A randomized, double-blind, placebo controlled, parallel group, proof of concept study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of QGE031 in the treatment of patients with moderate to severe atopic dermatitis (CQGE031X2201)

Published: 04-06-2012
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Primary: To demonstrate the efficacy of QGE031 relative to placebo at 12 weeks in patients withatopic dermatitis (AD) as assessed by Eczema Area and Severity Index (EASI).Secondary: efficacy assessed by Investigator Global Assessment (IGA, 12 weeks...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON37121

Source
ToetsingOnline

Brief title
CQGE031X2201

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
atopic dermatitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: atopic dermatitis, IgE, QGE031

Outcome measures

Primary outcome

EASI at week 12.

Secondary outcome

IGA, 12 weeks, EASI and IGA 6 weeks, adverse events, PK, PD, immunogenicity,

specific IgE, IgE autoantibodies and free IgE, Patient Reported Outcomes.

Study description

Background summary

Atopic dermatitis (AD) is a chronic atopic skin condition with a prevalence of at least 10-15% of children in Europe and it has continuously increased in recent decades. The persistence after puberty is approximately up to 50%. Topical corticosteroids are the current mainstay of therapy but their value in patients with extensive disease is limited. Long-term use of topical corticosteroids is not recommended due to the potential to cause local and systemic side effects. Treatment options for patients who are not controlled with topical drugs include phototherapy, systemic steroids, methotrexate, and cyclosporine.
Patients with AD often have elevated levels of serum IgE; however, the role of IgE and specific allergens in driving AD has not been fully characterized. Case series have been published demonstrating efficacy with omalizumab (Xolair®; the first registered therapeutic antibody against IgE), although a randomized

placebo-controlled trial did not demonstrate clinical efficacy in AD patients.
In this study, an observed response in skin biomarkers suggests that clinical efficacy in AD might be achieved with improved suppression of IgE.
QGE031 is a humanized monoclonal antibody directed against human IgE and is a highly potent inhibitor of human IgE binding to the IgE receptor. It is designed to overcome some of the limitations associated with omalizumab. Clinical efficacy in treating patients with AD is expected due to the increased affinity of QGE031 relative to omalizumab which allows for dosing of patients with higher baseline IgE levels and suppression of free IgE to lower levels than achievable with omalizumab.
This proof of concept study will assess the safety and efficacy of QGE031 in patients with AD.

During the EC-assessment abroad it was requested to ajust the selction criteria for the study in such a way that they would better reflect the approved indication for cyclosporin, i.e. make them more stringent. Because in the mean time in Austria 2 patiënts had been randomized to cyclosporin and 9 to either QGE031 or placebo, and because amendment of the selction criteria would result in a study population with 2 different grade of severity of the disease, it was decided to ammend the randomization scheme in such a way that only 2 (instead of 4) patients would be randomized to cyclosporin and 14 to QGE031 and 14 to placebo (amendment 5). This means that no new cyclosporin-patients will be enrolled.
In the Netherland no cyclosporin-patient will therefore be enrolled.
Cyclosporin will, however, remain in the protocol description in the ABR-form.

Study objective

Primary: To demonstrate the efficacy of QGE031 relative to placebo at 12 weeks in patients with
atopic dermatitis (AD) as assessed by Eczema Area and Severity Index (EASI).
Secondary: efficacy assessed by Investigator Global Assessment (IGA, 12 weeks), EASI and IGA (6 weeks), safety, PK, PD, immunogenicity, specific IgE, IgE autoantibodies and free IgE, Patient Reported Outcomes.

Study design

Multicenter randomized double-blind parallel-group placebo-controlled proof of concept study.
Randomisation (7:7:1) to:
* 280 mg QGE031 s.c. every 2 weeks (double-blind).
* Placebo s.c. every 2 weeks (double-blind).
* 2.5 * 5.0 mg/kg oral cyclosporin daily (open-label). Cyclosporin-arm has been closed in the mean time.
Continuation of current medication.
Screening period up to 4 weeks. Treatment period 12 weeks. Follow-up period 12

weeks.
Interim-analyses planned (see protocol paragraph 9.8, page 70).
Approx. 30 patients.

Intervention

Treatment with QGE031, placebo or cyclosporin.

Study burden and risks

Risk: Adverse effects of study medication and prick test.
Burden: Study duration 24-28 weeks. 14 visits. Duration 1-4 h.
During 12 weeks every 2 weeks sc injection of study medication (2 injections of 1 ml each per occasion).
Physical examination 5 times.
Blood tests during every visit, 15-25 ml/occasion.
Pregnancy test (if relevant) 6 times.
Stool sample at screening.
ECG 4 times.
Photographs of affected skin 7 times.
Prick test 4 times.
Skin biopsy 2 times.
Questionnaires (2) 3 times.
Optional pharmacogenetic blood test (10 ml).

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Male and female patients 18 to 65 (inclusive) years of age.
* Presence of atopic dermatitis confirmed by:
* Itchy skin condition in the past 12 months (must have), plus three, or more, of the following:
o History of involvement of the skin creases (fronts of elbows, behind knees, fronts of ankles, around neck or around eyes)
o Personal history of asthma or hay fever
o History of generally dry skin in the past year
o Onset before age of 2 years
o Visible flexural dermatitis
* EASI score of *20 at screening and stable AD (on current treatment regimen in the month prior to enrollment).
* Total IgE in the range of 30 to 5000 IU/mL inclusive.

Exclusion criteria

* Pregnant or nursing women.
* Women of child-bearing potential, unless using adequate contraceptive measures.
* Known hypersensitivity to any constituents of the study drugs, to murine, chimeric or human antibodies, or to drugs of similar chemical classes.

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:	Will not start
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Neoral
Generic name:	cyclosporin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	QGE031
Generic name:	QGE031

Ethics review

Approved WMO

Date:	04-06-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	05-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	20-09-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	21-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2013
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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2011-002112-84-NL
CCMO	NL40573.018.12