Clinical trial results:
A multicenter, open-label, 8 day treatment study to assess the pharmacokinetics, safety and tolerability of fevipiprant delivered via a once daily chewable tablet in children aged 6 to <12 years with asthma

Summary

EudraCT number	2018-003920-35
Trial protocol	ES
Global end of trial date	22 January 2020

Results information

Result version number	v1 (current)
This version publication date	27 July 2020
First version publication date	27 July 2020

Trial information

Trial identification

Sponsor protocol code	CQAW039B2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03650400
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-001315-PIP02-16
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	22 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the key pharmacokinetic parameters of fevipiprant at steady state (ss), after at least four consecutive days of dosing

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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	United States: 11
Worldwide total number of subjects	11
EEA total number of subjects	0

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)	11
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Six US centers recruited 11 subjects in the study. A total of 19 subjects were screened to enroll 11 subjects in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A Fevipiprant 75 mg

Arm description:

QAW039 75 mg Chewable tablet

Arm type	Experimental
Investigational medicinal product name	fevipiprant
Investigational medicinal product code	QAW039
Other name	
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg (cohort A) or 375 mg (cohort B).

Arm title	Cohort B Feviprant 375 mg

Arm description:

QAW039 375 mg Chewable tablet

Arm type	Cohort

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg
Started	6	5
Completed	6	0
Not completed	0	5
Study terminated by sponsor	-	5

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A Fevipiprant 75 mg
Reporting group description: QAW039 75 mg Chewable tablet	
Reporting group title	Cohort B Feviprant 375 mg
Reporting group description: QAW039 375 mg Chewable tablet	

Reporting group values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg	Total
Number of subjects	6	5	11
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)	6	5	11
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	8.2	9.4	
standard deviation	± 1.83	± 1.52	-
Sex: Female, Male Units: participants			
Female	4	3	7
Male	2	2	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	4	10
More than one race	0	1	1
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Cohort A Fevipiprant 75 mg
Reporting group description: QAW039 75 mg Chewable tablet	
Reporting group title	Cohort B Feviprant 375 mg
Reporting group description: QAW039 375 mg Chewable tablet	

Primary: Pharmacokinetics of fevipiprant by area under the curve from 0 to 24 hours at steady state (AUC0-24h,ss), after at least four consecutive days of dosing

End point title	Pharmacokinetics of fevipiprant by area under the curve from 0 to 24 hours at steady state (AUC0-24h,ss), after at least four consecutive days of dosing[1]
End point description: Area under the curve (AUC0-24h,ss), steady state following drug administration. No statistical analysis was planned for this primary outcome.	
End point type	Primary
End point timeframe: End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed for PK parameters and no PK samples were collected for PK analysis in Cohort B, because of early study termination.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[2]		
Units: h*ng/mL				
arithmetic mean (standard deviation)	2380 (± 1880)	()		

Notes:

[2] - Study terminated early.

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of fevipiprant by maximum plasma concentration at steady state (Cmax,ss), after at least four consecutive days of dosing

End point title	Pharmacokinetics of fevipiprant by maximum plasma concentration at steady state (Cmax,ss), after at least four consecutive days of dosing[3]
End point description: Maximum plasma concentration (Cmax,ss) steady state following drug administration. No statistical analysis was planned for this primary outcome.	
End point type	Primary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed for PK parameters and no PK samples were collected for PK analysis in Cohort B, because of early study termination.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[4]		
Units: ng/mL				
arithmetic mean (standard deviation)	394 (± 286)	()		

Notes:

[4] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of fevipiprant by oral clearance at steady state (CL/F), after at least four consecutive days of dosing

End point title	Pharmacokinetics of fevipiprant by oral clearance at steady state (CL/F), after at least four consecutive days of dosing[5]

End point description:

Oral clearance (CL/F), steady state following drug administration. No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed for PK parameters and no PK samples were collected for PK analysis in Cohort B, because of early study termination.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[6]		
Units: L/h				
arithmetic mean (standard deviation)	48.2 (± 32)	()		

Notes:

[6] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of fevipiprant by CL/F

End point title	Pharmacokinetics of fevipiprant by CL/F

End point description:

Pharmacokinetics of fevipiprant by oral clearance (CL/F) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[7]		
Units: L/h				
arithmetic mean (standard deviation)	48.2 (± 32.0)	()		

Notes:

[7] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of fevipiprant by Tmax,ss

End point title	Pharmacokinetics of fevipiprant by Tmax,ss

End point description:

Pharmacokinetics of fevipiprant by time of maximum plasma concentration (Tmax,ss) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[8]		
Units: hours				
arithmetic mean (standard deviation)	1.42 (± 0.916)	()		

Notes:

[8] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary excretion of fevipiprant

End point title	Urinary excretion of fevipiprant

End point description:

CLr, amount and fraction of dose excreted over the PK collection interval at steady state, of fevipiprant

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[9]		
Units: L/h				
arithmetic mean (standard deviation)	6.61 (± 4.88)	()		

Notes:

[9] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of fevipiprant by Cmin,ss

End point title	Pharmacokinetics of fevipiprant by Cmin,ss

End point description:

Pharmacokinetics of fevipiprant by minimum plasma concentration (Cmin,ss) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[10]		
Units: ng/mL				
arithmetic mean (standard deviation)	28.3 (± 13.8)	()		

Notes:

[10] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of the metabolite CCN362 by AUC0-24h,ss

End point title	Pharmacokinetics of the metabolite CCN362 by AUC0-24h,ss

End point description:

Pharmacokinetics of CCN362 metabolite of fevipiprant , area under the curve (AUC0-24h,ss) at steady state.

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[11]		
Units: h*ng/mL				
arithmetic mean (standard deviation)	2760 (± 1210)	()		

Notes:

[11] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of the metabolite CCN362 by Cmax,ss

End point title	Pharmacokinetics of the metabolite CCN362 by Cmax,ss

End point description:

Pharmacokinetics of CCN362 metabolite of fevipiprant by maximum plasma concentration (Cmax,ss) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[12]		
Units: ng/mL				
arithmetic mean (standard deviation)	302 (± 134)	()		

Notes:

[12] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of the metabolite CCN362 by Cmin,ss

End point title	Pharmacokinetics of the metabolite CCN362 by Cmin,ss

End point description:

Pharmacokinetics of CCN362 metabolite of fevipiprant by minimum plasma concentration (Cmin,ss) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[13]		
Units: ng/mL				
arithmetic mean (standard deviation)	33.6 (± 22.6)	()		

Notes:

[13] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of the metabolite CCN362 by Tmax,ss

End point title	Pharmacokinetics of the metabolite CCN362 by Tmax,ss

End point description:

Pharmacokinetics of CCN362 metabolite of fevipiprant by time of maximum plasma concentration (Tmax,ss) at steady state

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours)

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[14]		
Units: hours				
arithmetic mean (standard deviation)	2.69 (± 1.20)	()		

Notes:

[14] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary excretion of the metabolite, CCN362

End point title	Urinary excretion of the metabolite, CCN362

End point description:

CLr, amount and fraction of dose excreted over the PK collection interval at steady state, of the metabolite, CCN362

End point type	Secondary

End point timeframe:

End of Treatment (pre-dose, 0.5hours, 1 hour, 2 hours, 3 hours, 5 hours and 8 hours.

End point values	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0[15]		
Units: L/h				
arithmetic mean (standard deviation)	5.10 (± 1.96)	()		

Notes:

[15] - Study terminated early

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events (AEs) are presented from first dose of study treatment until last dose of study treatment plus 7 days post treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort A Fevipiprant 75 mg

Reporting group description:

QAW039 75 mg Chewable tablet

Reporting group title	Cohort B Feviprant 375 mg

Reporting group description:

QAW039 375 mg Chewable tablet

Serious adverse events	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Cohort A Fevipiprant 75 mg	Cohort B Feviprant 375 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events were reported in this study

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2019	This protocol was amended based on health authority feedback. Based on this feedback the following changes were implemented: Modified study protocol with regards to meal intake for all days to ensure that meal intake is consistent on all treatment days Cyclosporine has been added as a prohibited medication in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported