Clinical trial results:
A 2-treatment period, randomized, placebo-controlled, multicenter parallel-group study to assess the safety of QAW039 when added to existing asthma therapy in GINA steps 3, 4 and 5 patients with uncontrolled asthma

Summary

EudraCT number	2016-001560-11
Trial protocol	SK DE LV EE HU BE GR AT FR CZ LT ES NL GB PL FI BG RO
Global end of trial date	16 March 2020

Results information

Result version number	v2 (current)
This version publication date	20 June 2021
First version publication date	30 September 2020
Version creation reason	• Correction of full data set Correction to Adverse event reporting additional description section

Trial information

Trial identification

Sponsor protocol code	CQAW039A2315

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03052517
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives for Treatment Period 1 (double-blind, 52-week treatment period) and Treatment Period 1 and Period 2 combined is:
In patients with moderate-to-severe asthma receiving SoC asthma therapy, to evaluate the long-term safety of QAW039 (150 mg once daily and 450 mg once daily), compared with placebo, as assessed by:
treatment emergent adverse events (AEs);
treatment emergent serious adverse events (SAEs); and
study treatment discontinuations due to treatment emergent AEs.

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	21 March 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	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 33
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Peru: 69
Country: Number of subjects enrolled	Philippines: 76
Country: Number of subjects enrolled	Poland: 64
Country: Number of subjects enrolled	Romania: 100
Country: Number of subjects enrolled	Russian Federation: 204
Country: Number of subjects enrolled	Saudi Arabia: 2
Country: Number of subjects enrolled	Serbia: 56
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Slovakia: 116
Country: Number of subjects enrolled	Spain: 63
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Argentina: 308

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Austria: 22
Country: Number of subjects enrolled	Belgium: 35
Country: Number of subjects enrolled	Brazil: 101
Country: Number of subjects enrolled	Bulgaria: 58
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	China: 68
Country: Number of subjects enrolled	Colombia: 19
Country: Number of subjects enrolled	Czech Republic: 50
Country: Number of subjects enrolled	Estonia: 13
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 53
Country: Number of subjects enrolled	Greece: 31
Country: Number of subjects enrolled	Guatemala: 65
Country: Number of subjects enrolled	Hungary: 127
Country: Number of subjects enrolled	India: 57
Country: Number of subjects enrolled	Israel: 32
Country: Number of subjects enrolled	Japan: 274
Country: Number of subjects enrolled	Latvia: 29
Country: Number of subjects enrolled	Lebanon: 20
Country: Number of subjects enrolled	Lithuania: 21
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	United States: 203
Worldwide total number of subjects	2538
EEA total number of subjects	851

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)	118
Adults (18-64 years)	1972
From 65 to 84 years	448
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were from ARG, AUS, AUT, BEL, BRA, BGR, CAN, CHN, COL, CZE, EST, FIN, FRA, DEU, GRC, GTM, HUN, IND, ISR, JPN, LVA, LBN, LTU, MYS, MEX, NLD, PER, PHL, POL, ROU, RUS, SAU, SRB, SGP, SVK, ESP, CHE, TWN, TUR, GBR, USA

Pre-assignment

Screening details:

Eligible patients included patients completing a prior QAW039 Phase 3 study (CQAW039A2307, QAW039A2314, CQAW039A2316, or CQAW039A2317) and patients who had not previously participated in a QAW039 study.

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 150mg

Arm description:

QAW039 150mg once daily

Arm type	Experimental
Investigational medicinal product name	QAW039 150mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

QAW039 150mg once daily oral tablet

Arm title	QAW039 450 mg

Arm description:

QAW039 450mg once daily

Arm type	Experimental
Investigational medicinal product name	QAW039 450 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

QAW039 450 mg once daily oral tablet

Arm title	Placebo

Arm description:

Placebo once daily

Arm type	Placebo

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

Dosage and administration details:

Placebo to QAW039 once daily oral tablet

Number of subjects in period 1	QAW039 150mg	QAW039 450 mg	Placebo
Started	1093	1085	360
Completed	76	71	32
Not completed	1017	1014	328
Adverse event, serious fatal	3	-	1
Physician decision	4	5	1
Study Terminated By Sponsor	928	938	296
Adverse event, non-fatal	6	5	-
Technical Problems	-	1	-
Pregnancy	1	-	1
Non-Compliance With Study Treatment	-	2	-
Subject/Guardian Decision	50	45	22
Lost to follow-up	2	4	-
Lack of efficacy	23	14	7

Baseline characteristics

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

Reporting group values	QAW039 150mg	QAW039 450 mg	Placebo
Number of subjects	1093	1085	360
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)	48	53	17
Adults (18-64 years)	856	836	280
From 65-84 years	189	196	63
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	50.1	50.1	49.9
standard deviation	± 14.95	± 15.55	± 14.99
Sex: Female, Male Units: Participants			
Female	659	667	229
Male	434	418	131
Race/Ethnicity, Customized Units: Subjects			
Caucasian	758	757	242
Black	30	14	11
Asian	219	215	73
Native American	27	40	12
Pacific Islander	0	1	0
Unknown	0	9	2
Other	59	49	20

Reporting group values	Total		
Number of subjects	2538		

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)	118		
Adults (18-64 years)	1972		
From 65-84 years	448		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	1555		
Male	983		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	1757		
Black	55		
Asian	507		
Native American	79		
Pacific Islander	1		
Unknown	11		
Other	128		

End points

End points reporting groups

Reporting group title	QAW039 150mg
Reporting group description: QAW039 150mg once daily	
Reporting group title	QAW039 450 mg
Reporting group description: QAW039 450mg once daily	
Reporting group title	Placebo
Reporting group description: Placebo once daily	
Subject analysis set title	QAW039 150mg SAF
Subject analysis set type	Safety analysis
Subject analysis set description: One patient received placebo. This patient was not included in QAW039 150 mg group in the SAF	
Subject analysis set title	QAW039 450mg SAF
Subject analysis set type	Safety analysis
Subject analysis set description: One patient had no treatment administered and thus was excluded from the SAF	
Subject analysis set title	Placebo SAF
Subject analysis set type	Safety analysis
Subject analysis set description: One patient in QAW039 150 mg group received placebo and was included in the placebo group in the SAF	

Primary: Number of participants with treatment emergent adverse events (AEs) up to week 52 - Cox Regression Model

End point title	Number of participants with treatment emergent adverse events (AEs) up to week 52 - Cox Regression Model
End point description: Adverse events starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE) were classified as treatment emergent AEs. For this Outcome Measure, AE up to week 52 are reported.	
End point type	Primary
End point timeframe: 52 weeks	

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	675	654	237	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.97

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.09

Primary: Number of participants with treatment emergent adverse events (AEs) up

to week 156 - Cox Regression Model	
End point title	Number of participants with treatment emergent adverse events (AEs) up to week 156 - Cox Regression Model

End point description:

Adverse events starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE) were classified as treatment emergent AEs

End point type	Primary

End point timeframe:

156 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	709	681	243	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.02

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.99

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.08

Primary: Number of participants with treatment emergent serious adverse events (SAEs) up to week 52 - Cox Regression Model

End point title	Number of participants with treatment emergent serious adverse events (SAEs) up to week 52 - Cox Regression Model

End point description:

Serious Adverse events starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +30 days were classified as treatment emergent SAEs. For this Outcome Measure, AE up to week 52 are reported.

End point type	Primary

End point timeframe:

52 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	73	53	29	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo

Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.22

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.97

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.14

Primary: Number of participants with treatment emergent serious adverse events (SAEs) up to week 156 - Cox Regression Model

End point title	Number of participants with treatment emergent serious adverse events (SAEs) up to week 156 - Cox Regression Model

End point description:

Serious Adverse events starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +30 days were classified as treatment emergent SAEs.

End point type	Primary

End point timeframe:

156 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	86	63	33	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.22

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.97

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.11

Primary: Number of participants with treatment emergent AEs leading to discontinuation from study treatment up to week 52 - Cox Regression Model

End point title	Number of participants with treatment emergent AEs leading to discontinuation from study treatment up to week 52 - Cox Regression Model

End point description:

Adverse events leading to study treatment discontinuation starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE) were classified as treatment emergent AEs leading to study treatment discontinuation. For this Outcome Measure, AE up to week 52 are reported.

End point type	Primary

End point timeframe:

52 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	26	33	9	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo

Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	2.23

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.64

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.1

Primary: Number of participants with treatment emergent AEs leading to discontinuation from study treatment up to week 156 - Cox Regression Model

End point title	Number of participants with treatment emergent AEs leading to discontinuation from study treatment up to week 156 - Cox

	Regression Model

End point description:

Adverse events leading to study treatment discontinuation starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE) were classified as treatment emergent AEs leading to study treatment discontinuation

End point type	Primary

End point timeframe:

156 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants	30	37	9	

Statistical analyses

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.56

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.95

Statistical analysis title	Cox Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.96

Secondary: Number of patients with at least one treatment emergent AE by primary system organ class up to week 52

End point title	Number of patients with at least one treatment emergent AE by primary system organ class up to week 52

End point description:

The number of patients per patient year of follow-up having a treatment emergent adverse event, categorized by system organ class. Treatment emergent adverse events are defined as an AEs starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE)

End point type	Secondary

End point timeframe:

52 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants				
Number of patients with at least one AE	675	654	237	
Blood and lymphatic system disorders	21	10	5	
Cardiac disorders	11	26	7	
Congenital, familial and genetic disorders	1	3	0	
Ear and labyrinth disorders	16	9	8	
Endocrine disorders	2	6	0	
Eye disorders	13	11	9	
Gastrointestinal disorders	88	86	32	
General disorders & administration site conditions	38	33	7	
Hepatobiliary disorders	9	17	7	
Immune system disorders	11	10	6	

Infections and infestations	400	374	145	
Injury, poisoning and procedural complications	67	52	23	
Investigations	79	85	20	
Metabolism and nutrition disorders	53	50	21	
Musculoskeletal and connective tissue disorders	91	84	24	
Neoplasms benign, malignant and unspecified	13	9	3	
Nervous system disorders	67	73	29	
Product issues	1	0	0	
Psychiatric disorders	18	15	9	
Renal and urinary disorders	33	41	8	
Reproductive system and breast disorders	14	9	4	
Respiratory, thoracic and mediastinal disorders	308	304	135	
Skin and subcutaneous tissue disorders	38	39	13	
Social circumstances	1	1	3	
Vascular disorders	39	33	9	

Statistical analyses

Statistical analysis title	Logistic Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.626
upper limit	1.047

Statistical analysis title	Logistic Regression Model
Comparison groups	QAW039 450 mg v Placebo
Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.622
upper limit	1.038

Statistical analysis title	Logistic Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	1.2

Secondary: Number of patients with at least one treatment emergent AE by primary system organ class up to week 156

End point title	Number of patients with at least one treatment emergent AE by primary system organ class up to week 156

End point description:

The number of patients per patient year of follow-up having a treatment emergent adverse event, categorized by system organ class. Treatment emergent adverse events are defined as an AEs starting on or after the day of the first intake of study drug in this study and until the day of last intake of study drug +7 days (30 days in the case of a serious AE)

End point type	Secondary

End point timeframe:

156 weeks

End point values	QAW039 150mg	QAW039 450 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1081	1077	359	
Units: Participants				
Number of patients with at least one AE	710	682	243	
Blood and lymphatic system disorders	23	12	5	
Cardiac disorders	16	34	7	
Congenital, familial and genetic disorders	1	3	1	
Ear and labyrinth disorders	18	13	9	
Endocrine disorders	5	7	0	
Eye disorders	16	14	9	

Gastrointestinal disorders	101	96	38	
General disorders & administration site conditions	43	34	8	
Hepatobiliary disorders	10	21	8	
Immune system disorders	11	11	6	
Infections and infestations	436	415	151	
Injury, poisoning and procedural complications	80	63	28	
Investigations	90	102	24	
Metabolism and nutrition disorders	61	60	23	
Musculoskeletal and connective tissue disorders	102	92	31	
Neoplasms benign, malignant and unspecified	17	11	3	
Nervous system disorders	83	77	32	
Pregnancy, puerperium and perinatal conditions	1	0	0	
Product issues	1	0	0	
Psychiatric disorders	23	18	9	
Renal and urinary disorders	36	45	10	
Reproductive system and breast disorders	17	10	4	
Respiratory, thoracic and mediastinal disorders	336	341	144	
Skin and subcutaneous tissue disorders	45	45	15	
Social circumstances	1	1	3	
Vascular disorders	45	40	13	

Statistical analyses

Statistical analysis title	Logistc Regression Model
Comparison groups	QAW039 150mg v Placebo
Number of subjects included in analysis	1440
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.667
upper limit	1.125

Statistical analysis title	Logistic Regression Model
Comparison groups	QAW039 450 mg v Placebo

Number of subjects included in analysis	1436
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.643
upper limit	1.082

Statistical analysis title	Logistic Regression Model
Comparison groups	QAW039 150mg v QAW039 450 mg
Number of subjects included in analysis	2158
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.794
upper limit	1.167

Secondary: Number of treatment emergent patient deaths due to an asthma exacerbation up to week 52

End point title	Number of treatment emergent patient deaths due to an asthma exacerbation up to week 52

End point description:

The number of treatment emergent patient deaths due to an asthma exacerbation. Treatment emergent deaths are defined as deaths resulting from treatment emergent AEs.

End point type	Secondary

End point timeframe:

52 weeks

End point values	QAW039 150mg SAF	QAW039 450mg SAF	Placebo SAF	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1092	1084	361	
Units: Number of deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent patient deaths due to an asthma exacerbation up to week 156

End point title	Number of treatment emergent patient deaths due to an asthma exacerbation up to week 156

End point description:

The number of treatment emergent patient deaths due to an asthma exacerbation. Treatment emergent deaths are defined as deaths resulting from treatment emergent AEs.

End point type	Secondary

End point timeframe:

156 weeks

End point values	QAW039 150mg SAF	QAW039 450mg SAF	Placebo SAF	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1092	1084	361	
Units: Number of deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of treatment emergent severe asthma exacerbation episodes requiring hospitalizations per person year up to week 52

End point title	Rate of treatment emergent severe asthma exacerbation episodes requiring hospitalizations per person year up to week 52

End point description:

Number of treatment emergent severe asthma exacerbation episodes requiring hospitalizations (any visit to the hospital requiring an overnight stay or an emergency room visit greater than 24 hours) per person year of follow-up. Treatment emergent severe asthma exacerbation episodes are defined as episodes occurring on or after the day of the first intake of study drug and until the day of last intake of study drug +7 days (30 days in the case of a serious AE).
Rate of exacerbations per person year = total number of exacerbations / total number of treatment years

End point type	Secondary

End point timeframe:

52 weeks

End point values	QAW039 150mg SAF	QAW039 450mg SAF	Placebo SAF	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1092	1084	361	
Units: Hospitalizations per person year				
number (not applicable)	0.04	0.02	0.06	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of treatment emergent severe asthma exacerbation episodes requiring hospitalizations per person year up to week 156

End point title	Rate of treatment emergent severe asthma exacerbation episodes requiring hospitalizations per person year up to week 156

End point description:

Number of treatment emergent severe asthma exacerbation episodes requiring hospitalizations (any visit to the hospital requiring an overnight stay or an emergency room visit greater than 24 hours) per person year of follow-up. Treatment emergent severe asthma exacerbation episodes are defined as episodes occurring on or after the day of the first intake of study drug and until the day of last intake of study drug +7 days (30 days in the case of a serious AE).
Rate of exacerbations per person year = total number of exacerbations / total number of treatment years

End point type	Secondary

End point timeframe:

156 weeks

End point values	QAW039 150mg SAF	QAW039 450mg SAF	Placebo SAF	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1092	1084	361	
Units: Hospitalizations per person year				
number (not applicable)	0.04	0.02	0.05	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 7 days post treatment (30 days in the case of a serious AE), up to maximum duration of 156 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 450 mg

Reporting group description:

QAW039 450 mg

Reporting group title	QAW039 150 mg

Reporting group description:

QAW039 150 mg

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	QAW039 450 mg	QAW039 150 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 1084 (5.90%)	87 / 1092 (7.97%)	33 / 361 (9.14%)
number of deaths (all causes)	1	3	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Breast cancer			

subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (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
Cervix carcinoma			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Gastric cancer			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Malignant melanoma			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Myeloproliferative neoplasm			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Prostate cancer			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal neoplasm			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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 cancer			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Uterine leiomyoma			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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			
Aortic stenosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Hypertension			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Pregnancy, puerperium and perinatal conditions			

Pregnancy			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Hyperplasia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Swelling face			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Immune system disorders			
Eosinophilic granulomatosis with polyangiitis			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Uterine polyp			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aphonia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Asthma			
subjects affected / exposed	16 / 1084 (1.48%)	30 / 1092 (2.75%)	13 / 361 (3.60%)
occurrences causally related to treatment / all	2 / 21	2 / 44	2 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic paralysis			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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

Pulmonary embolism			
subjects affected / exposed	2 / 1084 (0.18%)	1 / 1092 (0.09%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Wheezing			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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			
Depression			
subjects affected / exposed	1 / 1084 (0.09%)	3 / 1092 (0.27%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram Q wave abnormal			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Oxygen saturation decreased			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Exposure to allergen			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Fall			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Femur fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Fracture displacement			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Joint injury			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Lumbar vertebral fracture			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Radius fracture			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Road traffic accident			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Skeletal injury			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Upper limb fracture			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Congenital, familial and genetic disorders			
Fibrous dysplasia of bone			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Skeletal dysplasia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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			
Angina pectoris			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Angina unstable			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1092 (0.18%)	0 / 361 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Atrial fibrillation			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Mitral valve incompetence			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Myocardial infarction			

subjects affected / exposed	2 / 1084 (0.18%)	0 / 1092 (0.00%)	0 / 361 (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
Pericardial effusion			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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 extrasystoles			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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 tachycardia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain stem haemorrhage			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Cerebral infarction			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 1084 (0.18%)	0 / 1092 (0.00%)	0 / 361 (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
Colloid brain cyst			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Dyspraxia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Facial paralysis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Guillain-Barre syndrome			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Headache			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Ischaemic stroke			
subjects affected / exposed	0 / 1084 (0.00%)	3 / 1092 (0.27%)	2 / 361 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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			
Blood loss anaemia			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Tympanic membrane perforation			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Vertigo			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Dyspepsia			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Haemorrhoids			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Large intestinal obstruction			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Melaena			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Pancreatitis acute			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	2 / 361 (0.55%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal cyst			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Peritoneal haemorrhage			

subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Strangulated umbilical hernia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 1084 (0.18%)	0 / 1092 (0.00%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 1084 (0.09%)	2 / 1092 (0.18%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	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 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Calculus urinary			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Nephrolithiasis			
subjects affected / exposed	2 / 1084 (0.18%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Ureterolithiasis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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			
Arthralgia			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Arthritis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Back pain			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (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
Intervertebral disc degeneration			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (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
Muscular weakness			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Infections and infestations			

Acute sinusitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Bacterial infection			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Bronchitis			
subjects affected / exposed	3 / 1084 (0.28%)	0 / 1092 (0.00%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Cellulitis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic sinusitis			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Dengue fever			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Dengue haemorrhagic fever			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Diverticulitis			

subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Influenza			
subjects affected / exposed	1 / 1084 (0.09%)	1 / 1092 (0.09%)	0 / 361 (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
Lung abscess			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Otitis media			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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	4 / 1084 (0.37%)	7 / 1092 (0.64%)	2 / 361 (0.55%)
occurrences causally related to treatment / all	0 / 4	2 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
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 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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 tract infection			

subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Septic shock			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Sinusitis			
subjects affected / exposed	0 / 1084 (0.00%)	2 / 1092 (0.18%)	0 / 361 (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
Tuberculosis			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 1084 (0.00%)	0 / 1092 (0.00%)	1 / 361 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal abscess			

subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 1084 (0.00%)	1 / 1092 (0.09%)	0 / 361 (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
Hyperlipidaemia			
subjects affected / exposed	1 / 1084 (0.09%)	0 / 1092 (0.00%)	0 / 361 (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: 2 %

Non-serious adverse events	QAW039 450 mg	QAW039 150 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	499 / 1084 (46.03%)	525 / 1092 (48.08%)	190 / 361 (52.63%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	42 / 1084 (3.87%)	30 / 1092 (2.75%)	2 / 361 (0.55%)
occurrences (all)	48	32	2
Vascular disorders			
Hypertension			
subjects affected / exposed	30 / 1084 (2.77%)	30 / 1092 (2.75%)	11 / 361 (3.05%)
occurrences (all)	34	33	11
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 1084 (2.68%)	41 / 1092 (3.75%)	24 / 361 (6.65%)
occurrences (all)	40	63	30
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	275 / 1084 (25.37%)	291 / 1092 (26.65%)	125 / 361 (34.63%)
occurrences (all)	485	523	270
Rhinitis allergic			
subjects affected / exposed	28 / 1084 (2.58%)	19 / 1092 (1.74%)	11 / 361 (3.05%)
occurrences (all)	29	22	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 1084 (1.01%)	22 / 1092 (2.01%)	8 / 361 (2.22%)
occurrences (all)	11	25	8
Back pain			
subjects affected / exposed	31 / 1084 (2.86%)	29 / 1092 (2.66%)	10 / 361 (2.77%)
occurrences (all)	36	32	11
Infections and infestations			
Bronchitis			
subjects affected / exposed	55 / 1084 (5.07%)	75 / 1092 (6.87%)	38 / 361 (10.53%)
occurrences (all)	69	89	54
Influenza			
subjects affected / exposed	28 / 1084 (2.58%)	30 / 1092 (2.75%)	9 / 361 (2.49%)
occurrences (all)	28	32	11
Nasopharyngitis			
subjects affected / exposed	106 / 1084 (9.78%)	110 / 1092 (10.07%)	36 / 361 (9.97%)
occurrences (all)	146	154	51
Pharyngitis			
subjects affected / exposed	22 / 1084 (2.03%)	34 / 1092 (3.11%)	15 / 361 (4.16%)
occurrences (all)	27	35	17
Sinusitis			
subjects affected / exposed	28 / 1084 (2.58%)	39 / 1092 (3.57%)	9 / 361 (2.49%)
occurrences (all)	35	43	9
Upper respiratory tract infection			
subjects affected / exposed	43 / 1084 (3.97%)	72 / 1092 (6.59%)	25 / 361 (6.93%)
occurrences (all)	56	83	33
Upper respiratory tract infection bacterial			
subjects affected / exposed	31 / 1084 (2.86%)	14 / 1092 (1.28%)	12 / 361 (3.32%)
occurrences (all)	33	15	14

Urinary tract infection			
subjects affected / exposed	37 / 1084 (3.41%)	23 / 1092 (2.11%)	11 / 361 (3.05%)
occurrences (all)	46	25	11
Viral upper respiratory tract infection			
subjects affected / exposed	31 / 1084 (2.86%)	34 / 1092 (3.11%)	9 / 361 (2.49%)
occurrences (all)	37	40	12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2018	The key change to the protocol related to the removal of references and discussions regarding the Oral Corticosteroid Tapering Study (QAW039A2319), a Phase 3 study that was cancelled for strategic reasons before being initiated. The sample size for Study A2315 was also increased to account for the number of planned patients from the cancelled Oral Corticosteroid Tapering study. This amendment was not considered to have affected the interpretation of study results, as the changes were minor and occurred prior to study unblinding.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported