



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 Adolescents With Symptomatic Gastroesophageal Reflux Disease

Summary

EudraCT number	2023-000179-10
Trial protocol	Outside EU/EEA
Global end of trial date	13 June 2023

Results information

Result version number	v1
This version publication date	25 December 2023
First version publication date	25 December 2023

Trial information

Trial identification

Sponsor protocol code	VPED-102
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05343364
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, United States, IL 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	13 June 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the pharmacokinetic profile of vonoprazan in adolescent participants with symptomatic gastroesophageal reflux disease (GERD).

Protection of trial subjects:

All aspects of the study were carefully monitored, by the sponsor or its designee, for compliance with applicable government regulation with respect to current good clinical practice and current standard operating procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2022
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: 24
Worldwide total number of subjects	24
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)	0
Adolescents (12-17 years)	24
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 24 participants were enrolled into this study in the United States between May 2022 and June 2023.

Pre-assignment

Screening details:

The total duration of the study was up to 8 weeks. The Screening Period was up to 4 weeks, Treatment Period was 2 weeks, and safety follow-up phone call was 2 weeks after last study drug administration.

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 QD

Arm description:

Participants were randomized to receive vonoprazan 10 mg once daily (QD) from Day 1 to Day 14.

Arm type	Experimental
Investigational medicinal product name	Vonoprazan
Investigational medicinal product code	TAK-438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet.

Arm title	Vonoprazan 20 mg QD
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Arm description:

Participants were randomized to receive vonoprazan 20 mg QD from Day 1 to Day 14.

Arm type	Experimental
Investigational medicinal product name	Vonoprazan
Investigational medicinal product code	TAK-438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet.

Number of subjects in period 1	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD
Started	12	12
Completed	12	11
Not completed	0	1
Miscellaneous	-	1

Baseline characteristics

Reporting groups

Reporting group title	Vonoprazan 10 mg QD
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Reporting group description:

Participants were randomized to receive vonoprazan 10 mg once daily (QD) from Day 1 to Day 14.

Reporting group title	Vonoprazan 20 mg QD
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Reporting group description:

Participants were randomized to receive vonoprazan 20 mg QD from Day 1 to Day 14.

Reporting group values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD	Total
Number of subjects	12	12	24
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	14.3 ± 1.78	15.2 ± 1.75	-
Gender categorical Units: Subjects			
Female	6	7	13
Male	6	5	11
Ethnicity Units: Subjects			
Hispanic or Latino	4	2	6
Not Hispanic or Latino	6	10	16
Unknown or Not Reported	2	0	2
Race 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	3	5	8
White	9	7	16
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Vonoprazan 10 mg QD
Reporting group description:	
Participants were randomized to receive vonoprazan 10 mg once daily (QD) from Day 1 to Day 14.	
Reporting group title	Vonoprazan 20 mg QD
Reporting group description:	
Participants were randomized to receive vonoprazan 20 mg QD from Day 1 to Day 14.	

Primary: Maximum Observed Drug Concentration at Steady State (C_{max-ss}) of Vonoprazan

End point title	Maximum Observed Drug Concentration at Steady State (C _{max-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. PK set: inclusive of all evaluable participants who had at least one measurable concentration result.	
End point type	Primary
End point timeframe:	
Blood samples were collected predose, once between 0.5 and 2 hours, and once between 2.5 and 4 hours post-dose on Days 7 and 14	

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 additional statistical analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: ng/mL				
arithmetic mean (full range (min-max))	13.4 (6.57 to 25.6)	26.7 (13.1 to 49.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve During the Dosing Interval τ (AUC _{τ}) of Vonoprazan

End point title	Area Under the Plasma Concentration-time Curve During the Dosing Interval τ (AUC _{τ}) of Vonoprazan ^[2]
End point description:	
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: inclusive of all evaluable participants who had at least one measurable concentration result.	
End point type	Primary

End point timeframe:

Blood samples were collected predose, once between 0.5 and 2 hours, and once between 2.5 and 4 hours post-dose on Days 7 and 14

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 additional statistical analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: h*ng/mL				
arithmetic mean (full range (min-max))	94.6 (56.0 to 165)	208 (95.6 to 381)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL) of Vonoprazan

End point title | Apparent Oral Clearance (CL) of Vonoprazan^[3]

End point description:

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: inclusive of all evaluable participants who had at least one measurable concentration result.

End point type | Primary

End point timeframe:

Blood samples were collected predose, once between 0.5 and 2 hours, and once between 2.5 and 4 hours post-dose on Days 7 and 14

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 additional statistical analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: L/h				
arithmetic mean (full range (min-max))	121 (49.5 to 182)	133 (73.3 to 209)		

Statistical analyses

No statistical analyses for this end point

Primary: Central Volume of Distribution (Vc) of Vonoprazan

End point title | Central Volume of Distribution (Vc) of Vonoprazan^[4]

End point description:

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: inclusive of all evaluable participants who had at least one measurable concentration result.

End point type Primary

End point timeframe:

Blood samples were collected predose, once between 0.5 and 2 hours, and once between 2.5 and 4 hours post-dose on Days 7 and 14

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 additional statistical analyses were pre-specified for this endpoint.

End point values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: liters				
arithmetic mean (full range (min-max))	661 (357 to 1040)	799 (435 to 1110)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AEs)

End point title Number of Participants Experiencing Adverse Events (AEs)

End point description:

AE: any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug. Treatment-emergent adverse event (TEAE): any AE that occurred after the first dose of study drug or at baseline that worsens in either intensity or frequency after the first dose of study drug. Serious AE: any AE for which the following occurred: death, was life threatening, hospitalization or prolongation of hospitalization, persistent or significant disability/incapacity, a congenital anomaly/birth defect, or the AE was deemed an important medical event. Related AE: any AE that follows a reasonable temporal sequence from administration of study drug, or for which possible involvement of the drug cannot be ruled out, although factors other than the study drug may also be responsible. Clinically significant changes from baseline in laboratory test values, (hematology, serum chemistry and urinalysis), electrocardiograms (ECG) and vital signs were reported as AEs.

End point type Secondary

End point timeframe:

Up to Day 28

End point values	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[5]	12 ^[6]		
Units: participants				
Any TEAEs	4	1		
Any Serious TEAEs	0	0		
Any Study Drug-related TEAEs	0	0		

Any Serious Study Drug-related TEAEs	0	0		
Any TEAE Leading to Treatment Discontinuation	0	0		
Any TEAE Leading to Study Discontinuation	0	0		
Any AEs Leading to Death	0	0		

Notes:

[5] - Safety Set: inclusive of all participants who received at least 1 dose of study drug.

[6] - Safety Set: inclusive of all participants who received at least 1 dose of study drug.

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: inclusive of all participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Vonoprazan 10 mg QD
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Reporting group description:

Participants were randomized to receive vonoprazan 10 mg QD from Day 1 to Day 14.

Reporting group title	Vonoprazan 20 mg QD
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Reporting group description:

Participants were randomized to receive vonoprazan 20 mg QD from Day 1 to Day 14.

Serious adverse events	Vonoprazan 10 mg QD	Vonoprazan 20 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (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 QD	Vonoprazan 20 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	1 / 12 (8.33%)	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0	
Infections and infestations Cellulitis subjects affected / exposed occurrences (all) Enterocolitis infectious subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2022	Reasons for amendment: <ul style="list-style-type: none">- To clarify that participants must be aged 12 to 17 years, inclusive, at time of informed consent and throughout study participation.- To clarify that only select sites will perform gastric pH monitoring in participants deemed clinically indicated by the principal investigator.- To add that all study drug doses be taken on an empty stomach.- To add that the time and content of any meals consumed prior to taking study drug on Day 6 or Day 7 be recorded.- To add details for Day 7 dosing with respect to allowed water and meals.- To clarify that Day -1 assessments are only required for participants undergoing gastric pH monitoring.- To clarify that Day 6 is an optional visit for participants that check in to the clinic in the evening before starting Day 7 assessments.- Remove the Day 14 PK blood collection.- Remove morphology from electrocardiogram assessments.
14 September 2022	Reasons for amendment: <ul style="list-style-type: none">- Increased number of sites from 5 to 12.- Updated information about vonoprazan.- Removed duplicate entry for sucralfate under excluded medications and treatments.- Removed gastrin and pepsinogen I and II assessments.- Removed optional Day 6 visit.- Modified strategy to estimate PK parameters to a population based approach; as a result adjusted PK sampling schedule on Day 7, added PK sampling on Day 14, provided information on when time of dosing and meals should be collected and remove Tmax,ss and t1/2z PK parameters.- Removed required overnight stay for PK sampling due to revised sampling schedule.- Added details to the 24-hour gastric pH monitoring.- Moved symptom assessments from Day 8 to Day 7.- Updated Schedule of Events and Study Design to reflect above changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported