



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 | 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 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

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|------------------|----------------------|
| 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: