Clinical trial results:
A multi-center, proof-of-mechanism study of multiple, oral doses of fevipiprant (QAW039) in COPD patients with eosinophilia

Summary

EudraCT number	2018-004267-32
Trial protocol	GB BE DE ES
Global end of trial date	16 January 2020

Results information

Result version number	v1 (current)
This version publication date	20 January 2021
First version publication date	20 January 2021

Trial information

Trial identification

Sponsor protocol code	CQAW039E12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03810183
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	16 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of the proof-of-mechanism study was to determine whether fevipiprant (QAW039), when administered to chronic obstructive pulmonary disease (COPD) patients with eosinophilic airway inflammation on standard of care therapy, reduced the burden of sputum eosinophilia.
Data from other trials did not confirm efficacy of fevipiprant and did not warrant the continuation of treatment in this study. As a result, this study was terminated early.

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.
Regarding rescue medication, the site was permitted to provide short-acting beta2 agonist to each subject, in accordance with local SmPC, for use prior to spirometry, sputum induction and/or as rescue medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 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	Germany: 6
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	4
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 4 investigative sites in 2 countries (Germany and United Kingdom).

Pre-assignment

Screening details:

Participants were randomized 3:2 to active (QAW039 450 mg orally daily) vs. placebo arms. Randomization was stratified by current smoking status (current vs. ex-smoker).

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	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	QAW039 450 mg

Arm description:

QAW039 (fevipiprant) 450 mg once daily for 6 weeks administered orally as a tablet.

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

Dosage and administration details:

QAW039 (fevipiprant) 450 mg once daily for 6 weeks

Arm title	Placebo

Arm description:

Placebo once daily for 6 weeks administered orally as a tablet.

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 for 6 weeks

Number of subjects in period 1	QAW039 450 mg	Placebo
Started	6	3
Completed	4	2
Not completed	2	1
Study terminated by Sponsor	2	1

Baseline characteristics

Reporting groups	
Reporting group title	QAW039 450 mg
Reporting group description:	
QAW039 (fevipiprant) 450 mg once daily for 6 weeks administered orally as a tablet.	
Reporting group title	Placebo
Reporting group description:	
Placebo once daily for 6 weeks administered orally as a tablet.	

Reporting group values	QAW039 450 mg	Placebo	Total
Number of subjects	6	3	9
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)	3	1	4
From 65-84 years	3	2	5
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	63.5	67.3	
standard deviation	± 9.71	± 6.35	-
Sex: Female, Male Units: Participants			
Female	1	1	2
Male	5	2	7
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	1
White	6	2	8

End points

End points reporting groups

Reporting group title	QAW039 450 mg
Reporting group description:	
QAW039 (fevipiprant) 450 mg once daily for 6 weeks administered orally as a tablet.	
Reporting group title	Placebo
Reporting group description:	
Placebo once daily for 6 weeks administered orally as a tablet.	

Primary: Change from baseline in sputum eosinophil percentage based on log-10 transformed scale at Week 6

End point title	Change from baseline in sputum eosinophil percentage based on log-10 transformed scale at Week 6[1]
End point description:	
Sputum eosinophil percentage of the total cell count was obtained from induced sputum samples. Sputum was processed to include preparation of slides for differential cellular count. As sputum eosinophil percentage has been found to follow a log-normal distribution, the analysis of this outcome measure was based on log10-transformed scale. The baseline measurement was defined as sputum eosinophil percentage prior to the first dosing (on log10-transformed scale).	
End point type	Primary
End point timeframe:	
Baseline, Week 6	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the limited sample size caused by early termination of the study, only descriptive statistics could be calculated.

End point values	QAW039 450 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Percentage				
arithmetic mean (standard deviation)	-0.43373 (± 0.39740)	-0.06689 (± 0.43094)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected from first dose of study treatment until last dose plus 30 days, up to a maximum of 72 days.	
Adverse event reporting additional description:	
Any signs or symptoms that occurs during study treatment plus the 30 days post treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	QAW039 450mg
Reporting group description:	
QAW039 450mg	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Total
Reporting group description:	
Total	

Serious adverse events	QAW039 450mg	Placebo	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 9 (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	QAW039 450mg	Placebo	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	2 / 3 (66.67%)	6 / 9 (66.67%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Foot fracture			

subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2019	The section for specific liver event and laboratory test trigger definitions and follow-up requirements was updated to reflect the change that ALT or AST ≥ 3 × ULN should be the trigger for discontinuation of study treatment (changed from ALT or AST ≥ 5 × ULN). Other liver events and triggers made redundant due to this change were deleted.
05 November 2019	Due to natural variation in blood eosinophils, inclusion criteria 7 (circulating eosinophils must be ≥ 300 cells/µL blood) was updated to add a three month window prior to the screening visit for the subject to meet the inclusion criteria. To facilitate the collection of blood eosinophil data prior to full screening, an optional pre-screen visit/hematology collection was added to the study design, scheduled from 3 months to the day prior to the screening visit. Exclusion criteria linked to safety was updated to require that they had to be met at both the screening and baseline visits, to align with the assessment schedule. The addition of a hematology sample on Day 21 allowed the stopping criteria related to white blood cells levels to be checked during the treatment period and for full interpretation of the ILC (innate lymphoid cell) data. Changes to the visit windows for each visit in the screening period were made to give greater flexibility to the site and subject for scheduling purposes, while maintaining the maximum screening window.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported