Clinical trial results:
An open-label, multi-center, extension study to evaluate the long-term safety of subcutaneous 240 mg QGE031 given every 4 weeks for 52 weeks in allergic asthma patients who completed study CQGE031B2201

Summary

EudraCT number	2013-003683-31
Trial protocol	SK CZ PL FI HU DE IT PT
Global end of trial date	22 March 2016

Results information

Result version number	v1
This version publication date	30 March 2017
First version publication date	30 March 2017

Trial information

Trial identification

Sponsor protocol code	CQGE031B2201E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02075008
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 March 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the long-term safety and tolerability of QGE031 (240 mg sc) given every 4 weeks for an additional 12 months in allergic asthma patients who completed the core study CQGE031B2201, as assessed by:

- Incidence and severity of adverse events (AEs) including serious adverse events (SAEs) including any events of special interest
- Changes in vital signs, laboratory assessments, and electrocardiogram (ECGs)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

All patients were provided with a short-acting β2-agonist (salbutamol/albuterol) which they were instructed to use throughout the study as rescue medication on an 'as needed basis' as was previously done in the core study. Patients were advised that between visits they could take their rescue medication for symptoms of intercurrent bronchospasm. In order to standardize measurements, patients were instructed to abstain from taking rescue salbutamol/albuterol within 6 hours of the start of each spirometry visit unless absolutely necessary.

Evidence for comparator: -

Actual start date of recruitment	27 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 37
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Korea, Republic of: 15
Country: Number of subjects enrolled	Mexico: 3

Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Romania: 26
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Slovakia: 18
Country: Number of subjects enrolled	Turkey: 12
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	270
EEA total number of subjects	147

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	237
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was an open-label, single arm study for participants who completed the core study CQGE031B2201 (NCT01716754).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	QGE031 every 4 weeks (q4w)

Arm description:

QGE031 240 mg subcutaneously q4w

Arm type	Experimental
Investigational medicinal product name	QGE031
Investigational medicinal product code	QGE031
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

QGE031 240 mg subcutaneously q4w

Number of subjects in period 1	QGE031 every 4 weeks (q4w)
Started	270
Completed	94
Not completed	176
Adverse event, serious fatal	1
Physician decision	1
Consent withdrawn by subject	6
Study terminated by Sponsor	159
Technical problems	1
Adverse event, non-fatal	5
Pregnancy	1
Lost to follow-up	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	QGE031 every 4 weeks (q4w)
Reporting group description:	
QGE031 240 mg subcutaneously q4w	

Reporting group values	QGE031 every 4 weeks (q4w)	Total	
Number of subjects	270	270	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	237	237	
From 65-84 years	33	33	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	48.2		
standard deviation	± 13.17	-	
Gender, Male/Female			
Units: Subjects			
Female	168	168	
Male	102	102	

End points

End points reporting groups

Reporting group title	QGE031 every 4 weeks (q4w)
Reporting group description:	
QGE031 240 mg subcutaneously q4w	

Primary: Numbers of participants with non-serious adverse events (AEs), serious AEs and deaths as a measure of safety and tolerability

End point title	Numbers of participants with non-serious adverse events (AEs), serious AEs and deaths as a measure of safety and tolerability[1]
End point description:	
Safety was monitored throughout the study.	
End point type	Primary
End point timeframe:	
52 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis does not apply to this end point.

End point values	QGE031 every 4 weeks (q4w)			
Subject group type	Reporting group			
Number of subjects analysed	270			
Units: Participants				
Non-serious AEs	176			
Serious AEs	19			
Deaths	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator. The one death reported was not related to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	QGE031 240 mg q4w

Reporting group description:

QGE031 240 mg q4w

Serious adverse events	QGE031 240 mg q4w		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 270 (7.04%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal neoplasm			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Varicose vein			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cerebrovascular accident			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Vertebral artery thrombosis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Drug hypersensitivity			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 270 (1.85%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Nasal septum deviation			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	QGE031 240 mg q4w		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 270 (48.15%)		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	45 / 270 (16.67%)		
occurrences (all)	143		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	80 / 270 (29.63%)		
occurrences (all)	140		
Infections and infestations			
Bronchitis			
subjects affected / exposed	20 / 270 (7.41%)		
occurrences (all)	26		
Nasopharyngitis			
subjects affected / exposed	33 / 270 (12.22%)		
occurrences (all)	40		
Upper respiratory tract infection			
subjects affected / exposed	17 / 270 (6.30%)		
occurrences (all)	26		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 April 2015	This amendment included one additional Adjudication Committees (AC) for the assessment of CCV events. While there was no known mechanism linking IgE suppression to CCV events, statistically non-significant imbalances of these events had been identified in selected omalizumab datasets and had been reflected in some Xolair country labeling. In order to closely monitor any potential relationship between IgE suppression and these events, and to strengthen patient safety in this trial and future trials, Novartis had decided to institute a CCV adjudication committee. The other key change in this amendment was the removal of some exploratory biomarkers from the study protocol. The high number of biomarkers sampled and the required shipping conditions had frequently been reported as very cumbersome and too complex by the sites. Novartis decided to remove some of the exploratory biomarkers from the protocol. Samples already collected were planned to be analyzed and corresponding results were planned to be included in the final Clinical Study Report (CSR).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The two anaphylaxis events reported as both related to study medication and as serious adverse events reflect two observations on the same patient and on the same day after one injection of study drug.

Notes: