory.
- History of malignancy with the exception of local basal cell carcinoma of the skin.
- Pregnant or nursing (lactating) women.
- Serious co-morbidities.
- Patients on greater than 20 mg of simvastatin

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):	07-11-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	QAW039
Generic name:	QAW039

Ethics review

Approved WMO Date:	04-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-10-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-001560-11-NL
ClinicalTrials.gov	NCT03052517
CCMO	NL61901.018.17