Clinical trial results:
A randomized, placebo-controlled, dose-ranging, multi-centre trial of QAW039 (1-450 mg p.o.), to investigate the effect on FEV1 and ACQ in patients with moderate-to-severe, persistent, allergic asthma, inadequately controlled with ICS therapy

Summary

EudraCT number	2011-001062-18
Trial protocol	GR GB AT HU PL NL IT BG
Global end of trial date	12 November 2013

Results information

Result version number	v1 (current)
This version publication date	05 August 2018
First version publication date	05 August 2018

Trial information

Trial identification

Sponsor protocol code	CQAW039A2206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01437735
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	12 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate a clinically significant improvement in morning FEV1 in moderate to severe allergic asthmatics inadequately controlled by ICS therapy treated with QAW039 for 12 weeks compared to 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.
At Visit 1 all patients were provided with a salbutamol/albuterol propellant –HFA 134a) inhaler which they were instructed to use throughout the study as rescue medication. The rescue medication usage was collected daily in the diary between study visits.

Background therapy:

All patients were treated with 200µg budesonide bid throughout the trial.

Evidence for comparator: -

Actual start date of recruitment	25 August 2011
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	Argentina: 47
Country: Number of subjects enrolled	Colombia: 26
Country: Number of subjects enrolled	Guatemala: 37
Country: Number of subjects enrolled	India: 104
Country: Number of subjects enrolled	Japan: 124
Country: Number of subjects enrolled	Mexico: 52
Country: Number of subjects enrolled	Peru: 53
Country: Number of subjects enrolled	Romania: 62
Country: Number of subjects enrolled	Russian Federation: 60
Country: Number of subjects enrolled	South Africa: 67
Country: Number of subjects enrolled	Turkey: 13
Country: Number of subjects enrolled	United States: 211
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	United Kingdom: 11

Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Bulgaria: 44
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Hungary: 79
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	1058
EEA total number of subjects	263

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)	1044
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After obtaining informed consent at Visit 1, the patients were advised on wash out requirements for prohibited medications prior to screening at Visit 2 or 3 .

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	1 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	3 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their

QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	10 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits

4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	30 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	50 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in

the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	75 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	150 mg bid QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm type	Experimental

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	300 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately

12 hours after their AM dose ± 30 minutes.

Arm title	450 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	2 mg bid QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in

the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	25 mg bid QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	75 mg bid QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm type	Experimental

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	150 mg qd QAW039

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately

12 hours after their AM dose ± 30 minutes.

Arm title	10 mg qd montelukas

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Arm title	Placebo

Arm description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

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

Dosage and administration details:

QAW039/placebo study medication to be taken in the morning between 08:00 and 11:00 am. At Visits 4 to 8; the study medication was administered in the clinic between 08:00 and 11:00 am. Patients were instructed to withhold the use rescue medication for at least 6 hours prior to all clinic visits, unless the use was absolutely necessary. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits.
On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo approximately 12 hours after their AM dose ± 30 minutes.

Number of subjects in period 1	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039
Started	52	54	48
Completed	41	44	41
Not completed	11	10	7
Abnormal laboratory value(s)	2	-	-
Consent withdrawn by subject	-	3	3
Patient's inability to use the device	-	1	-
Adverse event, non-fatal	4	2	2
Unsatisfactory therapeutic effect	2	-	-
Administrative problems	-	-	1
patients randomized in error/no data available	1	2	-
Lost to follow-up	-	-	-
Abnormal test procedure result(s)	-	1	-
Protocol deviation	2	1	1

Number of subjects in period 1	30 mg qd QAW039	50 mg qd QAW039	75 mg qd QAW039
Started	55	51	58
Completed	46	43	51
Not completed	9	8	7
Abnormal laboratory value(s)	-	1	-
Consent withdrawn by subject	-	-	-
Patient's inability to use the device	-	-	-
Adverse event, non-fatal	7	4	3
Unsatisfactory therapeutic effect	-	-	-
Administrative problems	-	-	1
patients randomized in error/no data available	1	2	-
Lost to follow-up	1	-	-
Abnormal test procedure result(s)	-	1	1
Protocol deviation	-	-	2

Number of subjects in period 1	150 mg bid QAW039	300 mg qd QAW039	450 mg qd QAW039
Started	56	57	134

Completed	50	51	107
Not completed	6	6	27
Abnormal laboratory value(s)	-	-	-
Consent withdrawn by subject	-	-	6
Patient's inability to use the device	-	-	1
Adverse event, non-fatal	4	2	14
Unsatisfactory therapeutic effect	-	1	1
Administrative problems	-	1	-
patients randomized in error/no data available	-	-	1
Lost to follow-up	2	1	2
Abnormal test procedure result(s)	-	1	1
Protocol deviation	-	-	1

Number of subjects in period 1	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Started	52	60	52
Completed	45	54	37
Not completed	7	6	15
Abnormal laboratory value(s)	-	-	-
Consent withdrawn by subject	1	1	1
Patient's inability to use the device	-	-	-
Adverse event, non-fatal	4	1	7
Unsatisfactory therapeutic effect	-	-	1
Administrative problems	-	2	-
patients randomized in error/no data available	1	1	1
Lost to follow-up	-	1	1
Abnormal test procedure result(s)	-	-	-
Protocol deviation	1	-	4

Number of subjects in period 1	150 mg qd QAW039	10 mg qd montelukas	Placebo
Started	53	139	137
Completed	43	113	111
Not completed	10	26	26
Abnormal laboratory value(s)	1	1	1
Consent withdrawn by subject	2	10	2
Patient's inability to use the device	-	-	-
Adverse event, non-fatal	4	5	16
Unsatisfactory therapeutic effect	1	1	1
Administrative problems	1	3	-
patients randomized in error/no data available	-	2	1
Lost to follow-up	1	1	2

Abnormal test procedure result(s)	-	1	2
Protocol deviation	-	2	1

Reporting groups

Reporting group title	1 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	3 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	10 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	30 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	50 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	75 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	150 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	300 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	450 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	2 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	25 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	75 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	150 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	10 mg qd montelukas

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	Placebo

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group values	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039
Number of subjects	52	54	48
Age categorical Units: Subjects			
Adults (18-64 years)	51	53	47
From 65-84 years	1	1	1

Age continuous			
Units: years			
arithmetic mean	45.4	44.2	43.1
standard deviation	± 11.69	± 13.22	± 12.19
Gender categorical			
Units: Subjects			
Female	35	32	23
Male	17	22	25

Reporting group values	30 mg qd QAW039	50 mg qd QAW039	75 mg qd QAW039
Number of subjects	55	51	58
Age categorical			
Units: Subjects			
Adults (18-64 years)	53	51	57
From 65-84 years	2	0	1
Age continuous			
Units: years			
arithmetic mean	44.7	46.9	46.4
standard deviation	± 14.15	± 10.11	± 12.45
Gender categorical			
Units: Subjects			
Female	29	25	30
Male	26	26	28

Reporting group values	150 mg bid QAW039	300 mg qd QAW039	450 mg qd QAW039
Number of subjects	56	57	134
Age categorical			
Units: Subjects			
Adults (18-64 years)	55	57	132
From 65-84 years	1	0	2
Age continuous			
Units: years			
arithmetic mean	45.6	40.8	45.8
standard deviation	± 13.52	± 12.07	± 12.51
Gender categorical			
Units: Subjects			
Female	36	33	74
Male	20	24	60

Reporting group values	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Number of subjects	52	60	52
Age categorical			
Units: Subjects			
Adults (18-64 years)	52	60	52
From 65-84 years	0	0	0
Age continuous			
Units: years			
arithmetic mean	48.1	44.7	45.4
standard deviation	± 11.1	± 11.54	± 10.44

Gender categorical Units: Subjects			
Female	32	39	35
Male	20	21	17

Reporting group values	150 mg qd QAW039	10 mg qd montelukas	Placebo
Number of subjects	53	139	137
Age categorical Units: Subjects			
Adults (18-64 years)	53	136	135
From 65-84 years	0	3	2
Age continuous Units: years			
arithmetic mean	42.4	44.5	44.6
standard deviation	± 12.6	± 11.25	± 12.46
Gender categorical Units: Subjects			
Female	29	81	79
Male	24	58	58

Reporting group values	Total		
Number of subjects	1058		
Age categorical Units: Subjects			
Adults (18-64 years)	1044		
From 65-84 years	14		
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	612		
Male	446		

End points

End points reporting groups

Reporting group title	1 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	3 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	10 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	30 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	50 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	75 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	150 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	300 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	450 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	2 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	25 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	75 mg bid QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	150 mg qd QAW039

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	10 mg qd montelukas

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Reporting group title	Placebo

Reporting group description:

The study medication was administered in the clinic in the morning. On non-visit days, patients were instructed to take all three capsules in the morning between 08:00 and 11:00 from their QAW039/placebo medication kits. On all days, patients were instructed to take their 3 evening capsules of QAW039/placebo and their capsule of montelukast/placebo approximately 12 hours after their AM dose ± 30 minutes.

Subject analysis set title	QAW039 75 mg qd v/s QAW039 25 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 150 mg qd v/s QAW039 75 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 50 mg qd v/s QAW039 25 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 10 mg qd v/s QAW039 2 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 150 mg qd v/s QAW039 150 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 450 mg qd v/s QAW039 150 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 300 mg qd v/s QAW039 150 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 75 mg qd v/s QAW039 75 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Subject analysis set title	QAW039 300 mg qd v/s QAW039 75 mg bid
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Comparison between regimens of selected doses

Primary: Dose-response results of trough Forced Expiratory Volume in 1 second (FEV1) after 12 weeks of treatment

End point title	Dose-response results of trough Forced Expiratory Volume in 1 second (FEV1) after 12 weeks of treatment[1][2]

End point description:

Forced Expiratory Volume in 1 second (FEV1) (measured in litters), and the trough measurement is taken 24 hours after morning dose on the previous day.

End point type	Primary

End point timeframe:

Week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been reported for this primary end point.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for the Placebo arm since it is not the arm that is being evaluated for this endpoint.

End point values	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039	30 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	54	48	55
Units: Liters				
number (confidence interval 95%)				

Absolute increase over Placebo	0.0054 (0 to 0.1473)	0.0189 (0 to 0.161)	0.0476 (0 to 0.1647)	0.0881 (0 to 0.1685)
% of projected effect of maximum QAW039 dose	4.9 (0 to 99.6)	16.8 (0 to 100)	42.4 (0 to 100)	95.5 (0 to 100)

End point values	50 mg qd QAW039	75 mg qd QAW039	150 mg bid QAW039	300 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	58	56	57
Units: Liters				
number (confidence interval 95%)				
Absolute increase over Placebo	0.0954 (0 to 0.1697)	0.1019 (0.0009 to 0.1708)	0.1122 (0.0036 to 0.1753)	0.1097 (0.0065 to 0.1739)
% of projected effect of maximum QAW039 dose	98.2 (0.8 to 100)	99.1 (16.7 to 100)	100.0 (67.3 to 221.9)	100 (66.7 to 100)

End point values	450 mg qd QAW039	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	52	60	52
Units: Liters				
number (confidence interval 95%)				
Absolute increase over Placebo	0.1107 (0.0104 to 0.1746)	0.0027 (0 to 10.1113)	0.1043 (0.0004 to 0.1668)	0.1104 (0.0016 to 0.1713)
% of projected effect of maximum QAW039 dose	0 (0 to 0)	5.8 (0 to 82.6)	100 (11.4 to 105.2)	100 (40.4 to 170)

End point values	150 mg qd QAW039	10 mg qd montelukas		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	139		
Units: Liters				
number (confidence interval 95%)				
Absolute increase over Placebo	0.1078 (0.0029 to 0.1725)	0.1324 (0.0427 to 0.2252)		
% of projected effect of maximum QAW039 dose	99.9 (33.3 to 100.0)	119.3 (32.1 to 227.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the Asthma Control Questionnaire (ACQ7) score from baseline

to week 12

End point title	Change in the Asthma Control Questionnaire (ACQ7) score from baseline to week 12

End point description:

The Asthma Control Questionnaire (ACQ) is a validated questionnaire consisting of 7 items: 5 on symptom assessment, 1 on rescue bronchodilator use and 1 assessing the patients Forced Expiratory Volume in 1 second (FEV1) result against the predicted result for a person of similar age and stature. Each item is graded on a scale of 0-6, and a mean score of 1.5 or greater is considered to demonstrate inadequate asthma control in this trial. The minimal important difference that is considered clinically important is a change of 0.5 in the mean score.

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039	30 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	54	48	55
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Change from baseline	-0.758 (-0.954 to -0.561)	-0.636 (-0.836 to -0.436)	-0.603 (-0.806 to -0.399)	-0.612 (-0.805 to -0.42)
Difference to Placebo	-0.127 (-0.351 to 0.098)	-0.005 (-0.23 to 0.22)	0.029 (-0.202 to 0.259)	0.019 (-0.197 to 0.235)
Difference to Montelukast	-0.078 (-0.3 to 0.144)	0.044 (-0.179 to 0.267)	0.077 (-0.152 to 0.306)	0.068 (-0.149 to 0.284)

End point values	50 mg qd QAW039	75 mg qd QAW039	150 mg bid QAW039	300 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	58	56	57
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Change from baseline	-0.529 (-0.722 to -0.337)	-0.617 (-0.805 to -0.428)	-0.548 (-0.731 to -0.365)	-0.721 (-0.908 to -0.533)
Difference to Placebo	0.102 (-0.119 to 0.323)	0.015 (-0.2 to 0.299)	0.083 (-0.126 to 0.293)	-0.089 (-0.303 to 0.124)
Difference to Montelukast	0.151 (-0.068 to 0.37)	0.063 (-0.151 to 0.277)	0.132 (-0.077 to 0.34)	-0.041 (-0.253 to 0.171)

End point values	450 mg qd QAW039	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	52	60	52
Units: Units on a scale				
least squares mean (confidence interval				

95%)				
Change from baseline	-0.666 (-0.795 to -0.537)	-0.681 (-0.872 to -0.49)	-0.563 (-0.745 to -0.381)	-0.737 (-0.95 to -0.523)
Difference to Placebo	-0.035 (-0.2 to 0.131)	-0.05 (-0.27 to 0.17)	0.068 (-0.141 to 0.277)	-0.105 (-0.345 to 0.134)
Difference to Montelukast	0.014 (-0.15 to 0.178)	-0.001 (-0.219 to 0.217)	0.117 (-0.091 to 0.324)	-0.057 (-0.294 to 0.181)

End point values	150 mg qd QAW039	10 mg qd montelukas	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	139	137	
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Change from baseline	-0.653 (-0.847 to -0.46)	-0.68 (-0.806 to -0.554)	-0.631 (-0.761 to -0.502)	
Difference to Placebo	-0.022 (-0.243 to 0.199)	-0.049 (-0.213 to 0.115)	0 (0 to 0)	
Difference to Montelukast	0.026 (-0.194 to 0.246)	0 (0 to 0)	0.049 (-0.115 to 0.213)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the dose response relationship among QAW039 doses with respect to Forced Expiratory Volume in 1 second (FEV1) after 12 weeks treatment

End point title	Change in the dose response relationship among QAW039 doses with respect to Forced Expiratory Volume in 1 second (FEV1) after 12 weeks treatment

End point description:

Forced Expiratory Volume in 1 second (FEV1) (measured in liters), and the measurement is taken 24 hours after the morning dose on the previous day.

End point type	Secondary

End point timeframe:

Week 12

End point values	QAW039 150 mg qd v/s QAW039 75 mg bid	QAW039 75 mg qd v/s QAW039 25 mg bid	QAW039 50 mg qd v/s QAW039 25 mg bid	QAW039 10 mg qd v/s QAW039 2 mg bid
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	105	118	111	100
Units: Liter				
least squares mean (confidence interval 95%)	0 (-0.0556 to 0.017)	0 (-0.0697 to 0.0423)	0 (-0.107 to 0.0313)	0.0111 (-0.0303 to 0.1515)

End point values	QAW039 150 mg qd v/s QAW039 150 mg bid	QAW039 450 mg qd v/s QAW039 150 mg bid	QAW039 300 mg qd v/s QAW039 150 mg bid	QAW039 75 mg qd v/s QAW039 75 mg bid
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	109	190	113	110
Units: Liter				
least squares mean (confidence interval 95%)	0 (-0.0755 to 0.0114)	0 (-0.048 to 0.02)	0 (-0.0576 to 0.016)	0 (-0.0889 to 0.0125)

End point values	QAW039 300 mg qd v/s QAW039 75 mg bid			
Subject group type	Subject analysis set			
Number of subjects analysed	109			
Units: Liter				
least squares mean (confidence interval 95%)	0 (-0.0397 to 0.0221)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of efficacy of QAW039 with that of montelukast as an add-on therapy to Inhaled Corticosteroids (ICS)

End point title	Comparison of efficacy of QAW039 with that of montelukast as an add-on therapy to Inhaled Corticosteroids (ICS)[3]

End point description:

Forced Expiratory Volume in 1 second (FEV1) measurement taken 24 hours after the morning dose on the previous day. The Asthma Control Questionnaire (ACQ)consisting of 7 items: 5 on system assessment, 1 on rescue bronchodilator use and 1 assessing the patients for FEV1 result against the predicted result for a person of similar age and stature. Each item is graded on a scale of 0-6, and a mean score of 1.5 or greater is considered to demonstrate inadequate asthma control in this trial. The minimal important difference that is considered clinically important is a change of 0.5 in the mean score.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for the Montelukast arm since it is not the arm that is being evaluated for this endpoint.

End point values	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039	30 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	54	48	55
Units: Liter				
least squares mean (confidence interval 95%)	-0.058 (-0.18 to 0.063)	-0.046 (-0.167 to 0.074)	-0.132 (-0.258 to -0.005)	-0.042 (-0.161 to 0.076)

End point values	50 mg qd QAW039	75 mg qd QAW039	150 mg bid QAW039	300 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	58	56	57
Units: Liter				
least squares mean (confidence interval 95%)	-0.082 (-0.204 to 0.041)	-0.022 (-0.14 to 0.096)	-0.07 (-0.187 to 0.047)	-0.014 (-0.13 to 0.103)

End point values	450 mg qd QAW039	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	52	60	52
Units: Liter				
least squares mean (confidence interval 95%)	-0.056 (-0.145 to 0.032)	-0.147 (-0.267 to -0.027)	0.012 (-0.103 to 0.126)	0.046 (-0.081 to 0.173)

End point values	150 mg qd QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	137		
Units: Liter				
least squares mean (confidence interval 95%)	0.031 (-0.089 to 0.15)	-0.134 (-0.222 to -0.045)		

Statistical analyses

No statistical analyses for this end point

Secondary: To assess the effect of QAW039 on asthma symptoms as measured by the Juniper asthma control diary (JACD).

End point title	To assess the effect of QAW039 on asthma symptoms as measured by the Juniper asthma control diary (JACD).

End point description:

The asthma control diary mimics the Asthma Control Questionnaire (ACQ), but is recorded daily by the patient, rather than at each visit. All patients were instructed to complete the patient diary twice daily, once in the
morning and once approximately 12 h later in the evening from screening through the study. As for the ACQ, the ACD consists of 7 questions.

The Modified Full analysis set was used. The modified full analysis set (mFAS) included all randomized patients who received at least one dose of study drug and who had valid baseline and post baseline spirometry data.

End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	1 mg qd QAW039	3 mg qd QAW039	10 mg qd QAW039	30 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	34	30	39
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	1.69 (± 0.546)	1.72 (± 0.583)	1.72 (± 0.606)	1.61 (± 0.58)
Post Baseline	1.44 (± 0.55)	1.59 (± 0.718)	1.43 (± 0.635)	1.51 (± 0.518)
Change from Baseline	-0.25 (± 0.446)	-0.12 (± 0.407)	-0.29 (± 0.526)	-0.09 (± 0.323)

End point values	50 mg qd QAW039	75 mg qd QAW039	150 mg bid QAW039	300 mg qd QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	39	55	37
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	1.74 (± 0.579)	1.86 (± 0.835)	1.65 (± 0.743)	1.86 (± 0.766)
Post Baseline	1.65 (± 0.651)	1.71 (± 1.007)	1.51 (± 0.713)	1.64 (± 0.662)
Change from Baseline	-0.09 (± 0.44)	-0.15 (± 0.589)	-0.14 (± 0.431)	-0.22 (± 0.512)

End point values	450 mg qd QAW039	2 mg bid QAW039	25 mg bid QAW039	75 mg bid QAW039
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	38	41	33
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	1.71 (± 0.721)	1.67 (± 0.605)	1.88 (± 0.784)	1.59 (± 0.662)
Post Baseline	1.49 (± 0.654)	1.49 (± 0.542)	1.68 (± 0.917)	1.45 (± 0.732)
Change from Baseline	-0.22 (± 0.47)	-0.18 (± 0.37)	-0.21 (± 0.646)	-0.14 (± 0.404)

End point values	150 mg qd QAW039	10 mg qd montelukas	Placebo	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	100	98	
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	1.77 (± 0.69)	1.7 (± 0.731)	1.79 (± 0.703)	
Post Baseline	1.55 (± 0.758)	1.47 (± 0.771)	1.64 (± 0.723)	
Change from Baseline	-0.21 (± 0.445)	-0.23 (± 0.46)	-0.15 (± 0.527)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	QAW039 450mg QD
Reporting group description:	
QAW039 450mg QD	
Reporting group title	Montelukast 10mg QD
Reporting group description:	
Montelukast 10mg QD	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	QAW039 low dose
Reporting group description:	
QAW039 low dose	
Reporting group title	QAW039 mid dose
Reporting group description:	
QAW039 mid dose	
Reporting group title	QAW039 top dose
Reporting group description:	
QAW039 top dose	

Serious adverse events	QAW039 450mg QD	Montelukast 10mg QD	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 133 (2.26%)	1 / 133 (0.75%)	2 / 136 (1.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostatic adenoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Injury, poisoning and procedural complications			

Foot fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Humerus fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	0 / 136 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	0 / 136 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	0 / 136 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Asthma exacerbation			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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
Meningitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 133 (0.00%)	0 / 136 (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 low dose	QAW039 mid dose	QAW039 top dose
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 201 (1.99%)	4 / 219 (1.83%)	2 / 212 (0.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostatic adenoma			
subjects affected / exposed	0 / 201 (0.00%)	1 / 219 (0.46%)	0 / 212 (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			
Foot fracture			

subjects affected / exposed	0 / 201 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
Humerus fracture			
subjects affected / exposed	1 / 201 (0.50%)	0 / 219 (0.00%)	0 / 212 (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			
Hypertension			
subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	0 / 212 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	0 / 212 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	0 / 212 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	0 / 212 (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
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	1 / 201 (0.50%)	0 / 219 (0.00%)	0 / 212 (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, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma exacerbation			
subjects affected / exposed	1 / 201 (0.50%)	1 / 219 (0.46%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 219 (0.00%)	0 / 212 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 201 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 219 (0.46%)	0 / 212 (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

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

Non-serious adverse events	QAW039 450mg QD	Montelukast 10mg QD	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 133 (16.54%)	27 / 133 (20.30%)	28 / 136 (20.59%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 133 (7.52%)	8 / 133 (6.02%)	8 / 136 (5.88%)
occurrences (all)	12	8	10
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	6 / 133 (4.51%)	4 / 133 (3.01%)	11 / 136 (8.09%)
occurrences (all)	6	4	11
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 133 (3.76%)	10 / 133 (7.52%)	7 / 136 (5.15%)
occurrences (all)	6	13	9
Upper respiratory tract infection			
subjects affected / exposed	3 / 133 (2.26%)	11 / 133 (8.27%)	4 / 136 (2.94%)
occurrences (all)	3	12	4

Non-serious adverse events	QAW039 low dose	QAW039 mid dose	QAW039 top dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 201 (14.93%)	40 / 219 (18.26%)	38 / 212 (17.92%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 201 (4.98%)	10 / 219 (4.57%)	9 / 212 (4.25%)
occurrences (all)	11	11	11
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 201 (1.99%)	5 / 219 (2.28%)	10 / 212 (4.72%)
occurrences (all)	4	6	10
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 201 (5.47%)	21 / 219 (9.59%)	15 / 212 (7.08%)
occurrences (all)	11	25	19
Upper respiratory tract infection			
subjects affected / exposed	9 / 201 (4.48%)	7 / 219 (3.20%)	8 / 212 (3.77%)
occurrences (all)	11	7	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 October 2011	The purpose of this amendment was to • widen the scope of the inclusion/exclusion criteria to allow more patients to participate, especially in Asia. These changes did not substantially change the study population and did not have an impact on the risk benefit for the patients. To allow patients with no suitable validated ACD translation to participate in the study, as translations are not currently available for all countries and languages. The Asthma Control Diary in the trial was not a safety measure in this trial, since the patients' safety on trial is monitored via the twice daily assessments recorded in the electronic diary. • to address some inconsistencies and errors in the text which were identified since the original submission.
26 March 2012	Due to the thorough QT (TQT) study (approximately 240 patients) that was performed in parallel with this study, ECG assessment in the current study was amended to reduce the patient burden. A2206 patients, who agreed to the extended PK sub-study, continued with comprehensive ECG assessment at all protocol defined time points, whereas, for the remainder of patients in study A2206 underwent, ECGs before predose and 1 hour post dose with optional ECGs at 3 and 6 hours post dose was retained while 3 and 6 hours post dose ECGs become optional.
12 October 2012	Due to lower than expected enrolment into the sputum sub-study, it was necessary to amend the protocol to allow patients to be placed into the restricted (1 of 3 treatment groups; QAW 450 mg qd, montelukast 10 mg qd and placebo) randomization list, even if they were not part of the sputum sub-study. This ensured that the total number of patients randomized to each of these three groups in the whole population remained at 125 in each group (to give 100 completers in each of these three groups, assuming a 20% dropout rate). In this way, sample size requirements for the primary endpoint analyses were met, without impact on the total number of patients required in the study.

01 February 2013	In order to assess the consistency in dose response between the Japanese and global populations, results from statistical modeling and simulations demonstrated that approximately 125 randomized Japanese patients should be included. This would provide a sample size of approximately 100 completed Japanese patients allowing for a 20% drop-out rate. Based on recruitment projections, additional time for recruitment in the clinical centers in Japan was required to allow for the requisite number of Japanese patients to be recruited. Therefore, to collect the planned Japanese sample size, continuation of Japanese enrollment and two database locks were performed. The first database lock was to be performed after approximately 950 randomized patients (including all patients, Japanese and non-Japanese) completed the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported