



## Clinical trial results:

**A multicenter, randomized, double-blind, parallel-group, placebo-controlled study of fevipiprant once daily plus standard-of-care (SoC) for assessment of the efficacy in reduction of nasal polyps size in patients with nasal polyposis and concomitant asthma**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-002073-22 |
| Trial protocol           | DE NL CZ BE IT |
| Global end of trial date | 10 June 2020   |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 25 December 2020 |
| First version publication date | 25 December 2020 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CQAW039A2322 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03681093 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                           |
|------------------------------|-------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Novartis Pharma AG                                                                        |
| Sponsor organisation address | CH-4002, Basel, Switzerland,                                                              |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |

Notes:

### Paediatric regulatory details

|                                                                      |    |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|                                                      |              |
|------------------------------------------------------|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 10 June 2020 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 10 June 2020 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of fevipirant 150 mg and 450 mg compared to placebo in the reduction of nasal polyps size and the effect on symptoms, quality of life and smell via patient-reported outcomes in patients with nasal polyposis and concomitant asthma.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

At the start of the Run-in period, all patients were provided with a short-acting bronchodilator (SABA, such as salbutamol 100 mcg or albuterol 90 mcg) which they were instructed to use throughout the study as rescue medication on an 'as needed basis'.

Background therapy:

During the Run-in period and Treatment period patients utilized mometasone furoate spray (200 µg once daily, administered as two 50 µg actuations into each nostril).

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 26 March 2019 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Argentina: 38    |
| Country: Number of subjects enrolled | Belgium: 6       |
| Country: Number of subjects enrolled | Canada: 7        |
| Country: Number of subjects enrolled | Czechia: 13      |
| Country: Number of subjects enrolled | Germany: 13      |
| Country: Number of subjects enrolled | Italy: 8         |
| Country: Number of subjects enrolled | Netherlands: 8   |
| Country: Number of subjects enrolled | Poland: 4        |
| Country: Number of subjects enrolled | United States: 1 |
| Worldwide total number of subjects   | 98               |
| EEA total number of subjects         | 52               |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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)                      | 82 |
| From 65 to 84 years                       | 16 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in 25 investigative sites in 9 countries.

### Pre-assignment

Screening details:

After the screening, participants went through a Run-in period of 4 weeks where they utilized mometasone furoate spray into each nostril. Afterwards, patients were randomized in 1:1:1 ratio in either of the 3 arms and continued to use the mometasone furoate spray.

### Period 1

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

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | Fevipirant 150 mg |

Arm description:

Fevipirant (QAW039) 150 mg once daily orally

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

Dosage and administration details:

Fevipirant (QAW039) 150 mg once daily administered orally for 16 weeks.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Fevipirant 450 mg |
|------------------|-------------------|

Arm description:

Fevipirant (QAW039) 450 mg once daily orally

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

Dosage and administration details:

Fevipirant (QAW039) 450 mg once daily administered orally for 16 weeks.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Placebo once daily orally

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|                                        |          |
|----------------------------------------|----------|
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Placebo once daily administered orally for 16 weeks.

| <b>Number of subjects in period 1</b> | Fevipirant 150 mg | Fevipirant 450 mg | Placebo |
|---------------------------------------|-------------------|-------------------|---------|
| Started                               | 32                | 34                | 32      |
| Completed                             | 32                | 32                | 31      |
| Not completed                         | 0                 | 2                 | 1       |
| Subject decision                      | -                 | 2                 | 1       |

## Baseline characteristics

### Reporting groups

|                                              |                   |
|----------------------------------------------|-------------------|
| Reporting group title                        | Fevipirant 150 mg |
| Reporting group description:                 |                   |
| Fevipirant (QAW039) 150 mg once daily orally |                   |
| Reporting group title                        | Fevipirant 450 mg |
| Reporting group description:                 |                   |
| Fevipirant (QAW039) 450 mg once daily orally |                   |
| Reporting group title                        | Placebo           |
| Reporting group description:                 |                   |
| Placebo once daily orally                    |                   |

| Reporting group values                             | Fevipirant 150 mg | Fevipirant 450 mg | Placebo |
|----------------------------------------------------|-------------------|-------------------|---------|
| Number of subjects                                 | 32                | 34                | 32      |
| Age categorical                                    |                   |                   |         |
| Units: Subjects                                    |                   |                   |         |
| In utero                                           | 0                 | 0                 | 0       |
| Preterm newborn infants (gestational age < 37 wks) | 0                 | 0                 | 0       |
| Newborns (0-27 days)                               | 0                 | 0                 | 0       |
| Infants and toddlers (28 days-23 months)           | 0                 | 0                 | 0       |
| Children (2-11 years)                              | 0                 | 0                 | 0       |
| Adolescents (12-17 years)                          | 0                 | 0                 | 0       |
| Adults (18-64 years)                               | 27                | 28                | 27      |
| From 65-84 years                                   | 5                 | 6                 | 5       |
| 85 years and over                                  | 0                 | 0                 | 0       |
| Age Continuous                                     |                   |                   |         |
| Units: years                                       |                   |                   |         |
| arithmetic mean                                    | 50.8              | 50.9              | 48.5    |
| standard deviation                                 | ± 13.36           | ± 13.10           | ± 13.43 |
| Sex: Female, Male                                  |                   |                   |         |
| Units: participants                                |                   |                   |         |
| Female                                             | 16                | 15                | 12      |
| Male                                               | 16                | 19                | 20      |
| Race/Ethnicity, Customized                         |                   |                   |         |
| Units: Subjects                                    |                   |                   |         |
| White                                              | 32                | 34                | 31      |
| Black                                              | 0                 | 0                 | 1       |

| Reporting group values                             | Total |  |  |
|----------------------------------------------------|-------|--|--|
| Number of subjects                                 | 98    |  |  |
| Age categorical                                    |       |  |  |
| Units: Subjects                                    |       |  |  |
| In utero                                           | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                               | 0     |  |  |

|                                                                         |    |  |  |
|-------------------------------------------------------------------------|----|--|--|
| Infants and toddlers (28 days-23 months)                                | 0  |  |  |
| Children (2-11 years)                                                   | 0  |  |  |
| Adolescents (12-17 years)                                               | 0  |  |  |
| Adults (18-64 years)                                                    | 82 |  |  |
| From 65-84 years                                                        | 16 |  |  |
| 85 years and over                                                       | 0  |  |  |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Sex: Female, Male<br>Units: participants                                |    |  |  |
| Female                                                                  | 43 |  |  |
| Male                                                                    | 55 |  |  |
| Race/Ethnicity, Customized<br>Units: Subjects                           |    |  |  |
| White                                                                   | 97 |  |  |
| Black                                                                   | 1  |  |  |

## End points

### End points reporting groups

|                                              |                   |
|----------------------------------------------|-------------------|
| Reporting group title                        | Fevipirant 150 mg |
| Reporting group description:                 |                   |
| Fevipirant (QAW039) 150 mg once daily orally |                   |
| Reporting group title                        | Fevipirant 450 mg |
| Reporting group description:                 |                   |
| Fevipirant (QAW039) 450 mg once daily orally |                   |
| Reporting group title                        | Placebo           |
| Reporting group description:                 |                   |
| Placebo once daily orally                    |                   |

### Primary: Change from baseline in Nasal Polyp Score at Week 16

|                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                     | Change from baseline in Nasal Polyp Score at Week 16 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                      |
| Nasal Polyp Score (NPS) is the sum of the right and left nostril scores, as evaluated by means of nasal endoscopy. Total score ranges from 0 to 8 (scored 0 [no polyp] to 4 [large polyps] for each nostril), with a lower score indicating smaller-sized polyps.<br>Baseline NPS is defined as the last measurement performed on or before the date of randomization.<br>A negative change from baseline in NPS is considered a favorable outcome. |                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                      | Primary                                              |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                      |
| Baseline, Week 16                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                      |

| End point values                    | Fevipirant 150 mg | Fevipirant 450 mg | Placebo         |  |
|-------------------------------------|-------------------|-------------------|-----------------|--|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group |  |
| Number of subjects analysed         | 31                | 32                | 28              |  |
| Units: score on scale               |                   |                   |                 |  |
| least squares mean (standard error) | 0.20 (± 0.224)    | -0.10 (± 0.216)   | 0.14 (± 0.233)  |  |

### Statistical analyses

|                                         |                                                 |
|-----------------------------------------|-------------------------------------------------|
| Statistical analysis title              | Change NPS score - fevipirant 150 mg vs placebo |
| Comparison groups                       | Fevipirant 150 mg v Placebo                     |
| Number of subjects included in analysis | 59                                              |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | superiority                                     |
| P-value                                 | = 0.979 <sup>[1]</sup>                          |
| Method                                  | Mixed Model for Repeated Measures (MMRM)        |
| Parameter estimate                      | Least Squares (LS) Mean                         |
| Point estimate                          | 0.05                                            |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.59                      |
| upper limit          | 0.7                        |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.323                      |

Notes:

[1] - Adjusted p-value is reported. The adjusted p-value was obtained from the Dunnett Multiplicity Correction applied to control the Type I error for the primary analysis.

|                                         |                                                 |
|-----------------------------------------|-------------------------------------------------|
| <b>Statistical analysis title</b>       | Change NPS score - fevipirant 450 mg vs placebo |
| Comparison groups                       | Fevipirant 450 mg v Placebo                     |
| Number of subjects included in analysis | 60                                              |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | superiority                                     |
| P-value                                 | = 0.656 <sup>[2]</sup>                          |
| Method                                  | MMRM                                            |
| Parameter estimate                      | LS Mean                                         |
| Point estimate                          | -0.25                                           |
| Confidence interval                     |                                                 |
| level                                   | 95 %                                            |
| sides                                   | 2-sided                                         |
| lower limit                             | -0.88                                           |
| upper limit                             | 0.39                                            |
| Variability estimate                    | Standard error of the mean                      |
| Dispersion value                        | 0.319                                           |

Notes:

[2] - Adjusted p-value is reported. The adjusted p-value was obtained from the Dunnett Multiplicity Correction applied to control the Type I error for the primary analysis.

### Secondary: Change from baseline in Nasal Congestion Score at Week 16

|                                                                                                                                                                                                                                                                                                                                                             |                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                             | Change from baseline in Nasal Congestion Score at Week 16 |
| End point description:                                                                                                                                                                                                                                                                                                                                      |                                                           |
| The nasal congestion score (NCS) is assessed via a questionnaire where patients are asked "Is your nose blocked?" with responses ranging from 0 = not at all, to 3=severe.<br>Baseline NCS is defined as the last assessment performed on or before the date of randomization.<br>A negative change from baseline in NCS is considered a favorable outcome. |                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                              | Secondary                                                 |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                        |                                                           |
| Baseline, Week 16                                                                                                                                                                                                                                                                                                                                           |                                                           |

| End point values                    | Fevipirant 150 mg | Fevipirant 450 mg | Placebo         |  |
|-------------------------------------|-------------------|-------------------|-----------------|--|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group |  |
| Number of subjects analysed         | 31                | 32                | 28              |  |
| Units: score on scale               |                   |                   |                 |  |
| least squares mean (standard error) | -0.15 (± 0.172)   | -0.35 (± 0.171)   | -0.80 (± 0.181) |  |

## Statistical analyses

|                                         |                                                 |
|-----------------------------------------|-------------------------------------------------|
| <b>Statistical analysis title</b>       | Change NCS score - fevipirant 150 mg vs placebo |
| Comparison groups                       | Fevipirant 150 mg v Placebo                     |
| Number of subjects included in analysis | 59                                              |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | superiority                                     |
| P-value                                 | = 0.012 <sup>[3]</sup>                          |
| Method                                  | MMRM                                            |
| Parameter estimate                      | LS Mean                                         |
| Point estimate                          | 0.64                                            |
| Confidence interval                     |                                                 |
| level                                   | 95 %                                            |
| sides                                   | 2-sided                                         |
| lower limit                             | 0.15                                            |
| upper limit                             | 1.14                                            |
| Variability estimate                    | Standard error of the mean                      |
| Dispersion value                        | 0.249                                           |

Notes:

[3] - Unadjusted p-value

|                                         |                                                 |
|-----------------------------------------|-------------------------------------------------|
| <b>Statistical analysis title</b>       | Change NCS score - fevipirant 450 mg vs placebo |
| Comparison groups                       | Fevipirant 450 mg v Placebo                     |
| Number of subjects included in analysis | 60                                              |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | superiority                                     |
| P-value                                 | = 0.074 <sup>[4]</sup>                          |
| Method                                  | MMRM                                            |
| Parameter estimate                      | LS Mean                                         |
| Point estimate                          | 0.45                                            |
| Confidence interval                     |                                                 |
| level                                   | 95 %                                            |
| sides                                   | 2-sided                                         |
| lower limit                             | -0.04                                           |
| upper limit                             | 0.94                                            |
| Variability estimate                    | Standard error of the mean                      |
| Dispersion value                        | 0.248                                           |

Notes:

[4] - Unadjusted p-value

## Secondary: Change from baseline in Quality of Life as assessed by the SNOT-22 questionnaire at Week 16

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Change from baseline in Quality of Life as assessed by the SNOT-22 questionnaire at Week 16 |
|-----------------|---------------------------------------------------------------------------------------------|

**End point description:**

SNOT-22 (Sino-Nasal Outcome Test) Questionnaire is a disease specific Health-Related Quality of Life (HRQoL) measure that comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant is asked to rate how severe each problem had been for them over the past 2 weeks on a scale from 0 (no problem) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating better HRQoL. Baseline SNOT-22 is defined as the last assessment performed on or before the date of randomization. A negative change from baseline in SNOT-22 is considered a favorable outcome.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 16

| End point values                    | Fevipirant 150 mg    | Fevipirant 450 mg     | Placebo              |  |
|-------------------------------------|----------------------|-----------------------|----------------------|--|
| Subject group type                  | Reporting group      | Reporting group       | Reporting group      |  |
| Number of subjects analysed         | 31                   | 32                    | 28                   |  |
| Units: score on scale               |                      |                       |                      |  |
| least squares mean (standard error) | -3.23 ( $\pm$ 3.349) | -10.61 ( $\pm$ 3.358) | -8.44 ( $\pm$ 3.571) |  |

**Statistical analyses**

|                                         |                                               |
|-----------------------------------------|-----------------------------------------------|
| <b>Statistical analysis title</b>       | Change SNOT-22 - fevipirant 150 mg vs placebo |
| Comparison groups                       | Fevipirant 150 mg v Placebo                   |
| Number of subjects included in analysis | 59                                            |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | = 0.288 <sup>[5]</sup>                        |
| Method                                  | MMRM                                          |
| Parameter estimate                      | LS Mean                                       |
| Point estimate                          | 5.22                                          |
| Confidence interval                     |                                               |
| level                                   | 95 %                                          |
| sides                                   | 2-sided                                       |
| lower limit                             | -4.49                                         |
| upper limit                             | 14.93                                         |
| Variability estimate                    | Standard error of the mean                    |
| Dispersion value                        | 4.881                                         |

Notes:

[5] - Unadjusted p-value

|                                   |                                               |
|-----------------------------------|-----------------------------------------------|
| <b>Statistical analysis title</b> | Change SNOT-22 - fevipirant 450 mg vs placebo |
| Comparison groups                 | Fevipirant 450 mg v Placebo                   |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 60                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.661 <sup>[6]</sup>     |
| Method                                  | MMRM                       |
| Parameter estimate                      | LS Mean                    |
| Point estimate                          | -2.17                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -11.99                     |
| upper limit                             | 7.65                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 4.936                      |

Notes:

[6] - Unadjusted p-value

### Secondary: Change from baseline in sense of smell as assessed by the University of Pennsylvania Smell Identification Test (UPSIT) at Week 16

|                 |                                                                                                                                   |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in sense of smell as assessed by the University of Pennsylvania Smell Identification Test (UPSIT) at Week 16 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|

End point description:

The UPSIT (University of Pennsylvania Smell Identification Test) is a test that measures an individual's ability to detect odors. It consists of 4 workbooks of 10 pages each. On each page there is a different "scratch and sniff" strip which is embedded with a microencapsulated odorant and a question regarding the smell detected with a four-choice option for the response. The total number of questions in UPSIT is 40. The number of correct responses regarding the smells being experienced is summed to provide a total score that ranges from 0 to 40, with a higher score indicating a better sense of smell. Baseline UPSIT is defined as the last assessment performed on or before the date of randomization. A positive change from baseline in UPSIT is considered a favorable outcome.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 16

| End point values                    | Fevipirant 150 mg | Fevipirant 450 mg | Placebo         |  |
|-------------------------------------|-------------------|-------------------|-----------------|--|
| Subject group type                  | Reporting group   | Reporting group   | Reporting group |  |
| Number of subjects analysed         | 31                | 32                | 28              |  |
| Units: score on scale               |                   |                   |                 |  |
| least squares mean (standard error) | 1.05 (± 1.242)    | 4.95 (± 1.259)    | 0.44 (± 1.315)  |  |

### Statistical analyses

|                            |                                             |
|----------------------------|---------------------------------------------|
| Statistical analysis title | Change UPSIT - fevipirant 150 mg vs placebo |
| Comparison groups          | Fevipirant 150 mg v Placebo                 |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 59                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.735 <sup>[7]</sup>     |
| Method                                  | MMRM                       |
| Parameter estimate                      | LS Mean                    |
| Point estimate                          | 0.61                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -2.98                      |
| upper limit                             | 4.21                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 1.809                      |

Notes:

[7] - Unadjusted p-value

|                                         |                                             |
|-----------------------------------------|---------------------------------------------|
| <b>Statistical analysis title</b>       | Change UPSIT - fevipirant 450 mg vs placebo |
| Comparison groups                       | Fevipirant 450 mg v Placebo                 |
| Number of subjects included in analysis | 60                                          |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           | superiority                                 |
| P-value                                 | = 0.015 <sup>[8]</sup>                      |
| Method                                  | MMRM                                        |
| Parameter estimate                      | LS Mean                                     |
| Point estimate                          | 4.51                                        |
| Confidence interval                     |                                             |
| level                                   | 95 %                                        |
| sides                                   | 2-sided                                     |
| lower limit                             | 0.89                                        |
| upper limit                             | 8.13                                        |
| Variability estimate                    | Standard error of the mean                  |
| Dispersion value                        | 1.821                                       |

Notes:

[8] - Unadjusted p-value

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment until end of study treatment plus 2 weeks post treatment, up to Week 18.

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus 2 weeks post treatment.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Fevipirant 150 mg |
|-----------------------|-------------------|

Reporting group description:

Fevipirant (QAW039) 150 mg once daily orally

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Fevipirant 450 mg |
|-----------------------|-------------------|

Reporting group description:

Fevipirant (QAW039) 450 mg once daily orally

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo once daily orally

| Serious adverse events                            | Fevipirant 150 mg | Fevipirant 450 mg | Placebo        |
|---------------------------------------------------|-------------------|-------------------|----------------|
| Total subjects affected by serious adverse events |                   |                   |                |
| subjects affected / exposed                       | 0 / 32 (0.00%)    | 0 / 34 (0.00%)    | 0 / 32 (0.00%) |
| number of deaths (all causes)                     | 0                 | 0                 | 0              |
| number of deaths resulting from adverse events    | 0                 | 0                 | 0              |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Fevipirant 150 mg | Fevipirant 450 mg | Placebo          |
|-------------------------------------------------------|-------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events |                   |                   |                  |
| subjects affected / exposed                           | 17 / 32 (53.13%)  | 13 / 34 (38.24%)  | 11 / 32 (34.38%) |
| Vascular disorders                                    |                   |                   |                  |
| Hypertension                                          |                   |                   |                  |
| subjects affected / exposed                           | 0 / 32 (0.00%)    | 1 / 34 (2.94%)    | 0 / 32 (0.00%)   |
| occurrences (all)                                     | 0                 | 1                 | 0                |
| General disorders and administration site conditions  |                   |                   |                  |

|                                                                                  |                     |                     |                     |
|----------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)          | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 32 (6.25%)<br>2 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                                  |                     |                     |                     |
| Asthma<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 32 (6.25%)<br>2 | 3 / 34 (8.82%)<br>3 | 1 / 32 (3.13%)<br>1 |
| Cough<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)             | 2 / 32 (6.25%)<br>2 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)           | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Paranasal sinus inflammation<br>subjects affected / exposed<br>occurrences (all) | 0 / 32 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 2 / 32 (6.25%)<br>2 |
| Respiratory disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 32 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 32 (3.13%)<br>1 |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |
| Investigations                                                                   |                     |                     |                     |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)            | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Blood creatine phosphokinase increased                                           |                     |                     |                     |

|                                                                                                                     |                     |                     |                     |
|---------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                    | 0 / 32 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 32 (3.13%)<br>1 |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                                                | 2 / 32 (6.25%)<br>2 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                                                | 2 / 32 (6.25%)<br>2 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>Contusion<br>subjects affected / exposed<br>occurrences (all)     | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Facial paralysis<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                                        | 2 / 32 (6.25%)<br>4 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 32 (3.13%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 |
| Tympanic membrane perforation<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 32 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 32 (0.00%)<br>0 |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Eye disorders                                   |                |                |                |
| Conjunctival haemorrhage                        |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Gastrointestinal disorders                      |                |                |                |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Mouth ulceration                                |                |                |                |
| subjects affected / exposed                     | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Tongue discomfort                               |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Vomiting                                        |                |                |                |
| subjects affected / exposed                     | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Alopecia                                        |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Scab                                            |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Renal and urinary disorders                     |                |                |                |
| Pollakiuria                                     |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Arthritis                                       |                |                |                |
| subjects affected / exposed                     | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Infections and infestations                     |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Acute sinusitis             |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)           | 0              | 0              | 1              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Ear infection               |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gastric infection           |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gastroenteritis viral       |                |                |                |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Gingivitis                  |                |                |                |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Influenza                   |                |                |                |
| subjects affected / exposed | 2 / 32 (6.25%) | 1 / 34 (2.94%) | 2 / 32 (6.25%) |
| occurrences (all)           | 2              | 1              | 2              |
| Laryngitis                  |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 2 / 32 (6.25%) |
| occurrences (all)           | 1              | 0              | 2              |
| Oral herpes                 |                |                |                |
| subjects affected / exposed | 1 / 32 (3.13%) | 2 / 34 (5.88%) | 0 / 32 (0.00%) |
| occurrences (all)           | 1              | 2              | 0              |
| Otitis media                |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Pharyngitis                 |                |                |                |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |

|                                         |                |                |                |
|-----------------------------------------|----------------|----------------|----------------|
| Sinusitis                               |                |                |                |
| subjects affected / exposed             | 3 / 32 (9.38%) | 1 / 34 (2.94%) | 2 / 32 (6.25%) |
| occurrences (all)                       | 3              | 1              | 2              |
| Tonsillitis                             |                |                |                |
| subjects affected / exposed             | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                       | 0              | 1              | 0              |
| Upper respiratory tract infection       |                |                |                |
| subjects affected / exposed             | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Viral upper respiratory tract infection |                |                |                |
| subjects affected / exposed             | 0 / 32 (0.00%) | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Metabolism and nutrition disorders      |                |                |                |
| Decreased appetite                      |                |                |                |
| subjects affected / exposed             | 0 / 32 (0.00%) | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
| occurrences (all)                       | 0              | 1              | 0              |
| Metabolic syndrome                      |                |                |                |
| subjects affected / exposed             | 1 / 32 (3.13%) | 0 / 34 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                           |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 12 December 2018  | The protocol was amended based on health authority feedback. Additional exclusion criteria were added to ensure that patients taking any of the prohibited medications were appropriately excluded. |
| 30 January 2019   | To align the safety requirements with other studies in the QAW039 program including addition of exclusion criteria.                                                                                 |
| 24 September 2019 | To provide clarification on the process for assessment of nasal endoscopy at baseline and management of protocol deviations in relation to the statistical analysis sets.                           |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported