Clinical trial results:
A randomized, double-blind, placebo controlled, parallel group study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of QGE031 in the treatment of patients with bullous pemphigoid with disease refractory to oral steroid treatment

Summary

EudraCT number	2012-003370-10
Trial protocol	AT DE FR
Global end of trial date	30 March 2015

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	13 April 2016

Trial information

Trial identification

Sponsor protocol code	CQGE031X2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01688882
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	30 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 March 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate the efficacy of QGE031 240mg q2w relative to placebo at 12 weeks in patients with BP by reducing disease activity as determined by Clinical Global Assessment of Change (CGA-C) responder rate.

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: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2013
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	Austria: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	20
EEA total number of subjects	11

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)	5
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part 1 was a multicenter, randomized, placebo-controlled study evaluating the efficacy, safety, PK and PD of multiple, subcutaneous doses of QGE031 in the treatment of patients with BP with disease refractory to oral steroid treatment. Patients were treated with QGE031 or placebo in a 2:1 ratio.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	QGE031

Arm description:

QGE031 240 mg Q2W s.c.

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 every 2 weeks for 12 weeks

Arm title	Placebo

Arm description:

Placebo to Match Q2W s.c.

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

Dosage and administration details:

Placebo subcutaneously every 2 weeks for 12 weeks

Number of subjects in period 1	QGE031	Placebo
Started	13	7
Safety Follow-up	11	5 [1]
Completed	10	6
Not completed	3	1
Adverse event, non-fatal	1	-
Unsatisfactory therapeutic effect	1	1
Administrative problems	1	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: [2] The one patient that discontinued was already switched to open-label QGE031 treatment.

Baseline characteristics

Reporting groups	
Reporting group title	QGE031
Reporting group description: QGE031 240 mg Q2W s.c.	
Reporting group title	Placebo
Reporting group description: Placebo to Match Q2W s.c.	

Reporting group values	QGE031	Placebo	Total
Number of subjects	13	7	20
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)	4	1	5
From 65-84 years	9	6	15
85 years and over	0	0	0
Age Continuous | Units: years			
arithmetic mean	63.7	67.9	
standard deviation	± 14.85	± 14.6	-
Gender, Male/Female Units: participants			
Male	10	3	13
Female	3	4	7

End points

End points reporting groups

Reporting group title	QGE031
Reporting group description: QGE031 240 mg Q2W s.c.	
Reporting group title	Placebo
Reporting group description: Placebo to Match Q2W s.c.	

Primary: Number of Patients that had a Clinical Global Assessment of Change (CGA-C) responder rate by Week 12

End point title	Number of Patients that had a Clinical Global Assessment of Change (CGA-C) responder rate by Week 12[1]

End point description:

Clinical Global Assessment of Change (CGA-C) responder rate was the responder rate at 12 weeks based on the CGA-C in bullous pemphigoid (BP). A patient with a CGA-C score of 3 or 4 indicating 'at least marked improvement from baseline' at 12 weeks was considered a responder. The CGA-C is an investigator assessment of change from baseline and is scored as follows: -4 = Very marked worsening (100% worsening); -3 = Marked worsening (67-99% worsening); -2 = Moderate worsening (34-66% worsening); -1 = Slight worsening (1-33% worsening); 1= Slight improvement (1-33% improvement); 2 = Moderate improvement (34-66% improvement); 3 = Marked improvement (67-99% improvement); 4 = Complete clearance (100% improvement)
No statistical analysis was planned for this primary outcome

End point type	Primary

End point timeframe:

12 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: No intergroup analysis were performed

End point values	QGE031	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: number of participants	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Response based on Clinical Global Assessment of Change CGA-C score at 6 weeks

End point title	Response based on Clinical Global Assessment of Change CGA-C score at 6 weeks

End point description:

Clinical Global Assessment of Change (CGA-C) responder rate was the responder rate at 6 weeks based on the CGA-C score in bullous pemphigoid (BP). A patient with a CGA-C score of 3 or 4 indicating marked improvement from baseline at 6 weeks was considered a responder. The CGA-C is an investigator assessment of change from baseline and is scored as follows: -4 = Very marked worsening

(100% worsening); -3 = Marked worsening (67-99% worsening); -2 = Moderate worsening (34-66% worsening); -1 = Slight worsening (1-33% worsening); 1= Slight improvement (1-33% improvement); 2 = Moderate improvement (34-66% improvement); 3 = Marked improvement (67-99% improvement); 4 = Complete clearance (100% improvement)

End point type	Secondary

End point timeframe:

6 weeks

End point values	QGE031	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: number of participants	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Investigator Global Assessment Score over 12 weeks

End point title	Number of Patients Investigator Global Assessment Score over 12 weeks

End point description:

Investigator’s Global Assessment (IGA) - (scale of 0 to 4, where 0=clear, 1=almost clear, 2=mild, 3=moderate and 4=severe)

End point type	Secondary

End point timeframe:

Baseline (week 0), week 6 and week 12

End point values	QGE031	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Number of participants				
Week 0 - IGA Score: 0	0	0		
Week 6 - IGA Score: 0	1	2		
Week 12 - IGA Score: 0	1	2		
Week 0 - IGA Score: 1	0	0		
Week 6 - IGA Score: 1	4	2		
Week 12 - IGA Score: 1	5	1		
Week 0 - IGA Score: 2	0	0		
Week 6 - IGA Score: 2	4	0		
Week 12 - IGA Score: 2	1	2		
Week 0 - IGA Score: 3	4	5		
Week 6 - IGA Score: 3	2	2		
Week 12 - IGA Score: 3	4	1		

Week 0 - IGA Score: 4	9	2		
Week 6 - IGA Score: 4	0	0		
Week 12- IGA Score: 4	0	0		

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	18.0

Reporting groups

Reporting group title	Treatment Period - QGE031 240mg q2w
Reporting group description:	
Treatment Period - QGE031 240mg q2w	
Reporting group title	Treatment Period - Placebo
Reporting group description:	
Treatment Period - Placebo	
Reporting group title	Treatment Period - Open-label QGE031
Reporting group description:	
Treatment Period - Open-label QGE031	
Reporting group title	Treatment Period - Total
Reporting group description:	
Treatment Period - Total	
Reporting group title	Follow-up Period - QGE031 240mg q2w
Reporting group description:	
Follow-up Period - QGE031 240mg q2w	
Reporting group title	Follow-up Period - Placebo
Reporting group description:	
Follow-up Period - Placebo	
Reporting group title	Follow-up Period - Open-label QGE031
Reporting group description:	
Follow-up Period - Open-label QGE031	
Reporting group title	Follow-up Period - Total
Reporting group description:	
Follow-up Period - Total	

Serious adverse events	Treatment Period - QGE031 240mg q2w	Treatment Period - Placebo	Treatment Period - Open-label QGE031
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	2 / 7 (28.57%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Meniscus injury			

subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Period - Total	Follow-up Period - QGE031 240mg q2w	Follow-up Period - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 20 (40.00%)	2 / 11 (18.18%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	3 / 20 (15.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Follow-up Period - Open-label QGE031	Follow-up Period - Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	2 / 18 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 18 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment Period - QGE031 240mg q2w	Treatment Period - Placebo	Treatment Period - Open-label QGE031
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	6 / 7 (85.71%)	2 / 4 (50.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Chest discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	5	6
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Haemoglobin urine present			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Neutrophil count increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neutrophil morphology abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Staphylococcus test positive			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			

subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sciatic nerve palsy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular dementia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Thrombocytosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Aphthous stomatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hepatobiliary disorders			

Hepatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Miliaria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pemphigoid			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Purpura senile			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Skin candida			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hyponatraemia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1

Non-serious adverse events	Treatment Period - Total	Follow-up Period - QGE031 240mg q2w	Follow-up Period - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)	10 / 11 (90.91%)	3 / 5 (60.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Chest discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	11	0	0
Malaise			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Xerosis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eosinophil count increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Haemoglobin urine present			

subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Neutrophil count increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutrophil morphology abnormal			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Staphylococcus test positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Burning sensation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Sciatic nerve palsy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular dementia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Thrombocytosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry eye			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Aphthous stomatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Miliaria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pemphigoid			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	3 / 11 (27.27%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Purpura senile			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin hyperpigmentation			

subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Urticaria			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin candida			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	3 / 20 (15.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gout			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hyponatraemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Follow-up Period - Open-label QGE031	Follow-up Period - Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	15 / 18 (83.33%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Injection site haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Injection site pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Xerosis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	2	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Investigations			

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Eosinophil count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Haemoglobin urine present			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Neutrophil count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Neutrophil morphology abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Staphylococcus test positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
White blood cells urine positive			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Ligament sprain			

subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Tooth fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Wound			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Sciatic nerve palsy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Vascular dementia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Aphthous stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Miliaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pemphigoid			
subjects affected / exposed	1 / 4 (25.00%)	3 / 18 (16.67%)	
occurrences (all)	1	3	
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	3	
Purpura senile			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Skin hyperpigmentation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Furuncle			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	1 / 4 (25.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Skin candida			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Urinary tract infection			

subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Glucose tolerance impaired			
subjects affected / exposed	1 / 4 (25.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Gout			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2013	Amendment 1: was generated in order to comply with a German health authority request relating to effective methods of contraception. Specifically,that the combined use of condoms and spermicides (foam/gel/film/cream/vaginal suppository)for contraception was not recommended in Germany. Therefore,the other described methods of contraception were to be used in Germany. The justification given was that since most of the spermicides are aliphatic, fat could make the condom leaky and potentially lead to unintentional pregnancy. The combination of these barrier methods of contraception has been accepted by other Health Authorities, and therefore changes in Section 4.2 pertain only to Germany. Other minor and administrative changes were made throughout the protocol for clarity and consistency.
03 April 2013	Amendment 2: was generated to comply with a Japanese health authority request given that this was the first multi-dosing study with QGE031 in Japan. Specifically,this related to the possibility of weekly unscheduled patient visits occurring during prednisone tapering, inclusion of blood sampling for hematology and clinical chemistry also during weeks 2 and 4, and clarification of the instructions provided to patients relating to epinephrine auto-injector use.Changes proposed within this amendment pertained to all countries.Other minor and administrative changes were made throughout the protocol for clarity and
17 May 2013	Amendment 3:was generated in response to a request from the French Health Authority(Agence nationale de sécurité du médicament et des produits de santé). Specifically,the protocol was revised to provide recommendations to Investigators regarding the treatment of adverse events. Changes contained within this amendment pertained to all countries.

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.

This study was stopped after Part 1 completed and was terminated because the predefined criteria of efficacy was not reached (>50% better then placebo)

Notes: