A Multi-Center, Randomized, Double-Blind, Placebo-Controlled study to investigate the efficacy and safety of 52 weeks treatment with QGE031 s.c. in Asthma Patients not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS

Published: 23-06-2015
Last updated: 16-04-2024

To evaluate the efficacy, safety and tolerability of QGE031 (24 mg, 72 mg, 240 mg s.c. q4w) compared to placebo on top of SoC in atopic patients with asthma.

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

Summary

ID

NL-OMON42235

Source
ToetsingOnline

Brief title
QGE031B2204

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 van dit onderzoek)

Intervention

Keyword: Asthma Exacerbations, Efficacy, QGE031, Safety

Outcome measures

Primary outcome

Rate of severe asthma exacerbations during 52 weeks of treatment

Secondary outcome

Key secondary objectives

* To evaluate the efficacy of QGE031 (24 mg, 72 mg, 240 mg s.c. q4w) compared to placebo on top of SoC in all asthma patients (atopic and non-atopic) who are not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS on the reduction in rate of severe asthma exacerbations during 52 weeks of treatment.

* To evaluate the efficacy of QGE031 (24 mg, 72 mg, 240 mg s.c. q4w) compared to placebo on top of SoC in non-atopic patients with asthma who are not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS on the reduction in rate of severe asthma exacerbations during 52 weeks of treatment.

Other secondary objectives

* Exacerbation (except listed above)

* ACQ5, 6, 7 scores

* ACD scores

* FEV1, FVC, FEV1/FVC

* PEF

ACQ5,6,7 scores

ACD scores

FEV1, FVC, FEV1/FVC

Study description

Background summary

QGE031 is a so-called monoclonal antibody, a drug that has been developed especially in the laboratory to inhibit the production of immunoglobulin E or IgE. IgE plays a role in allergic reactions. QGE031 resembles the drug Xolair (omalizumab), which is registered in the Netherlands for the treatment of asthma. Preclinical research showed QGE031 a more effective inhibitor than omalizumab which resulted in less allergic skin reactions. QGE031 has not been studied in patients with asthma. Through this study, the efficacy and safety of 52 weeks of treatment administered subcutaneously QGE031 (every 4 weeks) in patients with asthma is assessed.

Study objective

To evaluate the efficacy, safety and tolerability of QGE031 (24 mg, 72 mg, 240 mg s.c. q4w) compared to placebo on top of SoC in atopic patients with asthma.

Study design

A multicenter, randomised, placebocontrolled study to assess efficacy and safety of QGE031 (13 s.c. 4-weekly injections) in patients with asthma. It consists of 4 phases:
A screening epoch of up to 2 weeks duration during which patients who have given informed consent are assessed for study eligibility.

A 4 week run-in epoch where baseline data are collected. At the end of this epoch, eligible patients are randomized to double-blind treatment.
A 52 week double blind treatment epoch during which patients receive study drug every 4 weeks.
A follow-up epoch with the final visit occurring 20 weeks after the last treatment epoch visit (Visit 215) to allow for a complete wash out of the drug and assess persistency of efficacy and/or any
rebound.

Total duration of study is approx. 1.5 years.

Intervention

13 x 4-weekly s.c. injection 24 mg, 72 mg or 240 mg QGE031 or placebo

Study burden and risks

Burden:
13 s.c. injections, 4-weekly.
physical Examination: 6x
Assessment length 1x, weight 3x, bloodpressure and pulse 6x
Blood collection: 13 x, 5-32 ml per visit
Optional pharmacogenetic/-genomic blood collection: 4x (5 ml per visit), moreover nasal swab collection: 4x
Urine collection: 7x
female subjects: Pregnancy test: 18x (3x in serum, 15x in urine)
Stool/feces sample collection: 1x
Spirometry:14x
Teversibility test:1x
Skin prick tests: 1x
Completion of registration injection site reactions: Throughout treatment period
PEF and completion of diaries: Throughout duration study
FeNO: 9x
ECG:10x
Completion of 4 questionnaires: 11 x (not all 4 at each visit)

Risks:
Adverse Events QGE031 and risks/burden studyprocedures

Known Adverse events QGE031:
- Most common reported: Hives, approx. 2 hrs post injection. Disappeared quickly after treatment of this allergic reaction.
- Allergic reactions (e.g., rash, swelling of throat and/or tongue) and some which on rare occasion may be severe (e.g., very low blood pressure and difficulty with breathing). The risk for a severe allergic reaction caused by the study drug is not known yet, however there have been no occurrences so far

and the risk is considered low.
- Risks at s.c. injection site: Pain, swelling, redness and bruising.

Risks/burden studyprocedures:
- Venapuncture (blood collection): Fainting, pain and/or bruising. Rarely, there may be a small blood clot or infection at the site of the needle puncture.
- Skin Prick tests: Local redness, swelling and itching. Extremely rare, an allergic reaction involving the entire body with itching, hives, wheezing or in severe cases, low blood pressure, swelling of the throat and/or difficulty breathing.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male and female adult patients aged * 18 to * 75 years.
- Patients with a diagnosis of asthma according to GINA 2014 for a period of at least 12 months prior to Visit 1.
- Daily treatment with medium- or high-dose ICS plus LABA (b.i.d. or equivalent) for * 3 months prior to Visit 1 (stable regimen at least 4 weeks prior to Visit 1). If the patients are treated with OCS (* 10 mg/day of prednisone or equivalent), the regimen should be stable at least 4 weeks prior to Visit 1 (Appendix 3 for the definition of corticosteroid dose).
- A documented history of at least two asthma exacerbations in the 12 months prior to Visit 1 that had required treatment with systemic corticosteroids (SCS) for at least 3 continuous days or a depo-injectable corticosteroids, or that required hospitalization or ER visit.
- FEV1 of * 40% and * 80% of the predicted normal value for the patient, after withholding bronchodilators at Visit 101. Withholding period of bronchodilators prior to spirometry: SABA for * 6 hrs and LABA (or FDC of ICS/LABA) for * 24 hrs, SAMA for * 8 hrs, LAMA for * 24 hrs. If FEV1 is between * 35 to 40% or 80 to * 85% of the patient*s predicted normal value, a one-time re-testing is allowed. Re-assessment of % predicted FEV1 should be done in an ad-hoc visit to be scheduled on a date that would provide sufficient time to receive confirmation from the spirometry data central reviewer before randomization.
- Patients must demonstrate an increase in FEV1 of * 12% and 200 mL within 30 minutes after administration of 400 µg salbutamol/albuterol (or equivalent dose) at Visit 1.
If reversibility is not proven at Visit 101, patients may be permitted to enter the study with historical evidence of reversibility within 5 years prior to Visit 1.
- Body mass index (BMI) must be within the range of * 18 and * 45 kg/m2.
- Asthma which is not adequately controlled on current treatment, as demonstrated by an ACQ5 score of *1.5 at Visit 101 and at Visit 102.
- The atopic status will be assessed at Visit 1 by using *Skin Prick Test (SPT)* and blood multi-allergen testing (ImmunoCAP Phadiatop, Phadia AB)* during V1.

Exclusion criteria

- Patients who experience an asthma attack/exacerbation requiring a short burst of SCSs during screening and run-in, they may be rescreened 6 weeks after recovery from the attack/exacerbation
- Patients who have had a respiratory tract infection within 4 weeks prior to Visit 1
- Patients who experience a respiratory tract infection during screening and run-in, they may be rescreened 4 weeks after recovery from the respiratory tract infection
- History of life-threatening asthma in the previous ten years, including a history of significant hypercarbia (pCO_2 > 45 mmHg), prior intubation (endotracheal and NIPPV), respiratory arrest, or seizures as a result of asthma
- Patients who have smoked or inhaled tobacco products within the 6 month period prior to Visit 1, or who have a smoking history of greater than 10 pack years (e.g. 10 pack years = 1 pack/day x 10 years or * pack/day x 20 years, etc.).
- Patients who are participating in the active phase of a supervised pulmonary rehabilitation

program unless the patient is on a maintenance program that has been ongoing for at least 3 months.
- Patients who have not achieved acceptable spirometry results at Visit 101 in accordance with ATS/ERS criteria for acceptability and repeatability (rescreening allowed only once).
- Patients with chronic lung diseases other than asthma.
- History of generalized urticaria or who have an acute urticaria episode at time of screening or during run-in. If patients experience an acute urticaria episode during screening or run-in, they may be rescreened after recovery from the urticaria.
- Patients with a stool examination positive for ova/parasites at Visit 101. If a stool test is positive for Blastocystis hominis (a non-pathogenic parasite) and the patient is asymptomatic, the patient can continue the study without screening failure.

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):	06-11-2015
Enrollment:	38
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	QGE031
Generic name:	QGE031

Ethics review

Approved WMO Date:	23-06-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-10-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2014-003155-57-NL
ClinicalTrials.gov	NCT02336425
CCMO	NL52415.058.15