

**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	2017-001273-16
Trial protocol	DE HU SK
Global end of trial date	30 July 2019

Results information

Result version number	v1 (current)
This version publication date	15 February 2020
First version publication date	15 February 2020

Trial information**Trial identification**

Sponsor protocol code	CQAW039A2316
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03215758
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	30 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2019
Global end of trial reached?	Yes
Global end of trial date	30 July 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 as measured by change from baseline in pre-dose FEV₁, compared with placebo, at the end of the 12-week active-treatment period

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	01 November 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	Argentina: 195
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	Hungary: 38
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Philippines: 57
Country: Number of subjects enrolled	Slovakia: 67
Country: Number of subjects enrolled	South Africa: 26
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	United States: 220
Worldwide total number of subjects	675
EEA total number of subjects	156

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)	30
Adults (18-64 years)	553
From 65 to 84 years	91
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from centers in Argentina (20), Germany (12), Hungary (4), Mexico (2), Philippines (4), Slovakia (7), South Africa (5), Turkey (5), United States (29)

Pre-assignment

Screening details:

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	Fevipirant
Investigational medicinal product code	QAW039
Other name	QAW039
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150mg tablets

Arm title	Placebo
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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:

matching placebo

Number of subjects in period 1	QAW039	Placebo
Started	339	336
Completed	334	328
Not completed	5	8
Adverse event, serious fatal	-	1
Physician decision	-	1
Adverse event, non-fatal	1	2
Technical Problems	1	-
Protocol deviation	-	1
Subject/Guardian Decision	3	3

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	339	336	675
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)	15	15	30
Adults (18-64 years)	278	275	553
From 65-84 years	45	46	91
85 years and over	1	0	1
Age Continuous			
Units: Years			
arithmetic mean	48.1	47.7	-
standard deviation	± 15.15	± 15.40	-
Sex: Female, Male			
Units:			
Female	217	216	433
Male	122	120	242
Race/Ethnicity, Customized			
Units: Subjects			
Caucasian	274	281	555
Black	18	12	30
Asian	39	34	73
Native American	1	0	1
Pacific Islander	2	0	2
Unknown	0	3	3
Other	5	6	11

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 at week 12

End point title	Change from baseline in pre-dose FEV1 at week 12
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	339	336		
Units: Liters				
least squares mean (standard error)	0.112 (\pm 0.0167)	0.071 (\pm 0.0169)		

Statistical analyses

Statistical analysis title	change from baseline in pre-dose FEV1
Comparison groups	Placebo v QAW039
Number of subjects included in analysis	675
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.088
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.0238
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.006
upper limit	0.088

Secondary: Change from baseline in daytime asthma symptom score

End point title	Change from baseline in daytime asthma symptom score
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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
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End point timeframe:

12 weeks

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	339	336		
Units: Score				
least squares mean (standard error)	-0.56 (\pm 0.036)	-0.51 (\pm 0.037)		

Statistical analyses

Statistical analysis title	Change from baseline in daytime asthma symptoms
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	675
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.278
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.05

Secondary: Change from baseline in daily use of SABA

End point title	Change from baseline in daily use of SABA
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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
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End point timeframe:

12 weeks

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	339	336		
Units: Number of puffs				
least squares mean (standard error)	-1.11 (\pm 0.075)	-1.02 (\pm 0.076)		

Statistical analyses

Statistical analysis title	change from baseline in use of SABA
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	675
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.429
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.13

Secondary: Change from baseline in Asthma Quality of Life (AQLQ+12) score

End point title	Change from baseline in Asthma Quality of Life (AQLQ+12) score
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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
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End point timeframe:

Week 12

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	339	336		
Units: units on a scale				
least squares mean (standard error)	0.91 (\pm 0.048)	0.89 (\pm 0.049)		

Statistical analyses

Statistical analysis title	change from baseline in AQLQ+12
Comparison groups	QAW039 v Placebo
Number of subjects included in analysis	675
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.777
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.069
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.15

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After signing informed consent to 30 days after last dose

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	QAW039 150 mg
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Reporting group description:

QAW039 150 mg

Reporting group title	Placebo
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Reporting group description:

Placebo

Serious adverse events	QAW039 150 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 339 (0.29%)	5 / 336 (1.49%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 339 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Astrocytoma			
subjects affected / exposed	0 / 339 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 339 (0.29%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	0 / 339 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 339 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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 / 339 (27.73%)	102 / 336 (30.36%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 339 (0.59%)	5 / 336 (1.49%)	
occurrences (all)	2	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 339 (0.29%)	5 / 336 (1.49%)	
occurrences (all)	1	5	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 339 (1.77%)	7 / 336 (2.08%)	
occurrences (all)	6	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 339 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	2	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 339 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	2	4	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	43 / 339 (12.68%)	45 / 336 (13.39%)	
occurrences (all)	50	57	
Cough			
subjects affected / exposed	2 / 339 (0.59%)	5 / 336 (1.49%)	
occurrences (all)	2	5	
Nasal congestion			
subjects affected / exposed	0 / 339 (0.00%)	4 / 336 (1.19%)	
occurrences (all)	0	4	
Rhinitis allergic			
subjects affected / exposed	12 / 339 (3.54%)	6 / 336 (1.79%)	
occurrences (all)	12	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 339 (0.29%)	4 / 336 (1.19%)	
occurrences (all)	1	4	
Back pain			
subjects affected / exposed	4 / 339 (1.18%)	4 / 336 (1.19%)	
occurrences (all)	4	4	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	4 / 339 (1.18%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Bronchitis			
subjects affected / exposed	12 / 339 (3.54%)	10 / 336 (2.98%)	
occurrences (all)	12	10	
Nasopharyngitis			
subjects affected / exposed	13 / 339 (3.83%)	12 / 336 (3.57%)	
occurrences (all)	14	12	
Rhinitis			
subjects affected / exposed	1 / 339 (0.29%)	5 / 336 (1.49%)	
occurrences (all)	1	5	
Upper respiratory tract infection			
subjects affected / exposed	6 / 339 (1.77%)	10 / 336 (2.98%)	
occurrences (all)	6	11	
Upper respiratory tract infection bacterial			

subjects affected / exposed	5 / 339 (1.47%)	5 / 336 (1.49%)	
occurrences (all)	5	5	
Viral upper respiratory tract infection			
subjects affected / exposed	7 / 339 (2.06%)	6 / 336 (1.79%)	
occurrences (all)	9	8	

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