



Clinical trial results:

A 52-week, multicenter, randomized, double-blind, placebocontrolled study to assess the efficacy and safety of QAW039 when added to existing asthma therapy in patients with uncontrolled severe asthma

Summary

EudraCT number	2015-002553-35
Trial protocol	GB AT DE EE LV BE IS FI DK FR PL LT IE ES GR
Global end of trial date	04 November 2019

Results information

Result version number	v2 (current)
This version publication date	20 June 2021
First version publication date	20 May 2020
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Correction on Adverse event reporting additional description section

Trial information

Trial identification

Sponsor protocol code	CQAW039A2307
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02555683
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 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	04 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:

In patients with severe asthma and high eosinophil counts (≥ 250 cells/ μ L) receiving standard-of-care asthma therapy:

- To demonstrate the efficacy (as measured by rate of moderate-to-severe asthma exacerbations) of at least one dose level of QAW039 (150 mg or 450 mg once daily), compared with placebo, at the end of the 52-week active-treatment period.

In all patients with severe asthma receiving standard-of-care asthma therapy:

- To demonstrate the efficacy (as measured by rate of moderate-to-severe asthma exacerbations) of at least one dose level of QAW039 (150 mg or 450 mg once daily), compared with placebo, at the end of the 52-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:

All patients were provided with SABAs (Short-acting β_2 -agonist) (salbutamol/albuterol/other SABA) which they were instructed to use throughout the study as rescue medication on an 'as needed basis'.

Evidence for comparator: -

Actual start date of recruitment	11 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Austria: 19
Country: Number of subjects enrolled	Brazil: 44
Country: Number of subjects enrolled	China: 60
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Estonia: 12
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 50
Country: Number of subjects enrolled	Germany: 87

Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Guatemala: 80
Country: Number of subjects enrolled	Hungary: 64
Country: Number of subjects enrolled	Latvia: 18
Country: Number of subjects enrolled	Lithuania: 18
Country: Number of subjects enrolled	Philippines: 34
Country: Number of subjects enrolled	Poland: 51
Country: Number of subjects enrolled	Romania: 154
Country: Number of subjects enrolled	Singapore: 5
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	United States: 85
Country: Number of subjects enrolled	Vietnam: 20
Worldwide total number of subjects	894
EEA total number of subjects	539

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)	29
Adults (18-64 years)	705
From 65 to 84 years	159
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were from Argentina, Australia, Austria, Belgium, Brazil, China, Denmark, Estonia, Finland, France, Germany, Greece, Guatemala, Hungary, Latvia, Lithuania, Philippines, Poland, Romania, Singapore, Spain, Switzerland, UK, US, Vietnam.

Pre-assignment

Screening details:

The study included a Screening period of up to 2 weeks and a Placebo Run-in period of 2 to 6 weeks, during which eligibility for randomization was determined.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	QAW039 150 mg

Arm description:

QAW039 150 mg once daily

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

Dosage and administration details:

QAW039 150 mg once daily (one tablet of blinded QAW039 at 150 mg dosage strength given together with one tablet blinded placebo to QAW039 450 mg)

Arm title	QAW039 450 mg
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Arm description:

QAW039 450 mg once daily

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

Dosage and administration details:

QAW039 450 mg once daily (one tablet of blinded QAW039 at 450 mg dosage strength given together with one tablet blinded placebo to QAW039 150 mg)

Arm title	Placebo
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Arm description:

Placebo once daily

Arm type	Placebo
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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 (one tablet blinded placebo to QAW039 150 mg and one tablet blinded placebo to QAW039 450 mg)

Number of subjects in period 1	QAW039 150 mg	QAW039 450 mg	Placebo
Started	301	295	298
FAS/SAF: High eosinophil subpopulation	200 ^[1]	201 ^[2]	201 ^[3]
FAS/SAF: Overall population	299	293	298
Completed	282	278	269
Not completed	19	17	29
Adverse event, serious fatal	-	1	2
Physician decision	1	-	2
Adverse event, non-fatal	1	-	1
Technical Problems	1	1	-
Protocol deviation	-	1	-
Death post Treatment/safety period	-	1	-
Lost to follow-up	2	1	2
Subject/guardian decision	12	12	22
Lack of efficacy	2	-	-

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: The numbers described disposition data for subpopulation

[2] - 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: The numbers described disposition data for subpopulation

[3] - 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: The numbers described disposition data for subpopulation

Baseline characteristics

Reporting groups

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

Reporting group values	QAW039 150 mg	QAW039 450 mg	Placebo
Number of subjects	301	295	298
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)	14	7	8
Adults (18-64 years)	239	230	236
From 65-84 years	48	57	54
85 years and over	0	1	0
Age Continuous Units: years			
arithmetic mean	49.9	51.1	50.3
standard deviation	± 14.97	± 14.29	± 14.48
Sex: Female, Male Units: Participants			
Female	192	214	177
Male	109	81	121
Race/Ethnicity, Customized Units: Subjects			
Caucasian	214	215	213
Black	11	6	12
Asian	45	38	44
Native American	24	29	24
Unknown	1	2	3
Other	6	5	2

Reporting group values	Total		
Number of subjects	894		

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)	29		
Adults (18-64 years)	705		
From 65-84 years	159		
85 years and over	1		
Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: Participants			
Female	583		
Male	311		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	642		
Black	29		
Asian	127		
Native American	77		
Unknown	6		
Other	13		

End points

End points reporting groups

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

Primary: Rate of Moderate-to-severe Asthma Exacerbations During the 52-week Treatment Period in High Eosinophils Subpopulation

End point title	Rate of Moderate-to-severe Asthma Exacerbations During the 52-week Treatment Period in High Eosinophils Subpopulation
End point description:	<p>A severe asthma exacerbation is defined as treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days and hospitalization; or treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days and emergency department visit (greater than 24 hours*); or death due to asthma.</p> <p>A moderate asthma exacerbation is defined as treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days either as an outpatient or in emergency department visits (Emergency department visit less than or equal to 24 hours).</p> <p>The high eosinophils subpopulation consists of all patients with blood eosinophil count ≥ 250 cells/μL at baseline.</p>
End point type	Primary
End point timeframe:	Baseline, Week 52

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200 ^[1]	201 ^[2]	201 ^[3]	
Units: events/year				
least squares mean (confidence interval 95%)	0.97 (0.78 to 1.20)	0.77 (0.62 to 0.97)	0.93 (0.75 to 1.16)	

Notes:

[1] - High eosinophil subpopulation

[2] - High eosinophil subpopulation

[3] - High eosinophil subpopulation

Statistical analyses

Statistical analysis title	Regression
Comparison groups	QAW039 150 mg v Placebo

Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8 ^[4]
Method	negative binomial regression model
Parameter estimate	rate ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.41

Notes:

[4] - adjusted p-value

Statistical analysis title	Regression
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51 ^[5]
Method	negative binomial regression model
Parameter estimate	Rate Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.14

Notes:

[5] - adjusted p-value

Primary: Rate of Moderate-to-severe Asthma Exacerbations During the 52-week Treatment Period in Overall population

End point title	Rate of Moderate-to-severe Asthma Exacerbations During the 52-week Treatment Period in Overall population
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End point description:

A severe asthma exacerbation is defined as treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days and hospitalization; or treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days and emergency department visit (greater than 24 hours*); or death due to asthma.

A moderate asthma exacerbation is defined as treatment with 'rescue' systemic corticosteroids for greater than or equal to 3 days either as an outpatient or in emergency department visits (Emergency department visit less than or equal to 24 hours).

End point type	Primary
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End point timeframe:

Baseline, Week 52

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	299	293	298	
Units: events/year				
least squares mean (confidence interval 95%)	0.92 (0.77 to 1.09)	0.75 (0.62 to 0.90)	0.96 (0.80 to 1.15)	

Statistical analyses

Statistical analysis title	Regression
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[6]
Method	negative binomial regression model
Parameter estimate	rate ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.22

Notes:

[6] - adjusted p-value

Statistical analysis title	Regression
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51 ^[7]
Method	negative binomial regression model
Parameter estimate	Rate Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.01

Notes:

[7] - adjusted p-value

Secondary: Change from baseline to week 52 in Asthma Quality of Life Questionnaire for Participants 12 years and older (AQLQ+12) score in high eosinophils subpopulation

End point title	Change from baseline to week 52 in Asthma Quality of Life Questionnaire for Participants 12 years and older (AQLQ+12) score in high eosinophils subpopulation
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End point description:

The AQLQ+12 is comprised of a total of 32 individual questions that span a total of four domains: symptoms, activity limitation, emotional function, and environmental stimuli. Patients were asked to recall their experiences during the previous 2 weeks and to score each item on a 7-point scale (7 = not at all impaired to 1 = severely impaired). The AQLQ+12 yields individual domain scores, which is the mean of all items in each domain, and an overall score, which is the mean of all 32 individual responses. Higher scores indicate less impairment in health-related quality of life.

The

high eosinophils subpopulation consists of all patients with blood eosinophil count ≥ 250 cells/ μ L at baseline.

End point type	Secondary
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	200 ^[8]	201 ^[9]	201 ^[10]	
Units: units on scale				
least squares mean (standard error)	0.75 (\pm 0.067)	0.81 (\pm 0.067)	0.68 (\pm 0.067)	

Notes:

[8] - High eosinophil subpopulation

[9] - High eosinophil subpopulation

[10] - High eosinophil subpopulation

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[11]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.095

Notes:

[11] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.591 ^[12]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.095

Notes:

[12] - adjusted p-value

Secondary: Change from Baseline to Week 52 in Asthma Control Questionnaire-5(ACQ-5) score in high eosinophils subpopulation

End point title	Change from Baseline to Week 52 in Asthma Control Questionnaire-5(ACQ-5) score in high eosinophils subpopulation
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End point description:

The ACQ-5 is a five-item, self-completed questionnaire, which is used as a measure of asthma control of a participant. 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 are equally weighted and the ACQ-5 score is the mean of the 5 questions: therefore, between 0 (totally controlled) and 6 (severely uncontrolled). The high eosinophils subpopulation consists of all patients with blood eosinophil count ≥ 250 cells/ μ L at baseline.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200 ^[13]	201 ^[14]	201 ^[15]	
Units: units on scale				
least squares mean (standard error)	-0.88 (\pm 0.069)	-0.94 (\pm 0.069)	-0.76 (\pm 0.070)	

Notes:

[13] - High eosinophil subpopulation

[14] - High eosinophil subpopulation

[15] - High eosinophil subpopulation

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo

Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[16]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.098

Notes:

[16] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.591 ^[17]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.098

Notes:

[17] - adjusted p-value

Secondary: Change from Baseline to Week 52 in Pre-dose Forced Expiratory Volume in 1 second (FEV1) in high eosinophils subpopulation

End point title	Change from Baseline to Week 52 in Pre-dose Forced Expiratory Volume in 1 second (FEV1) in high eosinophils subpopulation
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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. The high eosinophils subpopulation consists of all patients with blood eosinophil count ≥ 250 cells/ μ L at baseline.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200 ^[18]	201 ^[19]	201 ^[20]	
Units: Liter				
least squares mean (standard error)	0.169 (± 0.0257)	0.153 (± 0.0255)	0.103 (± 0.0260)	

Notes:

[18] - High eosinophil subpopulation

[19] - High eosinophil subpopulation

[20] - High eosinophil subpopulation

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8 ^[21]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.067
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.005
upper limit	0.139
Variability estimate	Standard error of the mean
Dispersion value	0.0365

Notes:

[21] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.523 ^[22]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.021
upper limit	0.121

Variability estimate	Standard error of the mean
Dispersion value	0.0363

Notes:

[22] - adjusted p-value

Secondary: Change from baseline to week 52 in Asthma Quality of Life Questionnaire for Participants 12 years and older (AQLQ+12) score in overall population

End point title	Change from baseline to week 52 in Asthma Quality of Life Questionnaire for Participants 12 years and older (AQLQ+12) score in overall population
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End point description:

The AQLQ+12 is comprised of a total of 32 individual questions that span a total of four domains: symptoms, activity limitation, emotional function, and environmental stimuli. Patients were asked to recall their experiences during the previous 2 weeks and to score each item on a 7-point scale (7 = not at all impaired to 1 = severely impaired). The AQLQ+12 yields individual domain scores, which is the mean of all items in each domain, and an overall score, which is the mean of all 32 individual responses. Higher scores indicate less impairment in health-related quality of life.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	299	293	298	
Units: units on scale				
least squares mean (standard error)	0.68 (± 0.053)	0.73 (± 0.054)	0.61 (± 0.054)	

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[23]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.076

Notes:

[23] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.591 ^[24]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.076

Notes:

[24] - adjusted p-value

Secondary: Change from Baseline to Week 52 in Asthma Control Questionnaire-5(ACQ-5) score in overall population

End point title	Change from Baseline to Week 52 in Asthma Control Questionnaire-5(ACQ-5) score in overall population
End point description:	
The ACQ-5 is a five-item, self-completed questionnaire, which is used as a measure of asthma control of a participant. 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 are equally weighted and the ACQ-5 score is the mean of the 5 questions: therefore, between 0 (totally controlled) and 6 (severely uncontrolled).	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	299	293	298	
Units: units on scale				
least squares mean (standard error)	-0.83 (± 0.055)	-0.90 (± 0.056)	-0.71 (± 0.056)	

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[25]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.079

Notes:

[25] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.591 ^[26]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.079

Notes:

[26] - adjusted p-value

Secondary: Change from Baseline to Week 52 in Pre-dose Forced Expiratory Volume in 1 second (FEV1) in overall population

End point title	Change from Baseline to Week 52 in Pre-dose Forced Expiratory Volume in 1 second (FEV1) in overall population
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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	Secondary
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End point timeframe:

Baseline, Week 52

End point values	QAW039 150 mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	299	293	298	
Units: Liter				
least squares mean (standard error)	0.144 (\pm 0.0205)	0.108 (\pm 0.0206)	0.068 (\pm 0.0209)	

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	QAW039 150 mg v Placebo
Number of subjects included in analysis	597
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819 ^[27]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.019
upper limit	0.134
Variability estimate	Standard error of the mean
Dispersion value	0.0292

Notes:

[27] - adjusted p-value

Statistical analysis title	ANCOVA
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.591 ^[28]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	0.097
Variability estimate	Standard error of the mean
Dispersion value	0.0292

Notes:

[28] - adjusted p-value

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs are presented from the first dose of study treatment until last dose plus 7 days. SAEs (including All-Cause Mortality) are presented from first dose of study treatment until last dose plus 30 days, up to a maximum duration of 56 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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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	QAW039 450 mg
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Reporting group description:

QAW039 450 mg

Reporting group title	Placebo
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Reporting group description:

Placebo

Serious adverse events	QAW039 150 mg	QAW039 450 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 299 (11.04%)	30 / 293 (10.24%)	32 / 298 (10.74%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Epithelioid mesothelioma			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leiomyosarcoma			

subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Non-small cell lung cancer			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Testicular neoplasm			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Pyrexia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adnexa uteri cyst			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Ovarian cyst			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	10 / 299 (3.34%)	8 / 293 (2.73%)	14 / 298 (4.70%)
occurrences causally related to treatment / all	0 / 13	0 / 11	0 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			

subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Nasal polyps			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Pulmonary embolism			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Pulmonary oedema			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Depression			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Injury, poisoning and procedural			

complications			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Ankle fracture			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Femur fracture			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Incisional hernia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Radius fracture			
subjects affected / exposed	2 / 299 (0.67%)	0 / 293 (0.00%)	0 / 298 (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
Tendon rupture			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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 haematoma			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Ulna fracture			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Wrist fracture			

subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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 disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Atrial tachycardia			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Pericardial effusion			

subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Ventricular hypokinesia			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Essential tremor			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 299 (0.33%)	1 / 293 (0.34%)	0 / 298 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Migraine			

subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Superior sagittal sinus thrombosis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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			
Lymphadenopathy			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Gastrointestinal disorders			
Diaphragmatic hernia			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Faecaloma			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Hiatus hernia			

subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Intestinal obstruction			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Megacolon			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal food impaction			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Pancreatitis acute			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Umbilical hernia			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			

subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 299 (0.33%)	2 / 293 (0.68%)	0 / 298 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Glomerulonephritis chronic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Nephrolithiasis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tenosynovitis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic spinal stenosis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Chronic hepatitis C			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Cystitis			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Diverticulitis			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			

subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Influenza			
subjects affected / exposed	1 / 299 (0.33%)	2 / 293 (0.68%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 299 (1.00%)	5 / 293 (1.71%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 4	1 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia chlamydial			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Tracheobronchitis			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 299 (0.00%)	0 / 293 (0.00%)	1 / 298 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 299 (0.67%)	0 / 293 (0.00%)	0 / 298 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 293 (0.34%)	0 / 298 (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
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 299 (0.33%)	0 / 293 (0.00%)	0 / 298 (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: 4 %

Non-serious adverse events	QAW039 150 mg	QAW039 450 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	204 / 299 (68.23%)	193 / 293 (65.87%)	214 / 298 (71.81%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	13 / 299 (4.35%)	11 / 293 (3.75%)	9 / 298 (3.02%)
occurrences (all)	15	15	11
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 299 (9.36%)	22 / 293 (7.51%)	24 / 298 (8.05%)
occurrences (all)	53	28	40
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	151 / 299 (50.50%)	135 / 293 (46.08%)	155 / 298 (52.01%)
occurrences (all)	345	299	341
Cough			
subjects affected / exposed	11 / 299 (3.68%)	5 / 293 (1.71%)	13 / 298 (4.36%)
occurrences (all)	16	7	20
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed occurrences (all)	16 / 299 (5.35%) 19	16 / 293 (5.46%) 16	11 / 298 (3.69%) 13
Infections and infestations			
Bronchitis			
subjects affected / exposed	29 / 299 (9.70%)	22 / 293 (7.51%)	26 / 298 (8.72%)
occurrences (all)	42	37	35
Lower respiratory tract infection			
subjects affected / exposed	12 / 299 (4.01%)	10 / 293 (3.41%)	7 / 298 (2.35%)
occurrences (all)	17	13	8
Nasopharyngitis			
subjects affected / exposed	43 / 299 (14.38%)	37 / 293 (12.63%)	49 / 298 (16.44%)
occurrences (all)	63	50	74
Rhinitis			
subjects affected / exposed	8 / 299 (2.68%)	11 / 293 (3.75%)	12 / 298 (4.03%)
occurrences (all)	9	11	13
Sinusitis			
subjects affected / exposed	18 / 299 (6.02%)	19 / 293 (6.48%)	18 / 298 (6.04%)
occurrences (all)	25	22	31
Upper respiratory tract infection			
subjects affected / exposed	35 / 299 (11.71%)	35 / 293 (11.95%)	31 / 298 (10.40%)
occurrences (all)	49	48	47
Upper respiratory tract infection bacterial			
subjects affected / exposed	13 / 299 (4.35%)	14 / 293 (4.78%)	21 / 298 (7.05%)
occurrences (all)	16	16	23
Urinary tract infection			
subjects affected / exposed	11 / 299 (3.68%)	15 / 293 (5.12%)	18 / 298 (6.04%)
occurrences (all)	14	16	19
Viral upper respiratory tract infection			
subjects affected / exposed	29 / 299 (9.70%)	26 / 293 (8.87%)	26 / 298 (8.72%)
occurrences (all)	40	34	34

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2015	A literature review has identified additional statins that could interact with QAW039, and patients taking these statins were to be excluded from the study: Text was added to indicate that patients on doses of simvastatin >20 mg, doses of atorvastatin >40 mg, doses of pravastatin >40 mg, or doses of pitavastatin >2 mg per day should not be included in the study. Statin doses less than or equal to these doses as well as other statins were permitted during the study.
19 May 2016	<p>Protocol changes were implemented as requested from health authorities and/or ethics committees/institutional review boards in some countries where the study was planned to be conducted. These changes included:</p> <ul style="list-style-type: none">• Changed inclusion criterion #2 to allow for the lower age limit in the study to patients aged ≥ 12 years (or \geq lower age limit allowed by health authority and/or ethics committee/institutional review board approvals).• Added an exclusion criterion for patients below the 3rd percentile for weight by age for adolescent patients aged 12 to <18 years to ensure malnourished adolescents were excluded.• Added an exclusion criterion for lactose and milk sensitivity since the placebo tablets include lactose.• Added an exclusion criterion for patients with a history of conditions other than asthma that could result in elevated eosinophils (e.g., hypereosinophilic syndromes, Churg-Strauss Syndrome, eosinophilic esophagitis) and exclude patients with known parasitic infestation within 6 months prior to Visit 1.• Added country-required local contraception language for certain countries.
10 February 2017	<p>Protocol was amended to include updated renal guidelines and liver event and laboratory trigger definitions of Novartis. These changes included:</p> <ul style="list-style-type: none">• Updated definitions of urine events.• Updated follow-up requirements for liver events and laboratory triggers for ALT and AST (> 3 to $\leq 5 \times$ ULN [patient is asymptomatic]).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported