Clinical trial results:
A Phase 1, Randomized, Parallel-group, Open-label, Multicenter Study to Evaluate the Pharmacokinetics, Pharmacodynamics and Safety of Vonoprazan (10 or 20 mg Once Daily) in Children Aged 6 to < 12 Years Who Have Symptomatic Gastroesophageal Reflux Disease

Summary

EudraCT number	2022-003228-42
Trial protocol	Outside EU/EEA
Global end of trial date	29 April 2024

Results information

Result version number	v1 (current)
This version publication date	06 November 2024
First version publication date	06 November 2024

Trial information

Trial identification

Sponsor protocol code	VPED-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT06106022
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Phathom Pharmaceuticals, Inc.
Sponsor organisation address	2150 East Lake Cook Road, Suite 800, Buffalo Grove, IL, United States, 60089
Public contact	Phathom Medical Information, Phathom Pharmaceuticals, Inc., 1 888-775-7428, medicalinformation@phathompharma.com
Scientific contact	Phathom Medical Information, Phathom Pharmaceuticals, Inc., 1 888-775-7428, medicalinformation@phathompharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002703-PIP01-19
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	29 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the pharmacokinetic profile of vonoprazan (10 or 20 mg once daily [QD]) in children ≥ 6 to < 12 years of age who have symptomatic gastroesophageal reflux disease (GERD).

Protection of trial subjects:

This study was performed according to the International Council for Harmonisation harmonized tripartite guideline E6(R2): Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2023
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: 22
Worldwide total number of subjects	22
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)	22
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:

A total of 22 participants were enrolled at 6 study sites in the United States between November 2023 and April 2024.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vonoprazan 10 mg

Arm description:

Participants received vonoprazan 10 mg QD for 14 days.

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

Dosage and administration details:

Administered orally.

Arm title	Vonoprazan 20 mg

Arm description:

Participants received vonoprazan 20 mg QD for 14 days.

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

Dosage and administration details:

Administered orally.

Number of subjects in period 1	Vonoprazan 10 mg	Vonoprazan 20 mg
Started	11	11
Completed	10	9
Not completed	1	2
Voluntary Withdrawal	-	2
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Vonoprazan 10 mg
Reporting group description:	
Participants received vonoprazan 10 mg QD for 14 days.	
Reporting group title	Vonoprazan 20 mg
Reporting group description:	
Participants received vonoprazan 20 mg QD for 14 days.	

Reporting group values	Vonoprazan 10 mg	Vonoprazan 20 mg	Total
Number of subjects	11	11	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	9.1	8.6	
standard deviation	± 1.92	± 1.69	-
Gender categorical Units: Subjects			
Female	7	5	12
Male	4	6	10
Ethnicity Units: Subjects			
Hispanic or Latino	6	9	15
Not Hispanic or Latino	5	2	7
Unknown or Not Reported	0	0	0
Race Units: Subjects			
White	10	10	20
Black or African American	1	1	2

End points

End points reporting groups

Reporting group title	Vonoprazan 10 mg
Reporting group description:	
Participants received vonoprazan 10 mg QD for 14 days.	
Reporting group title	Vonoprazan 20 mg
Reporting group description:	
Participants received vonoprazan 20 mg QD for 14 days.	

Primary: Maximum Drug Concentration at Steady-state (Cmax,ss) of Vonoprazan

End point title	Maximum Drug Concentration at Steady-state (Cmax,ss) of Vonoprazan[1]

End point description:

Plasma pharmacokinetic (PK) parameters were estimated using a non-linear mixed effects model and were determined from the concentration-time data for all evaluable participants. Actual sampling times, rather than scheduled or nominal sampling times, were used in all computations using sampling time. Data presented based on collections on both Day 7 and Day 14.

PK Set: includes all participants who received at least 1 dose of study drug and had sufficient concentration data to support accurate estimation of at least 1 PK parameter.

End point type	Primary

End point timeframe:

Day 7: pre-dose, 0.5 to 1.5 hour and 2.5 to 3.5 hours post dose; Day 14: pre-dose, 1 to 2 hours and 3 to 4 hours post dose

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 analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg	Vonoprazan 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: ng/mL				
arithmetic mean (full range (min-max))	16.2 (9.31 to 27.1)	42.1 (10.1 to 72.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve During the Dosing Interval τ at Steady State (AUCτ,ss) of Vonoprazan

End point title	Area Under the Plasma Concentration-time Curve During the Dosing Interval τ at Steady State (AUCτ,ss) of Vonoprazan[2]

End point description:

Plasma PK parameters were estimated using a non-linear mixed effects model and were determined from the concentration-time data for all evaluable participants. Actual sampling times, rather than scheduled or nominal sampling times, were used in all computations using sampling time.

PK Set: includes all participants who received at least 1 dose of study drug and had sufficient concentration data to support accurate estimation of at least 1 PK parameter.

End point type	Primary

End point timeframe:

Day 7: pre-dose, 0.5 to 1.5 hour and 2.5 to 3.5 hours post dose; Day 14: pre-dose, 1 to 2 hours and 3 to 4 hours post dose

Notes:

[2] - 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 analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg	Vonoprazan 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: h*ng/mL				
arithmetic mean (full range (min-max))	88.3 (51.7 to 121)	251 (72.1 to 549)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F) at Steady State of Vonoprazan

End point title	Apparent Oral Clearance (CL/F) at Steady State of

End point description:

Oral PK parameters were estimated using a non-linear mixed effects model and were determined from the concentration-time data for all evaluable participants. Actual sampling times, rather than scheduled or nominal sampling times, were used in all computations using sampling time.

PK Set: includes all participants who received at least 1 dose of study drug and had sufficient concentration data to support accurate estimation of at least 1 PK parameter.

End point type	Primary

End point timeframe:

Day 7: pre-dose, 0.5 to 1.5 hour and 2.5 to 3.5 hours post dose; Day 14: pre-dose, 1 to 2 hours and 3 to 4 hours post dose

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 analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg	Vonoprazan 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: L/h				
arithmetic mean (full range (min-max))	125 (82.9 to 193)	118 (36.4 to 278)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Central Volume of Distribution (Vz/F) at Steady State of Vonoprazan

End point title	Apparent Central Volume of Distribution (Vz/F) at Steady State of Vonoprazan[4]

End point description:

Plasma PK parameters were estimated using a non-linear mixed effects model and were determined from the concentration-time data for all evaluable participants. Actual sampling times, rather than scheduled or nominal sampling times, were used in all computations using sampling time.

PK Set: includes all participants who received at least 1 dose of study drug and had sufficient concentration data to support accurate estimation of at least 1 PK parameter.

End point type	Primary

End point timeframe:

Day 7: pre-dose, 0.5 to 1.5 hour and 2.5 to 3.5 hours post dose; Day 14: pre-dose, 1 to 2 hours and 3 to 4 hours post dose

Notes:

[4] - 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 analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg	Vonoprazan 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: liters				
arithmetic mean (full range (min-max))	491 (227 to 828)	444 (164 to 1310)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Day 28	
Adverse event reporting additional description: Safety Set: includes all participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Vonoprazan 10 mg
Reporting group description: Participants received vonoprazan 10 mg QD for 14 days.	
Reporting group title	Vonoprazan 20 mg
Reporting group description: Participants received vonoprazan 20 mg QD for 14 days.	

Serious adverse events	Vonoprazan 10 mg	Vonoprazan 20 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (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: 0 %

Non-serious adverse events	Vonoprazan 10 mg	Vonoprazan 20 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Vomiting subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 11 (0.00%) 0	
Infections and infestations Otitis media subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 11 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2023	The purposes of the amendment were to: • Remove requirement that body weight be ≥30 kg. • Clarify that the primary endpoints comprise PK assessments from data collected on Day 7 and Day 14. • Revise justification for dose selection using an updated popPK model. • Add electrocardiograms to safety endpoints. • Add the following: Following completion of study drug dosing on Day 14 or early discontinuation, the subject will be transitioned to local standard of care for 14 days during the Follow-up Period. • Addition of inclusion and exclusion criteria. • Clarify instructions for administration of study drug by specifying when study drug will be taken. • Provide additional instructions for recording date/time of each dose and actions required for missed study drug doses and missed visits/poor compliance. • Differentiate timing of PK blood samples between Days 7 and 14. Sodium heparin vacutainer collection tubes were specified. • Add bone fracture and hematologic abnormalities as adverse event of special interest. • Add urine pregnancy tests for female participants who had experienced menarche to protocol-required safety laboratory assessments. • Add Tanner staging to the physical examination. • Remove the measurement of electrocardiogram intervals, and specify that electrocardiograms were to be read and interpreted centrally by a pediatric cardiologist. • Define the pharmacodynamic population to include participants who received at least 1 dose of study drug and had sufficient pH data to support calculation of pharmacodynamic parameters. • Include a potential popPK analysis of interim data from a subset of participants prior to completion of enrollment to assess whether plasma exposure in pediatric participants aged ≥6 to <12 years was within the range observed in adults receiving the same dose. • Add appendices for contraceptive guidance, Tanner Staging criteria and growth charts.
30 August 2023	The purposes of the amendment were to: • Change exclusion criterion for creatinine from >2 mg/dL (>177 µmol/L) to >0.8 mg/dL (>70 µmol/L). • Change the reporting period for pregnancy during administration of active study drug from 'after Visit 2 or within 4 weeks of the last dose of active study drug' to 'after Visit 2 or within 2 weeks of the last dose of active study drug'. • Remove the requirement for an 8-hour fast before obtaining a glucose measurement. • Require participants to be dressed in light clothing and without shoes when body weight was measured. • Remove the telephone call at the Day 14 in-clinic visit from the schedule of assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported