A randomized, placebo-controlled, dose-ranging, multi-centre trial of QAW039 (1-450 mg p.o.) to investigate the effect on FEV1 and ACQ in patients with moderate-to-severe, persistent, allergic asthma, inadequately controlled with ICS therapy (CQAW039A2206)

Published: 29-05-2012
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Primary objective: To demonstrate a clinically significant improvement in morning FEV1 in moderate to severe allergic asthmatics inadequately controlled by ICS therapy treated with QAW039 for 12 weeks compared to placebo.Secondary objectives:...

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

Summary

ID

NL-OMON37185

Source
ToetsingOnline

Brief title
CQAW039A2206

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma; allergic asthma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis Pharma BV
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: asthma, CRHT2, dose-ranging, QAW039

Outcome measures

Primary outcome

Trough FEV1 week 12.

Secondary outcome

Asthma symptoms (ACQ, Juniper diary), other spirometry parameters, adverse

events.

Study description

Background summary

Many adults with asthma have inadequate control of symptoms when receiving a low-to-medium dose of an inhaled corticosteroid. Treatment options include the addition of a leukotriene modifier (Montelukast), the addition of an inhaled long-acting beta-agonist (LABA) or an increased dose of an inhaled corticosteroid. There are weaknesses with the current treatments namely, patients have trouble accurately dosing with the ICS/LABA inhalers and compliance with these devices is less than that seen with oral medications. Further the efficacy of montelukast is lower than ICS. Thus there is a need for a new oral therapy that is more efficacious than montelukast and that would provide added benefit when added to ICS.
QAW039 is a highly selective and potent oral antagonist of prostaglandin D2 (PGD2) that binds to the CRTH2 receptor (CRTH2 is also known as the DP2 receptor). QAW039 is expected to work by binding CRTH2 receptors on eosinophils and CRTH2+ T lymphocytes in the blood. At high levels of receptor inhibition, the migration of eosinophils and CRTH2+ CD4+ lymphocytes into the airway tissues will be blocked. Since both cell types are thought to be major effector

cells that drive the allergic inflammation associated with asthma, the control of the signs and symptoms of the disease should be improved.
The purpose of this Phase IIb study is to support the dose selection decision by finding the dose and/or regimen of QAW039 that will provide the optimal benefit/risk ratio in patients with moderate to severe allergic asthma inadequately controlled by ICS therapy.

Study objective

Primary objective: To demonstrate a clinically significant improvement in morning FEV1 in moderate to severe allergic asthmatics inadequately controlled by ICS therapy treated with QAW039 for 12 weeks compared to placebo.
Secondary objectives: asthmatic symptoms (ACQ and Juniper diary), other spirometry parameters, dose response (trough FEV1), safety and tolerability, efficacy vs montelukast.

Study design

Randomized, double-blind parallel group, phase IIB dose-ranging study.
Screening, thereafter switch to inhaled budesonide, to be stepped down (2-4 weeks) to a low dose (200 ug bid). Washout of prohibited co-medication during washout period. Thereafter randomization to 12 weeks of treatment with:
• QAW039: 13 dosing groups 1-150 mg 1-2 times daily and 450 mg qd.
• Montelukast 10 mg qd (chance 1:9).
• Placebo (chance 1:9).
All treatments oral (7 capsules daily), in combination with inhaled budesonide.
After the treatment period all patients will be given placebo for 4 weeks.
Salbutamol rescue medication.
Total study duration 18-21 weeks.
Approx. 950 patients.

Intervention

Treatment with QAW039 in various doses, montelukast or placebo.

Study burden and risks

Risk: Adverse effects of study medication. Changes in current asthma medication. Stepping down budesonide.
Burden: 10 visits in 18-21 weeks. 3 visits 7-8 h, 7 visits 2-3 h.
Physical examination 3 times.
Blood tests 9 times (8-54 ml/occasion, 150 ml in total).
Pregnancy test 7 times.
Skin prick test once.
Lung function (reversibility) once.
Lung function 4 times 1 test, 1 time 2 tests.

FENO test 4 times 1 test, 1 time 2 tests.
ECG 3 times 1 ECG, 4 times 4 ECGs.
Questionnaires (1-2) 9 times.
Daily diary and peak flow measurements.
Optional substudy: pharmacogenetic blood test (10 ml).

Contacts

Public
Novartis Pharma BV

Raapopseweg 1
Arnhem 6834 DP
NL
Scientific
Novartis Pharma BV

Raapopseweg 1
Arnhem 6834 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female adults aged 18-65 years.
• Asthma as per [GINA] guidelines, and currently prescribed ICS therapy.
• Pre-bronchodilator FEV1 40% to 80% of predicted at screening and at randomization. Value at the randomization should be within 15% of the screening FEV1.
• Patients should be allergic or atopic, as diagnosed historically or prior to entry into the

study.
• Reversible airway obstruction or airways hyper-reactivity or have shown either of such responses in previous test(s) within the last 5 years.
• ACQ score >= 1.5 at randomization.

Exclusion criteria

• Recent use of other investigational drugs (see protocol page 13 for details).
• History of hypersensitivity to any of the study drugs or to drugs of similar chemical classes (CRTh2 antagonists).
• History of long QT syndrome or QTc measured at Visit 2 (Fridericia method) is prolonged (>450 ms for males and females).
• History of malignancy (see protocol page 14 for exceptions) in the last 5 years.
• Pregnancy and breast feeding. Inadequate contraception, if relevant.
• Serious co-morbidities (see protocol page 14 for details).

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):	01-07-2012
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	QAW039
Generic name:	QAW039
Product type:	Medicine
Brand name:	Singulair
Generic name:	montelukast
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-05-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	27-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-05-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-05-2013
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	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2011-001062-18-NL
CCMO	NL40858.060.12