Clinical trial results:
A randomized, double-blind, placebo-controlled three-period incomplete cross over study to compare the efficacy of QAW039 alone and in combination with Montelukast in patients with allergic rhinitis using an Environmental Exposure Chamber

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Summary

EudraCT number	2012-001389-14
Trial protocol	DE
Global end of trial date	02 October 2013
Results information	
Result version number	v1 (current)
This version publication date	07 July 2018
First version publication date	07 July 2018

Trial information

Trial identification	
Sponsor protocol code	CQAW039A2212
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01804400
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of QAW039 225 mg twice daily (b.i.d.) and Montelukast 10 mg once daily (q.d.) administered together as a free combination compared to QAW039 225 mg b.i.d monotherapy in patients with grass pollen-induced intermittent allergic rhinitis in an EEC challenge model. This was assessed by the Total Nasal Symptom Score (TNSS) averaged over the last two hours (2-4h) of exposure following 14 days treatment with QAW039 and/or Montelukast or matched placebo.

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.
After each challenge the subjects had an option to receive a Terbutaline Turbohaler as rescue medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 188
Worldwide total number of subjects	188
EEA total number of subjects	188

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	188
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a maximum 49-day screening period including a 2-hour exposure to grass pollen in the Environmental Exposure Chamber (EEC).

Period 1

Period 1 title	Treatment Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 2

Arm description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 3

Arm description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 4

Arm description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 5

Arm description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 6

Arm description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Arm title	Treatment Sequence 7

Arm description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Arm title	Treatment Sequence 8

Arm description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

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

Dosage and administration details:

Three 150 mg capsules once daily in the morning

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule once daily in the morning and four capsules once daily in the evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 9

Arm description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.

Arm type	Placebo
Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 10

Arm description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.

Arm type	Placebo
Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Number of subjects in period 1	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	19	19	18
Completed	19	19	18
Not completed	0	0	0
Subject withdrew consent	-	-	-
Administrative problem	-	-	-

Number of subjects in period 1	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	18	19	19
Completed	17	19	19
Not completed	1	0	0
Subject withdrew consent	1	-	-
Administrative problem	-	-	-

Number of subjects in period 1	Treatment Sequence 7	Treatment Sequence 8	Treatment Sequence 9
Started	19	19	19
Completed	19	18	19
Not completed	0	1	0
Subject withdrew consent	-	-	-
Administrative problem	-	1	-

Number of subjects in period 1	Treatment Sequence 10
Started	19

Completed	19
Not completed	0
Subject withdrew consent	-
Administrative problem	-

Period 2

Period 2 title	Washout Period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 2

Arm description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 3

Arm description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 4

Arm description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 5

Arm description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 6

Arm description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 7

Arm description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 8

Arm description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 9

Arm description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 10

Arm description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	19	19	18
Completed	19	19	18
Not completed	0	0	0
Administrative problem	-	-	-

Number of subjects in period 2	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	17	19	19
Completed	16	18	19
Not completed	1	1	0
Administrative problem	1	1	-

Number of subjects in period 2	Treatment Sequence 7	Treatment Sequence 8	Treatment Sequence 9
Started	19	18	19
Completed	19	18	19
Not completed	0	0	0
Administrative problem	-	-	-

Number of subjects in period 2	Treatment Sequence 10
Started	19
Completed	19
Not completed	0
Administrative problem	-

Period 3	
Period 3 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In Treatment Period 1 this arm received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 2

Arm description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Arm title	Treatment Sequence 3

Arm description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

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

Dosage and administration details:

Three 150 mg capsules once daily in the morning

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule once daily in the morning and four capsules once daily in the evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 4

Arm description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 5

Arm description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

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

Dosage and administration details:

Three 150 mg capsules once daily in the morning

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule once daily in the morning and four capsules once daily in the evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 6

Arm description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 7

Arm description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 8

Arm description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 9

Arm description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Arm type	Experimental

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 10

Arm description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Number of subjects in period 3	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	19	19	18
Completed	19	19	18
Not completed	0	0	0
Administrative problem	-	-	-

Number of subjects in period 3	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	16	18	19
Completed	16	16	19
Not completed	0	2	0
Administrative problem	-	2	-

Number of subjects in period 3	Treatment Sequence 7	Treatment Sequence 8	Treatment Sequence 9
Started	19	18	19
Completed	19	18	19
Not completed	0	0	0
Administrative problem	-	-	-

Number of subjects in period 3	Treatment Sequence 10
Started	19
Completed	19
Not completed	0
Administrative problem	-

Period 4

Period 4 title	Washout Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1

Arm description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 2

Arm description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 3

Arm description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 4

Arm description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 5

Arm description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 6

Arm description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 7

Arm description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 8

Arm description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 9

Arm description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 10

Arm description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	19	19	18
Completed	19	19	18
Not completed	0	0	0
Subject withdrew consent	-	-	-
Abnormal lab value	-	-	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 4	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	16	16	19
Completed	16	16	19
Not completed	0	0	0
Subject withdrew consent	-	-	-
Abnormal lab value	-	-	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 4	Treatment Sequence 7	Treatment Sequence 8	Treatment Sequence 9
Started	19	18	19
Completed	18	17	19
Not completed	1	1	0
Subject withdrew consent	-	-	-
Abnormal lab value	1	-	-
Adverse event, non-fatal	-	1	-

Number of subjects in period 4	Treatment Sequence 10
Started	19
Completed	18
Not completed	1
Subject withdrew consent	1
Abnormal lab value	-
Adverse event, non-fatal	-

Period 5	
Period 5 title	Treatment Period 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms	
Are arms mutually exclusive?	Yes

Arm title	Treatment Sequence 1

Arm description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Arm title	Treatment Sequence 2

Arm description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.

Arm type	Placebo
Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 3

Arm description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 4

Arm description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug E.

Arm type	Placebo
Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 5

Arm description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 6

Arm description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10

mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

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

Dosage and administration details:

Three 150 mg capsules once daily in the morning

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule once daily in the morning and four capsules once daily in the evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 7

Arm description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Arm title	Treatment Sequence 8

Arm description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Arm type	Active comparator

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 10 mg capsule once daily in the evening

Investigational medicinal product name	Placebo for QAW039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Four capsules twice daily in the morning and evening

Arm title	Treatment Sequence 9

Arm description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Placebo for montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule once daily in the evening

Arm title	Treatment Sequence 10

Arm description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

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

Dosage and administration details:

Three 25 mg capsules and one 150 mg capsule administered twice daily in the morning and evening

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
One 10 mg capsule once daily in the evening

Number of subjects in period 5	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	19	19	18
Completed	15	16	15
Not completed	4	3	3
Subject withdrew consent	-	1	-
Adverse event, non-fatal	4	2	3
Administrative problem	-	-	-

Number of subjects in period 5	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	16	16	19
Completed	13	15	17
Not completed	3	1	2
Subject withdrew consent	2	-	-
Adverse event, non-fatal	1	1	2
Administrative problem	-	-	-

Number of subjects in period 5	Treatment Sequence 7	Treatment Sequence 8	Treatment Sequence 9
Started	18	17	19
Completed	17	16	16
Not completed	1	1	3
Subject withdrew consent	-	-	-
Adverse event, non-fatal	1	-	3
Administrative problem	-	1	-

Number of subjects in period 5	Treatment Sequence 10
Started	18
Completed	16
Not completed	2
Subject withdrew consent	1
Adverse event, non-fatal	-
Administrative problem	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1
Reporting group description:	
All randomized subjects	

Reporting group values	Treatment Period 1	Total	
Number of subjects	188	188	
Age categorical Units: Subjects			
18-<65 years	188	188	
Age continuous Units: years			
arithmetic mean	36.8		
standard deviation	± 10.89	-	
Gender categorical Units: Subjects			
Female	76	76	
Male	112	112	

Subject analysis sets	
Subject analysis set title	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received both QAW039 225 mg and Montelukast twice daily for 2 weeks.	
Subject analysis set title	QAW039 225 mg Twice Daily Monotherapy
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received QAW039 225 mg twice daily for 2 weeks.	
Subject analysis set title	Montelukast 10 mg Once Daily Monotherapy
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received Montelukast once daily for 2 weeks.	
Subject analysis set title	QAW039 450mg Once Daily Monotherapy
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received QAW039 450 mg once daily for 2 weeks.	
Subject analysis set title	Placebo Twice Daily
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received placebo twice daily for 2 weeks.	

Reporting group values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	Montelukast 10 mg Once Daily Monotherapy
Number of subjects	176	107	108

Age categorical Units: Subjects			
18-<65 years	176	107	108
Age continuous Units: years			
arithmetic mean	37	35.4	37.8
standard deviation	± 10.9	± 10.25	± 11.14
Gender categorical Units: Subjects			
Female	70	45	38
Male	106	62	70

Reporting group values	QAW039 450mg Once Daily Monotherapy	Placebo Twice Daily	
Number of subjects	68	68	
Age categorical Units: Subjects			
18-<65 years	68	68	
Age continuous Units: years			
arithmetic mean	38.2	37	
standard deviation	± 11.71	± 10.82	
Gender categorical Units: Subjects			
Female	28	30	
Male	40	38	

End points

End points reporting groups

Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.	
Reporting group title	Treatment Sequence 2
Reporting group description:	
Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.	
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.	
Reporting group title	Treatment Sequence 4
Reporting group description:	
Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug B.	
Reporting group title	Treatment Sequence 5
Reporting group description:	
Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.	
Reporting group title	Treatment Sequence 6
Reporting group description:	
Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.	
Reporting group title	Treatment Sequence 7
Reporting group description:	
Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.	
Reporting group title	Treatment Sequence 8
Reporting group description:	
Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.	
Reporting group title	Treatment Sequence 9
Reporting group description:	
Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.	
Reporting group title	Treatment Sequence 10
Reporting group description:	
Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.	
Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo	

b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 7

Reporting group description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 8

Reporting group description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 9

Reporting group description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 10

Reporting group description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 1

Reporting group description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In Treatment Period 1 this arm received Drug B.

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug A.

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug D.

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Reporting group title	Treatment Sequence 7

Reporting group description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

Reporting group title	Treatment Sequence 8

Reporting group description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Reporting group title	Treatment Sequence 9

Reporting group description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Reporting group title	Treatment Sequence 10

Reporting group description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Reporting group title	Treatment Sequence 1

Reporting group description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 7

Reporting group description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 8

Reporting group description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 9

Reporting group description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 10

Reporting group description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this washout period subjects did not receive drug.

Reporting group title	Treatment Sequence 1

Reporting group description:

Treatment Sequence 1 = Drug A / Drug B / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Reporting group title	Treatment Sequence 2

Reporting group description:

Treatment Sequence 2 = Drug A / Drug C / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug E.

Reporting group title	Treatment Sequence 3

Reporting group description:

Treatment Sequence 3 was Drug A / Drug D / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

Reporting group title	Treatment Sequence 4

Reporting group description:

Treatment Sequence 4 = Drug B / Drug A / Drug E, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subject received Drug E.

Reporting group title	Treatment Sequence 5

Reporting group description:

Treatment Sequence 5 = Drug B / Drug D / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Reporting group title	Treatment Sequence 6

Reporting group description:

Treatment Sequence 6 = Drug C / Drug A / Drug D, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo

b.i.d. In this treatment period subjects received Drug D.

Reporting group title	Treatment Sequence 7

Reporting group description:

Treatment Sequence 7 = Drug C / Drug B / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Reporting group title	Treatment Sequence 8

Reporting group description:

Treatment Sequence 8 = Drug D / Drug A / Drug C, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug C.

Reporting group title	Treatment Sequence 9

Reporting group description:

Treatment Sequence 9 = Drug E / Drug A / Drug B, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug B.

Reporting group title	Treatment Sequence 10

Reporting group description:

Treatment Sequence 10 = Drug E / Drug C / Drug A, with A = QAW039 225 mg b.i.d plus Montelukast 10 mg q.d, B = QAW039 225 mg b.i.d, C = Montelukast 10 mg q.d, D = QAW039 450 mg q.d, E = Placebo b.i.d. In this treatment period subjects received Drug A.

Subject analysis set title	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received both QAW039 225 mg and Montelukast twice daily for 2 weeks.

Subject analysis set title	QAW039 225 mg Twice Daily Monotherapy
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received QAW039 225 mg twice daily for 2 weeks.

Subject analysis set title	Montelukast 10 mg Once Daily Monotherapy
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received Montelukast once daily for 2 weeks.

Subject analysis set title	QAW039 450mg Once Daily Monotherapy
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received QAW039 450 mg once daily for 2 weeks.

Subject analysis set title	Placebo Twice Daily
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received placebo twice daily for 2 weeks.

Primary: Change in Total Nasal Symptom Score (TNSS) From Baseline at 14 days

End point title	Change in Total Nasal Symptom Score (TNSS) From Baseline at 14 days

End point description:

Total Nasal Symptom Score (TNSS) was averaged over the last two hours (2-4hours) of exposure following 14 days treatment with QAW039 and/or Montelukast. The TNSS is a rating system of nasal symptoms, as assessed by the subject, of nasal congestion, rhinorrhea, nasal itch and sneezing, each of which is scored on a scale from 0 to 3 as follows:
0 - absent symptoms (no sign/symptoms evident);
1 - mild symptoms (sign symptom clearly present, but minimal awareness; easily tolerated);
2 - moderate symptoms (definite awareness of sign/symptom that is bothersome but tolerable);
3 - severe symptoms (sign/symptom that is hard to tolerate; causes interference with activities of daily living).
This results in a total nasal symptom score ranging between 0 and 12.

A negative change from baseline indicates a treatment benefit.
This endpoint analyzed the pharmacodynamic (PD) analysis set, which included all subjects with available PD data and no major protocol deviations.

End point type	Primary

End point timeframe:

Baseline, Day 14

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	Montelukast 10 mg Once Daily Monotherapy	QAW039 450mg Once Daily Monotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	168	94	104	63
Units: score on a scale				
least squares mean (confidence interval 90%)	-1.44 (-1.653 to -1.228)	-1.344 (-1.616 to -1.072)	-1.123 (-1.383 to -0.863)	-0.878 (-1.206 to -0.549)

End point values	Placebo Twice Daily			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: score on a scale				
least squares mean (confidence interval 90%)	-0.998 (-1.332 to -0.664)			

Statistical analyses

Statistical analysis title	Analysis of TNSS
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 225 mg Twice Daily Monotherapy
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6019
Method	Mixed models analysis

Statistical analysis title	Analysis of TNSS #2
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 450mg Once Daily Monotherapy

Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0091
Method	Mixed models analysis

Statistical analysis title	Analysis of TNSS #3
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v Montelukast 10 mg Once Daily Monotherapy
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0742
Method	Mixed models analysis

Statistical analysis title	Analysis of TNSS #4
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0448
Method	Mixed models analysis

Statistical analysis title	Analysis of TNSS #5
Comparison groups	QAW039 225 mg Twice Daily Monotherapy v QAW039 450mg Once Daily Monotherapy
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0526
Method	Mixed models analysis

Secondary: Change in Total Ocular Symptom Score (TOSS) From Baseline at 14 days

End point title	Change in Total Ocular Symptom Score (TOSS) From Baseline at 14 days

End point description:

Total Ocular Symptom Score (TOSS), defined as the sum of ocular symptoms of eye tearing, itching, watery eyes and redness. redness, each of which is scored on a scale from 0 and 3 as below:
0 - absent symptoms (no sign/symptoms evident);
1 - mild symptoms (sign symptom clearly present, but minimal awareness; easily tolerated);
2 - moderate symptoms (definite awareness of sign/symptom that is bothersome but tolerable);
3 - severe symptoms (sign/symptom that is hard to tolerate; causes interference with activities of daily living).

This results in a total nasal symptom score ranging between 0 to 12.
The lower TOSS values indicate less symptoms and a negative change from baseline indicates a treatment benefit.
This endpoint analyzed the pharmacodynamic (PD) analysis set, which included all subjects with available PD data and no major protocol deviations.

End point type	Secondary
End point timeframe:	
Baseline, Day 14	

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	168	94	63	
Units: scores on a scale				
least squares mean (confidence interval 90%)	-1.302 (-1.552 to -1.053)	-1.338 (-1.649 to -1.026)	-0.903 (-1.276 to -0.53)	

Statistical analyses

Statistical analysis title	Analysis of TOSS
Comparison groups	QAW039 225 mg Twice Daily Monotherapy v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8597
Method	Mixed models analysis

Statistical analysis title	Analysis of TOSS #2
Comparison groups	QAW039 225 mg Twice Daily Monotherapy v QAW039 450mg Once Daily Monotherapy
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0989
Method	Mixed models analysis

Statistical analysis title	Analysis of TOSS #3
Comparison groups	QAW039 450mg Once Daily Monotherapy v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily

Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0896
Method	Mixed models analysis

Secondary: Change in Nasal Flow From Baseline at 14 days

End point title	Change in Nasal Flow From Baseline at 14 days

End point description:

Measured using rhinomanometry. Flow rates at 150 Pa were obtained separately for the right and left nostrils (cm^3/second). The sum of the flow rates of both nostrils was calculated from the two measurements. For nasal flow a treatment benefit is indicated by positive values for change from baseline.
This endpoint analyzed the pharmacodynamic (PD) analysis set, which included all subjects with available PD data and no major protocol deviations.

End point type	Secondary

End point timeframe:

Prior to, and every 60 min during allergen exposure period

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	Montelukast 10 mg Once Daily Monotherapy	QAW039 450mg Once Daily Monotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	168	94	104	63
Units: millilitres/second				
least squares mean (confidence interval 90%)	65.868 (49.285 to 82.45)	23.494 (1.624 to 45.364)	39.66 (18.854 to 60.465)	16.715 (-10.033 to 43.462)

End point values	Placebo Twice Daily			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: millilitres/second				
least squares mean (confidence interval 90%)	-13.663 (-40.911 to 13.586)			

Statistical analyses

Statistical analysis title	Analysis of nasal flow
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 225 mg Twice Daily Monotherapy

Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0075
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal flow #2
Comparison groups	Montelukast 10 mg Once Daily Monotherapy v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0854
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal flow #3
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 450mg Once Daily Monotherapy
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0073
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal flow #4
Comparison groups	Placebo Twice Daily v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal flow #5
Comparison groups	QAW039 225 mg Twice Daily Monotherapy v Placebo Twice Daily

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0732
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal flow #6
Comparison groups	Placebo Twice Daily v Montelukast 10 mg Once Daily Monotherapy
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0085
Method	Mixed models analysis

Secondary: Change in Nasal Excretion Weight From Baseline at 14 days

End point title	Change in Nasal Excretion Weight From Baseline at 14 days

End point description:

Total weight of tissues (before and after use). Tissue packs were supplied with all tissues collected to measure weight of nasal secretions. Subjects blew their noses prior to the completion of each collection period. For nasal secretion weight a treatment benefit is indicated by negative changes from baseline. This endpoint analyzed the pharmacodynamic (PD) analysis set, which included all subjects with available PD data and no major protocol deviations.

End point type	Secondary

End point timeframe:

Baseline, Day 14

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	Montelukast 10 mg Once Daily Monotherapy	QAW039 450mg Once Daily Monotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	168	94	104	63
Units: gram(s)				
least squares mean (confidence interval 90%)	-1.212 (-1.558 to -0.865)	-0.284 (-0.728 to 0.16)	-0.619 (-1.042 to -0.196)	-0.572 (-1.106 to -0.038)

End point values	Placebo Twice Daily			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: gram(s)				
least squares mean (confidence interval	-0.147 (-0.691			

90%)	to 0.398)

Statistical analyses

Statistical analysis title	Analysis of nasal secretion weight
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 225 mg Twice Daily Monotherapy
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0019
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal secretion weight #2
Comparison groups	Montelukast 10 mg Once Daily Monotherapy v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0382
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal secretion weight #3
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 450mg Once Daily Monotherapy
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0652
Method	Mixed models analysis

Statistical analysis title	Analysis of nasal secretion weight #4
Comparison groups	Placebo Twice Daily v QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	Mixed models analysis

Secondary: Change in Forced Expiratory Volume in 1 Second (FEV1) From Baseline at 14 days

End point title	Change in Forced Expiratory Volume in 1 Second (FEV1) From Baseline at 14 days

End point description:

Change in FEV1 from Baseline. FEV1 was measured with spirometry conducted according to internationally accepted standards. FEV1 was calculated as the volume of air forcibly exhaled in one second.
This endpoint analyzed the pharmacodynamic (PD) analysis set, which included all subjects with available PD data and no major protocol deviations.

End point type	Secondary

End point timeframe:

Baseline, Day 14

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	Montelukast 10 mg Once Daily Monotherapy	QAW039 450mg Once Daily Monotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	168	94	104	63
Units: litre(s)				
least squares mean (confidence interval 90%)	0.01 (-0.008 to 0.028)	-0.007 (-0.03 to 0.016)	0.013 (-0.009 to 0.035)	-0.012 (-0.04 to 0.016)

End point values	Placebo Twice Daily			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: litre(s)				
least squares mean (confidence interval 90%)	-0.008 (-0.036 to 0.021)			

Statistical analyses

Statistical analysis title	Analysis of FEV1
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 225 mg Twice Daily Monotherapy

Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2842
Method	Mixed models analysis

Statistical analysis title	Analysis of FEV1 #2
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v Montelukast 10 mg Once Daily Monotherapy
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8482
Method	Mixed models analysis

Statistical analysis title	Analysis of FEV1 #3
Comparison groups	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily v QAW039 450mg Once Daily Monotherapy
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2309
Method	Mixed models analysis

Statistical analysis title	Analysis of FEV1 #4
Comparison groups	QAW039 450mg Once Daily Monotherapy v QAW039 225 mg Twice Daily Monotherapy
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8027
Method	Mixed models analysis

Statistical analysis title	Analysis of FEV1 #5
Comparison groups	QAW039 450mg Once Daily Monotherapy v Montelukast 10 mg Once Daily Monotherapy

Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2161
Method	Mixed models analysis

Secondary: Plasma Concentration Maximum (Cmax)

End point title	Plasma Concentration Maximum (Cmax)

End point description:

Determined at steady state in plasma. Pharmacokinetic parameters were calculated from plasma concentration-time data using non-compartmental methods.
This endpoint analyzed the pharmacokinetic (PK) analysis set, which included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

End point type	Secondary

End point timeframe:

Day 7

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	8	4	
Units: nanogram(s)/millilitre				
arithmetic mean (standard deviation)	1170 (± 892)	1110 (± 550)	1890 (± 310)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration Minimum (Cmin)

End point title	Plasma Concentration Minimum (Cmin)

End point description:

Determined at steady state in plasma. Pharmacokinetic parameters were calculated from plasma concentration-time data using non-compartmental methods.
This endpoint analyzed the pharmacokinetic (PK) analysis set, which included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

End point type	Secondary

End point timeframe:

Day 7

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	8	4	
Units: nanograms/millilitre				
arithmetic mean (standard deviation)	83.6 (± 32.2)	90.7 (± 60.3)	54.4 (± 29.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration Average (Cav)

End point title	Plasma Concentration Average (Cav)

End point description:

Determined at steady state in plasma. Pharmacokinetic parameters were calculated from plasma concentration-time data using non-compartmental methods.
This endpoint analyzed the pharmacokinetic (PK) analysis set, which included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

End point type	Secondary

End point timeframe:

Day 7

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	4	
Units: nanograms/millilitre				
arithmetic mean (standard deviation)	325 (± 162)	308 (± 127)	300 (± 38.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Cmax (Tmax)

End point title	Time of Cmax (Tmax)

End point description:

Determined at steady state in plasma. Pharmacokinetic parameters were calculated from plasma concentration-time data using non-compartmental methods.
This endpoint analyzed the pharmacokinetic (PK) analysis set, which included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

End point type	Secondary

End point timeframe:

Day 7

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	8	4	
Units: hours				
median (full range (min-max))	1.03 (0.55 to 3.97)	1.47 (0.933 to 2)	1.98 (0.55 to 2.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Curve (AUCtau)

End point title	Area Under Curve (AUCtau)

End point description:

Determined at steady state in plasma. Pharmacokinetic parameters were calculated from plasma concentration-time data using non-compartmental methods.
This endpoint analyzed the pharmacokinetic (PK) analysis set, which included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

End point type	Secondary

End point timeframe:

Day 7

End point values	QAW039 225 mg Twice Daily Plus Montelukast 10 mg Once Daily	QAW039 225 mg Twice Daily Monotherapy	QAW039 450mg Once Daily Monotherapy	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	4	
Units: hours*nanogram/millilitre				
arithmetic mean (standard deviation)	3900 (± 1940)	3700 (± 1530)	7210 (± 926)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	QAW039 225 mg bid plus montelukast 10 mg qd
Reporting group description:	
QAW039 225 mg bid plus montelukast 10 mg qd	
Reporting group title	QAW039 225 mg bid
Reporting group description:	
QAW039 225 mg bid	
Reporting group title	Placebo bid
Reporting group description:	
Placebo bid	
Reporting group title	QAW039 450 mg qd
Reporting group description:	
QAW039 450 mg qd	
Reporting group title	Total (for all treatment periods)
Reporting group description:	
Total (for all treatment periods)	
Reporting group title	montelukast 10 mg qd
Reporting group description:	
montelukast 10 mg qd	

Serious adverse events	QAW039 225 mg bid plus montelukast 10 mg qd	QAW039 225 mg bid	Placebo bid
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 176 (0.00%)	0 / 107 (0.00%)	0 / 68 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	0 / 176 (0.00%)	0 / 107 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	QAW039 450 mg qd	Total (for all treatment periods)	montelukast 10 mg qd
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 68 (0.00%)	1 / 188 (0.53%)	1 / 108 (0.93%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	0 / 68 (0.00%)	1 / 188 (0.53%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	QAW039 225 mg bid plus montelukast 10 mg qd	QAW039 225 mg bid	Placebo bid
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 176 (28.98%)	31 / 107 (28.97%)	17 / 68 (25.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 176 (15.91%)	22 / 107 (20.56%)	9 / 68 (13.24%)
occurrences (all)	36	27	13
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 176 (5.68%)	4 / 107 (3.74%)	4 / 68 (5.88%)
occurrences (all)	11	4	5
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	13 / 176 (7.39%)	2 / 107 (1.87%)	5 / 68 (7.35%)
occurrences (all)	13	2	5
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 176 (1.70%)	1 / 107 (0.93%)	3 / 68 (4.41%)
occurrences (all)	3	1	3
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	12 / 176 (6.82%)	11 / 107 (10.28%)	1 / 68 (1.47%)
occurrences (all)	12	11	1

Non-serious adverse events	QAW039 450 mg qd	Total (for all treatment periods)	montelukast 10 mg qd
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 68 (27.94%)	99 / 188 (52.66%)	28 / 108 (25.93%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 68 (8.82%)	61 / 188 (32.45%)	16 / 108 (14.81%)
occurrences (all)	7	103	20
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 68 (10.29%)	20 / 188 (10.64%)	2 / 108 (1.85%)
occurrences (all)	8	30	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 68 (4.41%)	24 / 188 (12.77%)	5 / 108 (4.63%)
occurrences (all)	3	28	5
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 68 (2.94%)	10 / 188 (5.32%)	2 / 108 (1.85%)
occurrences (all)	2	11	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 68 (7.35%)	36 / 188 (19.15%)	7 / 108 (6.48%)
occurrences (all)	5	37	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: