Clinical trial results:
A Multi-Center, Randomized, Double-Blind, Placebo-Controlled study to investigate the efficacy and safety of 52 weeks treatment with QGE031 subcutaneous (s.c). in Asthma Patients not adequately controlled by medium- or high-dose inhaled corticosteroid (ICS) plus long acting 2-agonist (LABA) with or without oral corticosteroid (OCS)

Summary

EudraCT number	2014-003155-57
Trial protocol	GB HU IT DE BE ES SK NL LU
Global end of trial date	07 March 2016

Results information

Result version number	v1 (current)
This version publication date	09 March 2017
First version publication date	09 March 2017

Trial information

Trial identification

Sponsor protocol code	CQGE031B2204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02336425
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	07 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of QGE031 (24 mg, 72 mg, 240 mg s.c. q4w) compared to placebo on top of standard of care (SoC) in atopic patients with asthma who were
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.

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:

A short-acting β2-agonist (SABA) (salbutamol/albuterol) was provided to patients for use as a rescue medication. For the treatment of potential anaphylactic reactions, patients were supplied epinephrine autoinjector. If an epinephrine auto-injector was not available locally, the administration of epinephrine followed local standard of care.

Evidence for comparator: -

Actual start date of recruitment	18 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Slovakia: 2
Worldwide total number of subjects	10
EEA total number of subjects	7

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)	9
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized to one of the four treatment arms.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	QGE031 240 mg

Arm description:

QGE031 240 mg subcutaneous injection every 4 weeks

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 subcutaneous injection every 4 weeks

Arm title	QGE031 72 mg

Arm description:

QGE031 72 mg subcutaneous injection every 4 weeks

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 72 mg subcutaneous injection every 4 weeks

Arm title	QGE031 24 mg

Arm description:

QGE031 24 mg subcutaneous injection every 4 weeks

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 24 mg subcutaneous injection every 4 weeks

Arm title	Placebo to QGE031

Arm description:

Placebo subcutaneous injection every 4 weeks

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

Dosage and administration details:

Matching placebo to QGE031 subcutaneous injection every 4 weeks

Number of subjects in period 1	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg
Started	2	2	3
Completed	0	0	0
Not completed	2	2	3
Study terminated.	2	2	3

Number of subjects in period 1	Placebo to QGE031
Started	3
Completed	0
Not completed	3
Study terminated.	3

Baseline characteristics

Reporting groups	
Reporting group title	QGE031 240 mg
Reporting group description:	
QGE031 240 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 72 mg
Reporting group description:	
QGE031 72 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 24 mg
Reporting group description:	
QGE031 24 mg subcutaneous injection every 4 weeks	
Reporting group title	Placebo to QGE031
Reporting group description:	
Placebo subcutaneous injection every 4 weeks	

Reporting group values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg
Number of subjects	2	2	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	2	2
From 65-84 years	0	0	1
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	46.5	47	53.7
standard deviation	± 16.26	± 1.41	± 11.59
Gender, Male/Female Units: Subjects			
Female	2	0	3
Male	0	2	0

Reporting group values	Placebo to QGE031	Total	
Number of subjects	3	10	
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)	3	9	
From 65-84 years	0	1	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	47.7		
standard deviation	± 2.89	-	
Gender, Male/Female			
Units: Subjects			
Female	2	7	
Male	1	3	

End points

End points reporting groups

Reporting group title	QGE031 240 mg
Reporting group description: QGE031 240 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 72 mg
Reporting group description: QGE031 72 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 24 mg
Reporting group description: QGE031 24 mg subcutaneous injection every 4 weeks	
Reporting group title	Placebo to QGE031
Reporting group description: Placebo subcutaneous injection every 4 weeks	

Primary: QGE031 compared to placebo in atopic asthma patients on the reduction in rate of severe asthma exacerbations

End point title	QGE031 compared to placebo in atopic asthma patients on the reduction in rate of severe asthma exacerbations[1]
End point description:	
End point type	Primary
End point timeframe: Week 52	

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: Due to the small number of patients randomized, the planned statistical analysis was not performed.

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: severe asthma exacerbations				
number (not applicable)				

Notes:

[2] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[3] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[4] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[5] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in all asthma patients on the reduction in

rate of severe asthma exacerbations	
End point title	QGE031 compared to placebo in all asthma patients on the reduction in rate of severe asthma exacerbations

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[6]	0[7]	0[8]	0[9]
Units: severe asthma exacerbations				
number (not applicable)				

Notes:

[6] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[7] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[8] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[9] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in non-atopic asthma patients on the reduction in rate of severe asthma exacerbations	
End point title	QGE031 compared to placebo in non-atopic asthma patients on the reduction in rate of severe asthma exacerbations

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[10]	0[11]	0[12]	0[13]
Units: severe asthma exacerbations				
number (not applicable)				

Notes:

[10] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[11] - Due to the small number of patients randomized, the planned statistical analysis was not

performed.

[12] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[13] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on the reduction in rate of asthma exacerbations (by severity)

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on the reduction in rate of asthma exacerbations (by severity)

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[14]	0[15]	0[16]	0[17]
Units: asthma exacerbations				
number (not applicable)				

Notes:

[14] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[15] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[16] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[17] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on time to first asthma exacerbations (by severity)

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on time to first asthma exacerbations (by severity)

End point description:

End point type	Secondary

End point timeframe:

Week 52

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[18] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[19] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[20] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[21] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on change from baseline in Asthma Control Questionnaire (ACQ)

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on change from baseline in Asthma Control Questionnaire (ACQ)

End point description:

End point type	Secondary

End point timeframe:

Baseline, Treatment (Weeks 4, 8, 12, 16, 24, 36, 52), follow up (Weeks 60 and 72)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[22]	0[23]	0[24]	0[25]
Units: score on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[22] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[23] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[24] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[25] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on change from baseline in Asthma Control Diary (ACD)

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on change from baseline in Asthma Control Diary (ACD)

End point description:

End point type	Secondary

End point timeframe:

Over 52 weeks (Treatment) and 20 weeks (follow-up)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[26]	0[27]	0[28]	0[29]
Units: score on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[26] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[27] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[28] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[29] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Forced Expiratory Volume in 1 second (FEV1)

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Forced Expiratory Volume in 1 second (FEV1)

End point description:

End point type	Secondary

End point timeframe:

Baseline, Treatment (Weeks 4, 8, 12, 16, 24, 36, 52), follow up (Weeks 60 and 72)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[30]	0[31]	0[32]	0[33]
Units: liters				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[30] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[31] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[32] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[33] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Peak expiratory flow (PEF) in the morning and evening

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Peak expiratory flow (PEF) in the morning and evening

End point description:

End point type	Secondary

End point timeframe:

Over 52 weeks (Treatment) and 20 weeks (follow-up)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[34]	0[35]	0[36]	0[37]
Units: liters/minute				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[34] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[35] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[36] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[37] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Total daily symptom score

End point title	QGE031 compared to placebo in asthma patients (all and either atopic or non-atopic) on Total daily symptom score

End point description:

End point type	Secondary

End point timeframe:

Over 52 weeks (Treatment) and 20 weeks (follow-up)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[38]	0[39]	0[40]	0[41]
Units: score on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[38] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[39] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[40] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[41] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Response to QGE031 between atopic asthma and non-atopic asthma

End point title	Response to QGE031 between atopic asthma and non-atopic asthma

End point description:

End point type	Secondary

End point timeframe:

Over 52 weeks (treatment) and 20 weeks (follow up)

End point values	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg	Placebo to QGE031
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[42]	0[43]	0[44]	0[45]
Units: Participants				
number (not applicable)				

Notes:

[42] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[43] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[44] - Due to the small number of patients randomized, the planned statistical analysis was not performed.
[45] - Due to the small number of patients randomized, the planned statistical analysis was not performed.

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	QGE031 240 mg
Reporting group description:	
QGE031 240 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 72 mg
Reporting group description:	
QGE031 72 mg subcutaneous injection every 4 weeks	
Reporting group title	QGE031 24 mg
Reporting group description:	
QGE031 24 mg subcutaneous injection every 4 weeks	
Reporting group title	Placebo to QGE031
Reporting group description:	
Placebo subcutaneous injection every 4 weeks	

Serious adverse events	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo to QGE031		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	QGE031 240 mg	QGE031 72 mg	QGE031 24 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	2 / 2 (100.00%)	1 / 3 (33.33%)
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Dysphagia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Productive cough			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthma			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Biliary colic			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Infections and infestations			
Conjunctivitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory tract infection			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo to QGE031		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dysphagia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Productive cough			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Asthma			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Hepatobiliary disorders			
Biliary colic			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			

alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2015	This amendment 1 was triggered by a request from the European Health Authorities as part of the VHP (Voluntary Harmonization Procedure) process. Specifically, VHP requested the clarifications for the composition and the independency of the review committees from Novartis. Accordingly this amendment provided further clarification of the two committees that were supposed to review the data from the two pre-specified interim analyses.
17 March 2015	This amendment 2 was triggered by a request from the European Health Authorities as part of the VHP (Voluntary Harmonization Procedure) process. VHP requested to change the contraception method in the exclusion criteria based on "Recommendations related to contraception and pregnancy testing in clinical trials" issued by Clinical Trial Facilitation Group on 15-Sep-2014.
24 April 2015	This amendment 3 was triggered by feasibility challenges potentially affecting the conduct of the study. The detailed changes are outlined in the study protocol

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.

Study was terminated due to the efficacy results from the Phase II study CQGE031B2201 (NCT01716754). Data analyses were not performed due to the very limited dataset (only 10 participants received study medication of the 440 participants planned).

Notes: