Clinical trial results:
A 12-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma

Summary

EudraCT number	2017-001272-40
Trial protocol	SE ES BG DE HU IT RO
Global end of trial date	01 August 2019

Results information

Result version number	v1 (current)
This version publication date	16 February 2020
First version publication date	16 February 2020

Trial information

Trial identification

Sponsor protocol code	CQAW039A2317

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03226392
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, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to demonstrate the efficacy of fevipiprant 150 mg once daily compared with placebo, as measured by change from baseline in pre-dose forced expiratory volume in 1 second (FEV1) at the end of the 12-week active-treatment period

Protection of trial subjects:

to demonstrate the efficacy of fevipiprant 150 mg once daily compared with placebo, as measured by change from baseline in pre-dose forced expiratory volume in 1 second (FEV1) at the end of the 12-week active-treatment period

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2017
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	Brazil: 41
Country: Number of subjects enrolled	Bulgaria: 48
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Colombia: 28
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	India: 40
Country: Number of subjects enrolled	Israel: 18
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 15
Country: Number of subjects enrolled	Peru: 91
Country: Number of subjects enrolled	Russian Federation: 109
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	United States: 186
Country: Number of subjects enrolled	Vietnam: 22
Worldwide total number of subjects	704
EEA total number of subjects	142

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)	13
Adults (18-64 years)	563
From 65 to 84 years	128
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from centers in Brazil (8), Bulgaria (4), Canada (3), Colombia (4), Germany (5), Hungary (7), India (5), Israel (5), Italy (4), Peru (6), Republic of Korea (5), Russian Federation (14), Spain (8), United States (36), Vietnam (3).

Pre-assignment

Screening details:

a Screening period of up to 2 weeks to assess eligibility during which patients practice completing the electronic peak expiratory flow eDiary/ePEF device.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	QAW039

Arm description:

QAW039 once daily

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

Dosage and administration details:

150mg tablet

Arm title	Placebo

Arm description:

Placebo once daily

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

Dosage and administration details:

tablets

Number of subjects in period 1[1]	QAW039	Placebo
Started	352	350
Completed	341	344
Not completed	11	6
Physician decision	1	-
Protocol Deviation	1	-
Adverse event, non-fatal	1	-
Subject/Guardian Decision	7	6
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 2 patients in the placebo were mis-randomized, not treated, not included due to "technical problems

Baseline characteristics

Reporting groups	
Reporting group title	QAW039
Reporting group description: QAW039 once daily	
Reporting group title	Placebo
Reporting group description: Placebo once daily	

Reporting group values	QAW039	Placebo	Total
Number of subjects	352	350	702
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)	7	6	13
Adults (18-64 years)	275	286	561
From 65-84 years	70	58	128
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	50.4	50.2	
standard deviation	± 14.87	± 14.39	-
Sex: Female, Male Units:			
Female	216	218	434
Male	136	132	268
Race/Ethnicity, Customized Units: Subjects			
Black	26	18	44
Asian	41	46	87
Native American	12	12	24
Pacific Islander	2	0	2
Other	55	58	113
Caucasian	216	216	432

End points

End points reporting groups	
Reporting group title	QAW039
Reporting group description:	
QAW039 once daily	
Reporting group title	Placebo
Reporting group description:	
Placebo once daily	

Primary: Change from baseline in pre-dose FEV1	
End point title	Change from baseline in pre-dose FEV1
End point description:	
Forced Expiratory Volume in one second (FEV1) is calculated as the volume of air forcibly exhaled in one second as measured by a spirometer. Baseline is defined as the last available FEV1 measurement taken prior to the first dose of randomized study drug	
End point type	Primary
End point timeframe:	
Week 12	

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	352	350		
Units: Liters				
least squares mean (standard error)	0.126 (± 0.00177)	0.157 (± 0.0177)		

Statistical analyses

Statistical analysis title	change from baseline in pre-dose FEV1
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.214
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.031
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.018

Secondary: Change from baseline in daytime asthma symptom score

End point title	Change from baseline in daytime asthma symptom score

End point description:

Daytime asthma symptoms are evaluated through four questions and each of them will be rated on a scale of 0 to 6. Higher scores indicate more severe asthma-related symptoms. A mean score is calculated for the responses to 4 questions

End point type	Secondary

End point timeframe:

12 weeks

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	352	350		
Units: Score				
least squares mean (standard error)	-0.55 (± 0.034)	-0.45 (± 0.034)		

Statistical analyses

Statistical analysis title	change in mean daytime asthma symptom
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.035
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	Other: 0.04 %
sides	2-sided
lower limit	-0.19
upper limit	0.01

Secondary: Change from baseline in number of puffs of SABA taken per day

End point title	Change from baseline in number of puffs of SABA taken per day

End point description:

Daily use of SABA (the number of rescue medication puffs taken in the previous 12 hours) was recorded using a patient electronic diary (referred to as eDiary or eDiary/ePEF). Patients were instructed to routinely complete the patient diary twice daily – at the same time each morning and each evening, approximately 12 hours apart.

End point type	Secondary
End point timeframe:	
12 weeks	

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	352	350		
Units: Number of puffs				
least squares mean (standard error)	-0.89 (± 0.066)	-0.88 (± 0.066)		

Statistical analyses

Statistical analysis title	change in mean total daily use of SABA
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.893
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17

Secondary: Change from baseline in Asthma Quality of Life Questionnaire for 12 years and older (AQLQ+12) score

End point title	Change from baseline in Asthma Quality of Life Questionnaire for 12 years and older (AQLQ+12) score

End point description:

AQLQ is a 32-item instrument administered as a self-assessment. AQLQ+12 is a modified version of AQLQ developed to measure functional impairments of participants aged 12-70 years. It is divided into 4 domains: activity limitation, symptoms, emotional function, and environmental stimuli. Participants were asked to recall their experiences during the last 2 weeks and respond to each question on a 7-point scale (1=severe impairment, 7=no impairment), where higher scores indicated "better quality of life." Overall AQLQ+12 score is the mean of all 32 responses

End point type	Secondary
End point timeframe:	
Week 12	

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	352	350		
Units: units on a scale				
least squares mean (standard error)	0.77 (± 0.043)	0.72 (± 0.043)		

Statistical analyses

Statistical analysis title	change from baseline in AQLQ+12
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.448
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.17

Adverse events

Adverse events information	
Timeframe for reporting adverse events: After signing informed consent to 30 days after last dose	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	QAW039 150 mg
Reporting group description: QAW039 150 mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	QAW039 150 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 352 (1.99%)	3 / 350 (0.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 352 (0.00%)	1 / 350 (0.29%)	
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 / 352 (0.00%)	1 / 350 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 352 (0.00%)	1 / 350 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 352 (0.85%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 352 (0.28%)	0 / 350 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	QAW039 150 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 352 (26.70%)	116 / 350 (33.14%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 352 (0.00%)	5 / 350 (1.43%)	
occurrences (all)	0	6	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 352 (1.42%)	14 / 350 (4.00%)	
occurrences (all)	5	15	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	46 / 352 (13.07%)	61 / 350 (17.43%)	
occurrences (all)	56	79	
Cough			
subjects affected / exposed	2 / 352 (0.57%)	5 / 350 (1.43%)	
occurrences (all)	2	7	
Dyspnoea			
subjects affected / exposed	3 / 352 (0.85%)	5 / 350 (1.43%)	
occurrences (all)	5	7	
Oropharyngeal pain			
subjects affected / exposed	6 / 352 (1.70%)	4 / 350 (1.14%)	
occurrences (all)	6	4	
Rhinitis allergic			
subjects affected / exposed	3 / 352 (0.85%)	5 / 350 (1.43%)	
occurrences (all)	3	5	
Wheezing			
subjects affected / exposed	1 / 352 (0.28%)	4 / 350 (1.14%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	7 / 352 (1.99%)	7 / 350 (2.00%)	
occurrences (all)	7	8	
Infections and infestations			
Bronchitis			
subjects affected / exposed	9 / 352 (2.56%)	6 / 350 (1.71%)	
occurrences (all)	9	6	
Influenza			
subjects affected / exposed	4 / 352 (1.14%)	1 / 350 (0.29%)	
occurrences (all)	4	1	
Nasopharyngitis			
subjects affected / exposed	10 / 352 (2.84%)	24 / 350 (6.86%)	
occurrences (all)	10	27	
Pharyngitis			
subjects affected / exposed	5 / 352 (1.42%)	2 / 350 (0.57%)	
occurrences (all)	5	2	
Respiratory tract infection viral			
subjects affected / exposed	5 / 352 (1.42%)	1 / 350 (0.29%)	
occurrences (all)	5	1	
Upper respiratory tract infection			
subjects affected / exposed	7 / 352 (1.99%)	10 / 350 (2.86%)	
occurrences (all)	7	10	
Upper respiratory tract infection bacterial			
subjects affected / exposed	3 / 352 (0.85%)	6 / 350 (1.71%)	
occurrences (all)	3	6	
Viral upper respiratory tract infection			
subjects affected / exposed	12 / 352 (3.41%)	8 / 350 (2.29%)	
occurrences (all)	13	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported