



Clinical trial results:

A Phase 3 Randomized Multicenter Study to Evaluate the Efficacy and Safety of Open-Label Dual Therapy with Oral Vonoprazan 20 mg or Double-Blind Triple Therapy with Oral Vonoprazan 20 mg Compared to Double-Blind Triple Therapy with Oral Lansoprazole 30 mg Daily in Patients with Helicobacter Pylori Infection

Summary

EudraCT number	2019-002668-28
Trial protocol	HU GB CZ PL BG
Global end of trial date	18 March 2021

Results information

Result version number	v1 (current)
This version publication date	25 March 2022
First version publication date	25 March 2022

Trial information

Trial identification

Sponsor protocol code	HP-301
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04167670
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, Illinois, United States, 60089
Public contact	Phathom Medical Information, Phathom Pharmaceuticals, Inc., medicalinformation@phathompharma.com
Scientific contact	Phathom Medical Information, Phathom Pharmaceuticals, Inc., medicalinformation@phathompharma.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	18 March 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 March 2021
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 compare the efficacy of Helicobacter pylori (H pylori) eradication with vonoprazan dual and triple therapy regimens versus lansoprazole triple therapy regimen in participants with H pylori infection, excluding participants who had a clarithromycin or amoxicillin resistant strain of H pylori at baseline.

Protection of trial subjects:

This study was conducted in compliance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E6(R2) Section 3, Institutional Review Board (IRB)/Independent Ethics Committee (IEC) guidelines, Good Clinical Practice regulations and guidelines, and all applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 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	Poland: 426
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Bulgaria: 122
Country: Number of subjects enrolled	Czechia: 18
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	United States: 447
Worldwide total number of subjects	1046
EEA total number of subjects	591

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)	828
From 65 to 84 years	217
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

1046 participants were randomized at 103 study sites, including 71 in the United States and 32 in Europe.

Pre-assignment

Screening details:

A ^{13}C -urea breath test (^{13}C -UBT) was performed within 34 days prior to treatment to establish *Helicobacter pylori* (H pylori) infection status. 6 gastric mucosal biopsy specimens were collected to determine resistance of bacteria to clarithromycin, amoxicillin, and metronidazole antibiotics and to document H pylori infection.

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

Blinding implementation details:

Vonoprazan Dual Therapy was open label and Vonoprazan Triple Therapy was double blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Vonoprazan Dual Therapy

Arm description:

Participants were administered 20 milligrams (mg) vonoprazan twice daily (BID) and 1000 mg amoxicillin 3 times daily (TID) from Day 1 to Day 14.

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:

Vonoprazan was administered orally as over-encapsulated tablets.

Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Amoxicillin was administered orally as capsules.

Arm title	Vonoprazan Triple Therapy
------------------	---------------------------

Arm description:

Participants were administered 20 mg vonoprazan BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.

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:	
Vonoprazan was administered orally as over-encapsulated tablets.	
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Amoxicillin was administered orally as capsules.	
Investigational medicinal product name	Clarithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Clarithromycin was administered orally as tablets.	
Arm title	Lansoprazole Triple Therapy
Arm description:	
Participants were administered 30 mg lansoprazole BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.	
Arm type	Active comparator
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Amoxicillin was administered orally as capsules.	
Investigational medicinal product name	Clarithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Clarithromycin was administered orally as tablets.	
Investigational medicinal product name	Lansoprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Lansoprazole was administered orally as over-encapsulated capsules.	

Number of subjects in period 1	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy
Started	349	349	348
Received Study Drugs	348	346	345
Completed	334	331	334
Not completed	15	18	14
Significant protocol deviation	3	1	-
Withdrawal of Consent	4	1	3
Pretreatment event, AE, or SAE	1	7	4
Miscellaneous	7	5	3
Lost to follow-up	-	3	3
Voluntary withdrawal	-	1	1

Baseline characteristics

Reporting groups

Reporting group title	Vonoprazan Dual Therapy
Reporting group description:	
Participants were administered 20 milligrams (mg) vonoprazan twice daily (BID) and 1000 mg amoxicillin 3 times daily (TID) from Day 1 to Day 14.	
Reporting group title	Vonoprazan Triple Therapy
Reporting group description:	
Participants were administered 20 mg vonoprazan BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.	
Reporting group title	Lansoprazole Triple Therapy
Reporting group description:	
Participants were administered 30 mg lansoprazole BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.	

Reporting group values	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy
Number of subjects	349	349	348
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	51.9283668	50.7220630	51.6379310
standard deviation	± 13.4524716	± 13.8812741	± 13.5714970
Gender categorical			
Units: Subjects			
Female	210	226	216
Male	139	123	132
Ethnicity			
Units: Subjects			
Hispanic or Latino	95	99	89
Not Hispanic or Latino	251	249	259
Unknown or Not Reported	3	1	0
Race/Ethnicity			
Units: Subjects			
White	316	307	312
Black or African- American	22	30	25
Asian	4	6	6
American Indian or Alaska Native	0	1	1
Native Hawaiian or Other Pacific Islander	1	0	0
Other	4	1	3
Unknown	1	1	1
Not Reported	1	3	0

Reporting group values	Total		
Number of subjects	1046		

Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	652		
Male	394		
Ethnicity Units: Subjects			
Hispanic or Latino	283		
Not Hispanic or Latino	759		
Unknown or Not Reported	4		
Race/Ethnicity Units: Subjects			
White	935		
Black or African- American	77		
Asian	16		
American Indian or Alaska Native	2		
Native Hawaiian or Other Pacific Islander	1		
Other	8		
Unknown	3		
Not Reported	4		

End points

End points reporting groups

Reporting group title	Vonoprazan Dual Therapy
Reporting group description: Participants were administered 20 milligrams (mg) vonoprazan twice daily (BID) and 1000 mg amoxicillin 3 times daily (TID) from Day 1 to Day 14.	
Reporting group title	Vonoprazan Triple Therapy
Reporting group description: Participants were administered 20 mg vonoprazan BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.	
Reporting group title	Lansoprazole Triple Therapy
Reporting group description: Participants were administered 30 mg lansoprazole BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.	

Primary: Percentage of Participants With Successful Helicobacter Pylori (H Pylori) Eradication in Participants Without a Clarithromycin- or Amoxicillin-resistant Strain of H Pylori at Baseline

End point title	Percentage of Participants With Successful Helicobacter Pylori (H Pylori) Eradication in Participants Without a Clarithromycin- or Amoxicillin-resistant Strain of H Pylori at Baseline
End point description: H pylori eradication was determined by the ¹³ C-UBT test. The analysis set used was the Modified Intent-to-Treat Primary (MITTp) analysis set which included all participants randomized into the study who had a H pylori infection documented by ¹³ C-UBT and biopsy (ie, culture or histology) at baseline and did not have a clarithromycin- or amoxicillin-resistant strain of H pylori at baseline.	
End point type	Primary
End point timeframe: 4 weeks after the last dose of study drugs (maximum duration of treatment was 2 weeks)	

End point values	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	265	262	255	
Units: percentage of participants				
number (not applicable)	78.5	84.7	78.8	

Statistical analyses

Statistical analysis title	Vonoprazan Dual vs Lansoprazole Triple
Comparison groups	Vonoprazan Dual Therapy v Lansoprazole Triple Therapy

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.0037 ^[2]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.39
upper limit	6.76

Notes:

[1] - Noninferiority of vonoprazan dual therapy to lansoprazole triple therapy.

[2] - P-value based on a Farrington and Manning test with a noninferiority margin of 10%.

Statistical analysis title	Vonoprazan Triple vs Lansoprazole Triple
Comparison groups	Lansoprazole Triple Therapy v Vonoprazan Triple Therapy
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	< 0.0001 ^[4]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	12.62

Notes:

[3] - Noninferiority of vonoprazan triple therapy to lansoprazole triple therapy.

[4] - P-value based on a Farrington and Manning test with a noninferiority margin of 10%.

Secondary: Percentage of Participants With Successful Helicobacter Pylori (H Pylori) Eradication in Participants With a Clarithromycin-resistant Strain of H Pylori at Baseline

End point title	Percentage of Participants With Successful Helicobacter Pylori (H Pylori) Eradication in Participants With a Clarithromycin-resistant Strain of H Pylori at Baseline
-----------------	--

End point description:

H pylori eradication was determined by the ¹³C-UBT test. The analysis population included all participants randomized into the study who had H pylori infection documented by ¹³C-UBT and biopsy (ie, culture or histology) at baseline and had a clarithromycin-resistant strain of H pylori at baseline.

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

End point timeframe:

4 weeks after the last dose of study drugs (maximum duration of treatment was 2 weeks)

End point values	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	73	72	
Units: percentage of participants				
number (not applicable)	69.6	65.8	31.9	

Statistical analyses

Statistical analysis title	Vonoprazan Dual vs Lansoprazole Triple
Comparison groups	Vonoprazan Dual Therapy v Lansoprazole Triple Therapy
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.0001 ^[6]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	37.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.54
upper limit	52.56

Notes:

[5] - Superiority of vonoprazan dual therapy to lansoprazole triple therapy.

[6] - P-value based on a Farrington and Manning test with the null hypothesis difference ≤ 0 versus the alternative hypothesis difference > 0 .

Statistical analysis title	Vonoprazan Triple vs Lansoprazole Triple
Comparison groups	Lansoprazole Triple Therapy v Vonoprazan Triple Therapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.0001 ^[8]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	33.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.74
upper limit	48.12

Notes:

[7] - Superiority of vonoprazan triple therapy to lansoprazole triple therapy.

[8] - P-value based on a Farrington and Manning test with the null hypothesis difference ≤ 0 versus the alternative hypothesis difference > 0 .

Secondary: Percentage of All Participants With Successful Helicobacter Pylori (H Pylori) Eradication

End point title	Percentage of All Participants With Successful Helicobacter Pylori (H Pylori) Eradication
-----------------	---

End point description:

H pylori eradication was determined by the ¹³C-UBT test. The analysis set used was the modified intent-to-treat (MITT) analysis set which included all participants randomized into the study who had H pylori infection documented by ¹³C-UBT and biopsy (ie, culture or histology) at baseline.

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

End point timeframe:

4 weeks after the last dose of study drugs (maximum duration of treatment was 2 weeks)

End point values	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	324	338	330	
Units: percentage of participants				
number (not applicable)	77.2	80.8	68.5	

Statistical analyses

Statistical analysis title	Vonoprazan Dual vs Lansoprazole Triple
Comparison groups	Vonoprazan Dual Therapy v Lansoprazole Triple Therapy
Number of subjects included in analysis	654
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	= 0.0063 ^[10]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	15.44

Notes:

[9] - Superiority of vonoprazan dual therapy to lansoprazole triple therapy.

[10] - P-value based on a Farrington and Manning test with the null hypothesis difference ≤ 0 versus the alternative hypothesis difference > 0 .

Statistical analysis title	Vonoprazan Triple vs Lansoprazole Triple
Comparison groups	Lansoprazole Triple Therapy v Vonoprazan Triple Therapy
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	= 0.0001 ^[12]
Method	Farrington and Manning test
Parameter estimate	Percentage Difference
Point estimate	12.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.72
upper limit	18.81

Notes:

[11] - Superiority of vonoprazan triple therapy to lansoprazole triple therapy.

[12] - P-value based on a Farrington and Manning test with the null hypothesis difference ≤ 0 versus the alternative hypothesis difference > 0 .

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 4 weeks after the last dose of study drugs (maximum duration of treatment was 2 weeks)

Adverse event reporting additional description:

The analysis set used was the safety analysis set which included all participants who received at least 1 dose of study drugs.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Vonoprazan Dual Therapy
-----------------------	-------------------------

Reporting group description:

Participants were administered 20 milligrams (mg) vonoprazan twice daily (BID) and 1000 mg amoxicillin 3 times daily (TID) from Day 1 to Day 14.

Reporting group title	Vonoprazan Triple Therapy
-----------------------	---------------------------

Reporting group description:

Participants were administered 20 mg vonoprazan BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.

Reporting group title	Lansoprazole Triple Therapy
-----------------------	-----------------------------

Reporting group description:

Participants were administered 30 mg lansoprazole BID from Day 1 to Day 14. Participants were also administered 1000 mg amoxicillin BID and 500 mg clarithromycin BID from Day 1 to Day 14.

Serious adverse events	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 348 (1.44%)	6 / 346 (1.73%)	3 / 345 (0.87%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events	0	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic			
subjects affected / exposed	1 / 348 (0.29%)	0 / 346 (0.00%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 348 (0.00%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lower limb fracture			
subjects affected / exposed	1 / 348 (0.29%)	0 / 346 (0.00%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 348 (0.00%)	0 / 346 (0.00%)	1 / 345 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 348 (0.29%)	0 / 346 (0.00%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 348 (0.00%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 348 (0.00%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 348 (0.29%)	0 / 346 (0.00%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal polyp			
subjects affected / exposed	0 / 348 (0.00%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 348 (0.29%)	0 / 346 (0.00%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 348 (0.00%)	0 / 346 (0.00%)	1 / 345 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	0 / 348 (0.00%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Corona virus infection			
subjects affected / exposed	1 / 348 (0.29%)	1 / 346 (0.29%)	0 / 345 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 348 (0.00%)	0 / 346 (0.00%)	1 / 345 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

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

Non-serious adverse events	Vonoprazan Dual Therapy	Vonoprazan Triple Therapy	Lansoprazole Triple Therapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 348 (5.75%)	27 / 346 (7.80%)	48 / 345 (13.91%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 348 (0.57%)	15 / 346 (4.34%)	21 / 345 (6.09%)
occurrences (all)	2	15	21
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	18 / 348 (5.17%)	14 / 346 (4.05%)	33 / 345 (9.57%)
occurrences (all)	18	14	33

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2019	<p>The purposes of this amendment were to:</p> <ul style="list-style-type: none">• Change the primary objective and primary endpoint to exclude participants who had a clarithromycin- or amoxicillin-resistant strain of H pylori at baseline• Indicate that cytochrome P450 Family 2 Subfamily C Member 19 (CYP2C19) genotyping was optional• Remove wording that allowed a participant's legally acceptable representative as a party capable of giving consent for the study• Clarify that contraception must have been double barrier and that adequate double-barrier contraception must have been used from the signing of informed consent until Day -2 and 2 forms of adequate contraception must have been used from Day -1 until 4 weeks after the last dose of study drug• Allow rescreening of participants with approval from the medical monitor• Clarify that participants who discontinued study drug or withdrew from the study prematurely were to undergo early termination assessments• Redefine noncompliance as taking either less than 75% or more than 120% of study drug during any evaluation period• Exclude the use of cytochrome P450 3A4 (CYP3A4) substrates with a narrow therapeutic index from 14 days prior to Day 1 through the end of treatment• Update the resistance breakpoint for amoxicillin to >0.125 mcg/mL from >0.03 mcg/mL• Add overall study stopping criteria• Remove the requirement for at least 1 dose of study drug to be taken as a condition for inclusion in the MITT analysis set• Add collection of smoking status and alcohol use in the Schedule of Events and to include smoking status, alcohol use, and clinical condition as variables for subgroup analyses• Redefine the 4-week Post-Treatment Period in the Schedule of Events to be Days 42 to 70• Remove the requirement that the Early Termination Visit be conducted within 14 days of the last dose of study drug being taken• Clarify that ¹³C-UBT testing for H pylori infection status should be performed at least 4 weeks after the last dose of study drug
11 May 2020	<p>The purposes of this amendment were to:</p> <ul style="list-style-type: none">• Add a pre-screen optional fingerstick test to evaluate H pylori status• Clarify that participants must have had a negative urine drug test result for cannabinoids/tetrahydrocannabinol and non-prescribed medications at screening• Add a Week 1 phone call to remind participants about study drug compliance and other assessments• Add the collection of pharmacokinetic samples on Day 15• Clarify that pretreatment event and AE collection and reporting time windows also included those events considered serious• Clarify that serious AE electronic case report forms (eCRFs) be completed and submitted within 24 hours of the investigator first becoming aware of the serious AE (including serious AEs that were pretreatment events)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
------	--------------	--------------

19 March 2020	Study enrollment was paused between March 19, 2020 and May 11, 2020 due to the COVID-19 pandemic. Participants in screening were discontinued and subjects randomized were allowed to continue in the study.	19 May 2020
---------------	--	-------------

Notes:

Limitations and caveats

None reported