# Clinical trial results:
# A 12-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma

## Summary

| | |
|---|---|
| EudraCT number | 2017-001272-40 |
| Trial protocol | SE ES BG DE HU IT RO |
| Global end of trial date | 01 August 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 February 2020 |
| First version publication date | 16 February 2020 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CQAW039A2317 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03226392 |
| 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, Novartis.email@novartis.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 01 August 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 August 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

to demonstrate the efficacy of fevipiprant 150 mg once daily compared with placebo, as measured by change from baseline in pre-dose forced expiratory volume in 1 second (FEV1) at the end of the 12-week active-treatment period

Protection of trial subjects:

to demonstrate the efficacy of fevipiprant 150 mg once daily compared with placebo, as measured by change from baseline in pre-dose forced expiratory volume in 1 second (FEV1) at the end of the 12-week active-treatment period

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 31 October 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Brazil: 41 |
| Country: Number of subjects enrolled | Bulgaria: 48 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Colombia: 28 |
| Country: Number of subjects enrolled | Germany: 11 |
| Country: Number of subjects enrolled | Hungary: 30 |
| Country: Number of subjects enrolled | India: 40 |
| Country: Number of subjects enrolled | Israel: 18 |
| Country: Number of subjects enrolled | Italy: 10 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 15 |
| Country: Number of subjects enrolled | Peru: 91 |
| Country: Number of subjects enrolled | Russian Federation: 109 |
| Country: Number of subjects enrolled | Spain: 43 |
| Country: Number of subjects enrolled | United States: 186 |
| Country: Number of subjects enrolled | Vietnam: 22 |
| Worldwide total number of subjects | 704 |
| EEA total number of subjects | 142 |

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) | 13 |
| Adults (18-64 years) | 563 |
| From 65 to 84 years | 128 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from centers in Brazil (8), Bulgaria (4), Canada (3), Colombia (4), Germany (5), Hungary (7), India (5), Israel (5), Italy (4), Peru (6), Republic of Korea (5), Russian Federation (14), Spain (8), United States (36), Vietnam (3).

### Pre-assignment

Screening details:

a Screening period of up to 2 weeks to assess eligibility during which patients practice completing the electronic peak expiratory flow eDiary/ePEF device.

### 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, Subject |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | QAW039 |

Arm description:

QAW039 once daily

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

Dosage and administration details:

150mg tablet

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Placebo once daily

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

Dosage and administration details:

tablets

| **Number of subjects in period 1[1]** | QAW039 | Placebo |
|---|---|---|
| Started | 352 | 350 |
| Completed | 341 | 344 |
| Not completed | 11 | 6 |
| Physician decision | 1 | - |
| Protocol Deviation | 1 | - |
| Adverse event, non-fatal | 1 | - |
| Subject/Guardian Decision | 7 | 6 |
| Lost to follow-up | 1 | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 2 patients in the placebo were mis-randomized, not treated, not included due to "technical problems

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | QAW039 |
| Reporting group description: QAW039 once daily | |
| Reporting group title | Placebo |
| Reporting group description: Placebo once daily | |

| Reporting group values | QAW039 | Placebo | Total |
|---|---|---|---|
| Number of subjects | 352 | 350 | 702 |
| Age categorical<br>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) | 7 | 6 | 13 |
| Adults (18-64 years) | 275 | 286 | 561 |
| From 65-84 years | 70 | 58 | 128 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 50.4 | 50.2 | |
| standard deviation | ± 14.87 | ± 14.39 | - |
| Sex: Female, Male<br>Units: | | | |
| Female | 216 | 218 | 434 |
| Male | 136 | 132 | 268 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Black | 26 | 18 | 44 |
| Asian | 41 | 46 | 87 |
| Native American | 12 | 12 | 24 |
| Pacific Islander | 2 | 0 | 2 |
| Other | 55 | 58 | 113 |
| Caucasian | 216 | 216 | 432 |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | QAW039 |
| Reporting group description: | |
| QAW039 once daily | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo once daily | |

| Primary: Change from baseline in pre-dose FEV1 | |
|---|---|
| End point title | Change from baseline in pre-dose FEV1 |
| End point description: | |
| Forced Expiratory Volume in one second (FEV1) is calculated as the volume of air forcibly exhaled in one second as measured by a spirometer. Baseline is defined as the last available FEV1 measurement taken prior to the first dose of randomized study drug | |
| End point type | Primary |
| End point timeframe: | |
| Week 12 | |

| End point values | QAW039 | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 352 | 350 | | |
| Units: Liters | | | | |
| least squares mean (standard error) | 0.126 (± 0.00177) | 0.157 (± 0.0177) | | |

### Statistical analyses

| Statistical analysis title | change from baseline in pre-dose FEV1 |
|---|---|
| Comparison groups | QAW039 v Placebo |
| Number of subjects included in analysis | 702 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.214 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.031 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.08 |
| upper limit | 0.018 |

## Secondary: Change from baseline in daytime asthma symptom score

| End point title | Change from baseline in daytime asthma symptom score |
|---|---|

End point description:

Daytime asthma symptoms are evaluated through four questions and each of them will be rated on a scale of 0 to 6. Higher scores indicate more severe asthma-related symptoms. A mean score is calculated for the responses to 4 questions

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

End point timeframe:

12 weeks

| End point values | QAW039 | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 352 | 350 | | |
| Units: Score | | | | |
| least squares mean (standard error) | -0.55 (± 0.034) | -0.45 (± 0.034) | | |

### Statistical analyses

| Statistical analysis title | change in mean daytime asthma symptom |
|---|---|
| Comparison groups | QAW039 v Placebo |
| Number of subjects included in analysis | 702 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.035 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.1 |
| Confidence interval | |
| level | Other: 0.04 % |
| sides | 2-sided |
| lower limit | -0.19 |
| upper limit | 0.01 |

## Secondary: Change from baseline in number of puffs of SABA taken per day

| End point title | Change from baseline in number of puffs of SABA taken per day |
|---|---|

End point description:

Daily use of SABA (the number of rescue medication puffs taken in the previous 12 hours) was recorded using a patient electronic diary (referred to as eDiary or eDiary/ePEF). Patients were instructed to routinely complete the patient diary twice daily – at the same time each morning and each evening, approximately 12 hours apart.

| | |
|---|---|
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| **End point values** | QAW039 | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 352 | 350 | | |
| Units: Number of puffs | | | | |
| least squares mean (standard error) | -0.89 (± 0.066) | -0.88 (± 0.066) | | |

**Statistical analyses**

| **Statistical analysis title** | change in mean total daily use of SABA |
|---|---|
| Comparison groups | QAW039 v Placebo |
| Number of subjects included in analysis | 702 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.893 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.17 |

**Secondary: Change from baseline in Asthma Quality of Life Questionnaire for 12 years and older (AQLQ+12) score**

| End point title | Change from baseline in Asthma Quality of Life Questionnaire for 12 years and older (AQLQ+12) score |
|---|---|

End point description:

AQLQ is a 32-item instrument administered as a self-assessment. AQLQ+12 is a modified version of AQLQ developed to measure functional impairments of participants aged 12-70 years. It is divided into 4 domains: activity limitation, symptoms, emotional function, and environmental stimuli. Participants were asked to recall their experiences during the last 2 weeks and respond to each question on a 7-point scale (1=severe impairment, 7=no impairment), where higher scores indicated "better quality of life." Overall AQLQ+12 score is the mean of all 32 responses

| | |
|---|---|
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | QAW039 | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 352 | 350 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | 0.77 (± 0.043) | 0.72 (± 0.043) | | |

**Statistical analyses**

| Statistical analysis title | change from baseline in AQLQ+12 |
|---|---|
| Comparison groups | QAW039 v Placebo |
| Number of subjects included in analysis | 702 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.448 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.061 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.07 |
| upper limit | 0.17 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: After signing informed consent to 30 days after last dose | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |
| **Reporting groups** | |
| Reporting group title | QAW039 150 mg |
| Reporting group description: QAW039 150 mg | |
| Reporting group title | Placebo |
| Reporting group description: Placebo | |

| Serious adverse events | QAW039 150 mg | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 352 (1.99%) | 3 / 350 (0.86%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 352 (0.00%) | 1 / 350 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |

| | | | |
|---|---|---|---|
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 352 (0.00%) | 1 / 350 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 352 (0.00%) | 1 / 350 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 3 / 352 (0.85%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 0 / 350 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| **Non-serious adverse events** | QAW039 150 mg | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 94 / 352 (26.70%) | 116 / 350 (33.14%) | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 352 (0.00%) | 5 / 350 (1.43%) | |
| occurrences (all) | 0 | 6 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 352 (1.42%) | 14 / 350 (4.00%) | |
| occurrences (all) | 5 | 15 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 46 / 352 (13.07%) | 61 / 350 (17.43%) | |
| occurrences (all) | 56 | 79 | |
| Cough | | | |
| subjects affected / exposed | 2 / 352 (0.57%) | 5 / 350 (1.43%) | |
| occurrences (all) | 2 | 7 | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 352 (0.85%) | 5 / 350 (1.43%) | |
| occurrences (all) | 5 | 7 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 6 / 352 (1.70%) | 4 / 350 (1.14%) | |
| occurrences (all) | 6 | 4 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 3 / 352 (0.85%) | 5 / 350 (1.43%) | |
| occurrences (all) | 3 | 5 | |
| Wheezing | | | |
| subjects affected / exposed | 1 / 352 (0.28%) | 4 / 350 (1.14%) | |
| occurrences (all) | 1 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 352 (1.99%) | 7 / 350 (2.00%) | |
| occurrences (all) | 7 | 8 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 9 / 352 (2.56%) | 6 / 350 (1.71%) | |
| occurrences (all) | 9 | 6 | |
| Influenza | | | |
| subjects affected / exposed | 4 / 352 (1.14%) | 1 / 350 (0.29%) | |
| occurrences (all) | 4 | 1 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 352 (2.84%) | 24 / 350 (6.86%) | |
| occurrences (all) | 10 | 27 | |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 352 (1.42%) | 2 / 350 (0.57%) | |
| occurrences (all) | 5 | 2 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 5 / 352 (1.42%) | 1 / 350 (0.29%) | |
| occurrences (all) | 5 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 352 (1.99%) | 10 / 350 (2.86%) | |
| occurrences (all) | 7 | 10 | |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 3 / 352 (0.85%) | 6 / 350 (1.71%) | |
| occurrences (all) | 3 | 6 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 12 / 352 (3.41%) | 8 / 350 (2.29%) | |
| occurrences (all) | 13 | 10 | |

## 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

None reported