Clinical trial results:
A 52-week, multicenter, randomized, double-blind, double-dummy, parallel-group, placebo-controlled study of fevipiprant once daily plus standard-of-care (SoC) for reduction of systemic corticosteroids (oral and parenteral) use in patients with severe asthma

Summary

EudraCT number	2018-000212-25
Trial protocol	DE GB CZ SK ES BE FR GR BG HU
Global end of trial date	06 February 2020

Results information

Result version number	v2 (current)
This version publication date	21 May 2021
First version publication date	29 January 2021
Version creation reason	• Correction of full data set Additional text added in the field Adverse Events reporting additional description.

Trial information

Trial identification

Sponsor protocol code	CQAW039A2323

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03629249
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, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

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	06 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to determine the efficacy of fevipiprant (150 mg and 450 mg once daily), compared with placebo, as add-on to GINA (Global Initiative for Asthma) treatment step 4 or 5 standard-of-care (SoC) asthma therapy in terms of avoidance of systemic corticosteroids (SCS) use over 52 weeks in patients with inadequately controlled severe asthma and high eosinophil counts (eosinophil count at Visit 1 ≥250 cells/ µl) and in the overall patient population regardless of eosinophil counts.

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. Patients were provided SABA (primary rescue medication such as salbutamol 100 mcg or albuterol 90 mcg) as rescue medication to be used on an 'as needed basis' during the study. Nebulized formulation of salbutamol/albuterol was not permitted. Oral corticosteroids (add on rescue medication such as prednisone/prednisolone (or equivalent) tablets) were permitted, as instructed by the treating physician, as part of a written asthma plan for the treatment of acute asthma exacerbations and/or symptoms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2018
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: 153
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Peru: 17
Country: Number of subjects enrolled	Philippines: 22
Country: Number of subjects enrolled	Russian Federation: 54
Country: Number of subjects enrolled	South Africa: 15
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Turkey: 9
Country: Number of subjects enrolled	United States: 36
Country: Number of subjects enrolled	Vietnam: 14
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Czechia: 31

Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 106
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hungary: 63
Country: Number of subjects enrolled	Slovakia: 17
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 7
Worldwide total number of subjects	604
EEA total number of subjects	262

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)	498
From 65 to 84 years	106
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 122 investigative sites in 21 countries.

Pre-assignment

Screening details:

After the screening, participants went through a Run-in period of 4 or 10 weeks to evaluate maintenance of asthma control and to collect baseline safety data.

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, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	QAW039 150 mg

Arm description:

QAW039 150 mg once daily orally

Arm type	Experimental
Investigational medicinal product name	fevipiprant
Investigational medicinal product code	QAW039
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

QAW039 150 mg once daily orally

Arm title	QAW039 450 mg

Arm description:

QAW039 450 mg once daily orally

Arm type	Experimental
Investigational medicinal product name	fevipiprant
Investigational medicinal product code	QAW039
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

QAW039 450 mg once daily orally

Arm title	Placebo

Arm description:

Placebo to QAW039 once daily orally

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Placebo to QAW039 once daily orally

Number of subjects in period 1	QAW039 150 mg	QAW039 450 mg	Placebo
Started	201	201	202
Full Analysis Set (FAS)	201	200	201
Safety Set (SAF)	201	200	201
Completed	0	0	0
Not completed	201	201	202
Physician decision	1	-	-
Subject decision	1	1	3
Adverse event, non-fatal	1	1	-
Death	1	-	-
Protocol deviation	-	2	5
Study terminated by sponsor	197	197	194

Baseline characteristics

Reporting groups	
Reporting group title	QAW039 150 mg
Reporting group description: QAW039 150 mg once daily orally	
Reporting group title	QAW039 450 mg
Reporting group description: QAW039 450 mg once daily orally	
Reporting group title	Placebo
Reporting group description: Placebo to QAW039 once daily orally	

Reporting group values	QAW039 150 mg	QAW039 450 mg	Placebo
Number of subjects	201	201	202
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)	168	166	164
From 65-84 years	33	35	38
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	53.4	53.0	52.8
standard deviation	± 12.14	± 11.99	± 12.81
Sex: Female, Male Units: participants			
Female	121	136	125
Male	80	65	77
Race/Ethnicity, Customized Units: Subjects			
White	180	176	174
Black or African American	2	2	2
Asian	10	12	9
American Indian or Alaska Native	3	5	13
Missing	6	6	4

Reporting group values	Total		
Number of subjects	604		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	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)	498		
From 65-84 years	106		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	382		
Male	222		
Race/Ethnicity, Customized			
Units: Subjects			
White	530		
Black or African American	6		
Asian	31		
American Indian or Alaska Native	21		
Missing	16		

End points

End points reporting groups

Reporting group title	QAW039 150 mg
Reporting group description: QAW039 150 mg once daily orally	
Reporting group title	QAW039 450 mg
Reporting group description: QAW039 450 mg once daily orally	
Reporting group title	Placebo
Reporting group description: Placebo to QAW039 once daily orally	

Primary: Total systemic corticosteroid dose in mg prednisone/prednisolone or equivalent over 52 weeks in the overall population

End point title	Total systemic corticosteroid dose in mg prednisone/prednisolone or equivalent over 52 weeks in the overall population

End point description:

All participants were provided with prednisone/prednisolone (or equivalent) tablets that could be used according to the asthma plan along with an electronic diary (e-Diary/ePEF). Daily use of oral corticosteroids (number of tablets taken in the previous 12 hours) was recorded once in the morning and once in the evening by the subject in the eDiary/PEF device. In case of use of injectable corticosteroids during certain circumstances (eg. hospitalization) the data was collected on the eCRF (electronic case report form). The total systemic corticosteroids (SCS) dose data was aggregated into monthly data for analysis. For the patients discontinuing treatment early, the total SCS dose for 52 weeks was obtained as annualized SCS dose. For example if patient took 120 mg for 3 months then for 12 months patient will be taking 120*12/3=480mg total SCS dose. The mean values over 52 weeks in the overall patient population regardless of peripheral blood eosinophil counts are reported here.

End point type	Primary

End point timeframe:

52 weeks

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: milligrams (mg)				
arithmetic mean (full range (min-max))	219.67 (0 to 9241.27)	193.02 (0 to 5184.19)	223.22 (0 to 9552.69)	

Statistical analyses

Statistical analysis title	Total SCS dose - overall population
Comparison groups	QAW039 150 mg v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.714
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total SCS dose - overall population
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.734
Method	Wilcoxon (Mann-Whitney)

Primary: Total systemic corticosteroid dose in mg prednisone/prednisolone or equivalent over 52 weeks in the subpopulation of patients with high eosinophil count (≥ 250 cells/µl)

End point title	Total systemic corticosteroid dose in mg prednisone/prednisolone or equivalent over 52 weeks in the subpopulation of patients with high eosinophil count (≥ 250 cells/µl)

End point description:

All participants were provided with prednisone/prednisolone (or equivalent) tablets that could be used according to the asthma plan along with an electronic diary (e-Diary/ePEF). Daily use of oral corticosteroids (number of tablets taken in the previous 12 hours) was recorded once in the morning and once in the evening by the subject in the eDiary/PEF device. In case of use of injectable corticosteroids during certain circumstances (eg. hospitalization) the data was collected on the eCRF (electronic case report form). The total systemic corticosteroids (SCS) dose data was aggregated into monthly data for analysis. For the patients discontinuing treatment early, the total SCS dose for 52 weeks was obtained as annualized SCS dose. For example if patient took 120 mg for 3 months then for 12 months patient will be taking 120*12/3=480mg total SCS dose. The mean values over 52 weeks in the subpopulation of patients with high peripheral blood eosinophil count at baseline are reported here.

End point type	Primary

End point timeframe:

52 weeks

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	131	127	
Units: milligrams (mg)				
arithmetic mean (full range (min-max))	210.88 (0 to 5352.80)	185.29 (0 to 5184.19)	212.66 (0 to 9552.69)	

Statistical analyses

Statistical analysis title	Total SCS dose - high blood eosinophil count
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.665
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total SCS dose - high blood eosinophil count
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	Wilcoxon (Mann-Whitney)

Secondary: Change from baseline in daytime symptom scores

End point title	Change from baseline in daytime symptom scores

End point description:

All participants were provided with an electronic diary (eDiary/ePEF) to record asthma symptom twice per day. Daytime asthma symptoms were assessed before bed and nighttime asthma symptoms on awakening. The daytime asthma symptom score included 4 questions with a range of response categories for each question from 0 to 6 (0 = totally controlled; 6 = extremely poorly controlled). The questions were equally weighted and the overall score (from 0 to 6) was calculated as the average of the 4 questions with higher values indicating more asthma symptoms. Mean values of daytime asthma symptom scores were calculated over 4-week intervals during the treatment period. The baseline values of daytime asthma symptoms scores were defined as the average score during the run-in period. A negative change from baseline in daytime asthma symptom score is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, up to Week 29-32

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: score on scale				
arithmetic mean (standard deviation)				
Week 1-4 (n = 185, 184, 187)	-0.12 (± 0.494)	-0.12 (± 0.497)	-0.09 (± 0.459)	
Week 5-8 (n= 162, 155, 159)	-0.21 (± 0.615)	-0.25 (± 0.570)	-0.17 (± 0.561)	
Week 9-12 (n= 134, 133, 136)	-0.29 (± 0.632)	-0.36 (± 0.588)	-0.17 (± 0.605)	
Week 13-16 (n= 98, 96, 95)	-0.32 (± 0.644)	-0.37 (± 0.653)	-0.17 (± 0.629)	

Week 17-20 (n= 67, 68, 69)	-0.30 (± 0.570)	-0.35 (± 0.759)	-0.12 (± 0.622)	
Week 21-24 (n= 41, 34, 39)	-0.31 (± 0.536)	-0.49 (± 0.760)	-0.07 (± 0.688)	
Week 25-28 (n= 19, 17, 20)	-0.13 (± 0.519)	-0.65 (± 0.751)	-0.14 (± 0.726)	
Week 29-32 (n= 6, 4, 9)	-0.54 (± 0.546)	-0.83 (± 1.072)	-0.20 (± 0.887)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in nighttime symptom scores

End point title	Change from baseline in nighttime symptom scores

End point description:

All participants were provided with an electronic diary (eDiary/ePEF) to record asthma symptom twice per day. Daytime asthma symptoms were assessed before bed and nighttime asthma symptoms on awakening. The nighttime asthma symptom score included 1 question with a range of response categories from 0 to 3 (0 = no awakening with asthma symptoms; 3 = awake all night). Mean values of nighttime asthma symptom scores were calculated over 4-week intervals during the treatment period. The baseline values of nighttime asthma symptoms scores were defined as the average score during the run-in period. A negative change from baseline in nighttime asthma symptom score is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, up to Week 29-32

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: score on scale				
arithmetic mean (standard deviation)				
Week 1-4 (n= 185, 185, 188)	-0.08 (± 0.267)	-0.05 (± 0.281)	-0.07 (± 0.253)	
Week 5-8 (n= 163, 156, 159)	-0.11 (± 0.313)	-0.12 (± 0.314)	-0.13 (± 0.322)	
Week 9-12 (n= 136, 132, 135)	-0.15 (± 0.317)	-0.19 (± 0.369)	-0.12 (± 0.379)	
Week 13-16 (n= 101, 100, 96)	-0.19 (± 0.328)	-0.18 (± 0.360)	-0.12 (± 0.364)	
Week 17-20 (n= 70, 69, 69)	-0.21 (± 0.355)	-0.18 (± 0.397)	-0.17 (± 0.424)	
Week 21-24 (n= 43, 37, 41)	-0.17 (± 0.284)	-0.16 (± 0.323)	-0.14 (± 0.311)	
Week 25-28 (n= 20, 16, 20)	-0.17 (± 0.311)	-0.29 (± 0.355)	-0.15 (± 0.467)	
Week 29-32 (n= 8, 6, 9)	-0.12 (± 0.176)	-0.46 (± 0.505)	-0.24 (± 0.540)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ACQ-5 total score up to end of treatment visit

End point title	Change from baseline in ACQ-5 total score up to end of treatment visit

End point description:

The Asthma Control Questionnaire (ACQ-5) was completed by the patients at the investigator's site. Patients were asked to recall how their asthma had been during the previous week and to respond to the symptom questions on a 7-point scale (0=no impairment, 6=maximum impairment). The questions were equally weighted and the ACQ-5 score was the mean of the 5 questions and therefore between 0 (totally controlled) and 6 (severely uncontrolled). The baseline values of ACQ-5 score were defined as the ACQ-5 scores obtained on Day 1. A negative change from baseline in ACQ-5 score is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, up to Week 28

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: score on scale				
arithmetic mean (standard deviation)				
Week 6 (n= 166, 158, 160)	-0.74 (± 0.852)	-0.94 (± 0.870)	-0.85 (± 0.926)	
Week 12 (n= 120, 119, 119)	-0.97 (± 0.948)	-1.11 (± 0.904)	-1.05 (± 0.884)	
Week 20 (n= 60, 58, 53)	-1.08 (± 0.967)	-1.13 (± 1.075)	-1.22 (± 0.900)	
Week 28 (n= 19, 13, 15)	-1.14 (± 0.943)	-1.52 (± 1.079)	-1.15 (± 1.150)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in AQLQ+12 total score up to end of treatment visit

End point title	Change from baseline in AQLQ+12 total score up to end of treatment visit

End point description:

The Asthma Quality of Life Questionnaire (AQLQ+12) was completed by the patients at the investigator'

s site. The AQLQ+12 is a 32-item disease specific questionnaire designed to measure functional impairments that are most important to patients with asthma. Patients were asked to recall their experiences during the previous 2 weeks and to score each of the 32 items on a 7-point scale, where 1 indicates maximal impairment and 7 indicates no impairment. Thus, higher scores indicate better asthma-related quality of life. Each item of the AQLQ+12 was equally weighted and the overall score was the mean score of all 32 items and therefore ranged between 1 and 7. The baseline values of AQLQ+12 score were defined as the AQLQ+12 scores obtained on Day 1. A positive change from baseline in AQLQ+12 score is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, up to Week 28

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: score on scale				
arithmetic mean (standard deviation)				
Week 6 (n= 166, 159, 162)	0.43 (± 0.757)	0.43 (± 0.762)	0.40 (± 0.854)	
Week 12 (n= 120, 119, 120)	0.55 (± 0.884)	0.60 (± 0.876)	0.52 (± 0.833)	
Week 20 (n= 60, 58, 53)	0.64 (± 0.903)	0.67 (± 0.883)	0.60 (± 0.867)	
Week 28 (n= 19, 13, 15)	0.43 (± 0.662)	1.03 (± 1.178)	0.55 (± 1.053)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients requiring ≥ 7.5 mg systemic corticosteroid dose in mg prednisone/prednisolone or equivalent per day continuously for at least 30 days

End point title	Percentage of patients requiring ≥ 7.5 mg systemic corticosteroid dose in mg prednisone/prednisolone or equivalent per day continuously for at least 30 days

End point description:

All participants were provided with prednisone/prednisolone (or equivalent) tablets that could be used according to the asthma plan along with an electronic diary (e-Diary/ePEF) to record medication use. Daily use of oral corticosteroids (the number of tablets taken in the previous 12 hours) was recorded once in the morning and once in the evening by the subject using the eDiary/PEF device. In case of use of injectable corticosteroids during certain circumstances (eg. hospitalization) the data was collected on the eCRF (electronic case report form). The percentage of patients requiring ≥ 7.5 mg systemic corticosteroid dose in mg prednisone/prednisolone (or equivalent) per day continuously for at least 30 days within the on-treatment period is presented in this record.

End point type	Secondary

End point timeframe:

Up to 36 weeks

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: percentage of participants				
number (not applicable)	0.5	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with no systemic corticosteroids use

End point title	Percentage of patients with no systemic corticosteroids use

End point description:

All participants were provided with prednisone/prednisolone (or equivalent) tablets that could be used according to the asthma plan along with an electronic diary (e-Diary/ePEF) to record medication use. Daily use of oral corticosteroids (the number of tablets taken in the previous 12 hours) was recorded once in the morning and once in the evening by the subject using the eDiary/PEF device. In case of use of injectable corticosteroids during certain circumstances (eg. hospitalization) the data was collected on the eCRF (electronic case report form). The percentage of patients with no systemic corticosteroids use up to visit on Week 36 is presented in this record.

End point type	Secondary

End point timeframe:

Week 36

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: percentage of participants				
number (not applicable)	84.6	82.0	83.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with prescription of biologic therapy

End point title	Percentage of patients with prescription of biologic therapy

End point description:

As part of the flexible therapy, investigators were allowed to prescribe biologics approved for asthma from randomization visit onwards. Prescription of biologic therapy during the treatment period was recorded. The proportion of patients with prescription of biologic therapy during the on-treatment period is presented in this record.

End point type	Secondary

End point timeframe:

Up to 36 weeks

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	201	200	201	
Units: percentage of participants				
number (not applicable)	0.5	0.5	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) are presented from first dose of study treatment until last dose plus 14 days. Serious AEs are presented from first dose of study treatment until last dose plus 30 days, up to maximum duration of 40 weeks.

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.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	QAW039 150mg

Reporting group description:

QAW039 150mg

Reporting group title	QAW039 450mg

Reporting group description:

QAW039 450mg

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	QAW039 150mg	QAW039 450mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 201 (3.48%)	5 / 200 (2.50%)	4 / 201 (1.99%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Intentional product misuse			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (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
Traumatic fracture			

subjects affected / exposed	1 / 201 (0.50%)	0 / 200 (0.00%)	0 / 201 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 201 (0.50%)	0 / 200 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (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
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (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
Blood and lymphatic system disorders			
Anaemia macrocytic			
subjects affected / exposed	0 / 201 (0.00%)	0 / 200 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 200 (0.00%)	0 / 201 (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			
Asthma			
subjects affected / exposed	3 / 201 (1.49%)	0 / 200 (0.00%)	3 / 201 (1.49%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Osteoarthritis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 200 (0.00%)	0 / 201 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (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
Pneumonia			
subjects affected / exposed	0 / 201 (0.00%)	1 / 200 (0.50%)	0 / 201 (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
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 201 (0.50%)	0 / 200 (0.00%)	0 / 201 (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

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

Non-serious adverse events	QAW039 150mg	QAW039 450mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 201 (23.88%)	45 / 200 (22.50%)	44 / 201 (21.89%)
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	39 / 201 (19.40%)	41 / 200 (20.50%)	38 / 201 (18.91%)
occurrences (all)	47	60	53
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 201 (6.47%)	10 / 200 (5.00%)	13 / 201 (6.47%)
occurrences (all)	13	10	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 December 2018	The protocol was amended based on health authority feedback. The in-clinic study visit frequencies were modified to 8 weeks intervals after week 12, interspaced with telephone contacts. Additional collection of hematology, clinical chemistry and urinalysis samples were added to all in-clinic visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported