



Clinical trial results:

A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Adults with Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection

Summary

EudraCT number	2016-003192-22
Trial protocol	BE
Global end of trial date	29 August 2018

Results information

Result version number	v1 (current)
This version publication date	14 July 2019
First version publication date	14 July 2019

Trial information

Trial identification

Sponsor protocol code	M16-126
-----------------------	---------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02966795
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 011 800-633-9110,
Scientific contact	Betty Yao, AbbVie, betty.yao@abbvie.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	29 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of glecaprevir/pibrentasvir for an 8- or 12-week treatment duration in participants with chronic hepatitis C virus (HCV) genotype (GT) 5 or 6 infection, with or without compensated cirrhosis respectively.

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 January 2017
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	Australia: 8
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Vietnam: 12
Worldwide total number of subjects	84
EEA total number of subjects	24

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)	53
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 24 hospitals or clinics in Europe (Belgium, France), Oceania (Australia, New Zealand), North America (Canada, USA), South Africa, and southeast Asia (Singapore, Vietnam). Participants were screened between January 17, 2017, and December 26, 2017.

Pre-assignment

Screening details:

Enrolled participants with genotype 5 or 6 hepatitis C (HCV) were assigned to treatment with glecaprevir/pibrentasir for either 8 weeks or 12 weeks based on cirrhotic status.

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	Genotype 5-infected

Arm description:

Participants with HCV genotype 5 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Arm type	Experimental
Investigational medicinal product name	Glecaprevir/Pibrentasvir
Investigational medicinal product code	ABT-493/ABT-530
Other name	MAVYRET™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fixed-dose combination tablets taken orally once a day.

Arm title	Genotype 6-infected
------------------	---------------------

Arm description:

Participants with HCV genotype 6 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Arm type	Experimental
Investigational medicinal product name	Glecaprevir/Pibrentasvir
Investigational medicinal product code	ABT-493/ABT-530
Other name	MAVYRET™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fixed-dose combination tablets taken orally once a day.

Number of subjects in period 1	Genotype 5-infected	Genotype 6-infected
Started	23	61
Completed	23	60
Not completed	0	1
Patient Left the Country	-	1

Baseline characteristics

Reporting groups

Reporting group title	Genotype 5-infected
-----------------------	---------------------

Reporting group description:

Participants with HCV genotype 5 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Reporting group title	Genotype 6-infected
-----------------------	---------------------

Reporting group description:

Participants with HCV genotype 6 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Reporting group values	Genotype 5-infected	Genotype 6-infected	Total
Number of subjects	23	61	84
Age categorical Units: Subjects			
< 65 years	8	45	53
≥ 65 years	15	16	31
Age continuous Units: years			
median	68.0	54.0	-
full range (min-max)	24 to 76	30 to 79	-
Gender categorical Units: Subjects			
Female	13	32	45
Male	10	29	39
Race Units: Subjects			
White	21	4	25
Black or African American	1	0	1
Asian	1	56	57
Multi-race	0	1	1
Cirrhosis Status Units: Subjects			
Cirrhotic	3	6	9
Non-cirrhotic	20	55	75
Prior HCV Treatment History Units: Subjects			
Naive	19	57	76
Experienced	4	4	8
HCV Ribonucleic Acid (RNA) Concentration Units: log10 IU/mL			
arithmetic mean	6.52	6.64	-
standard deviation	± 0.53	± 0.74	-

End points

End points reporting groups

Reporting group title	Genotype 5-infected
-----------------------	---------------------

Reporting group description:

Participants with HCV genotype 5 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Reporting group title	Genotype 6-infected
-----------------------	---------------------

Reporting group description:

Participants with HCV genotype 6 infection received oral glecaprevir/pibrentasir (300 mg/120 mg) once daily with food for either 8 weeks (those without cirrhosis) or 12 weeks (those with compensated cirrhosis), according to label.

Primary: Percentage of Participants With Sustained Virologic Response 12 Weeks Post Treatment (SVR12)

End point title	Percentage of Participants With Sustained Virologic Response 12 Weeks Post Treatment (SVR12) ^[1]
-----------------	-------------------------------------------------------------------------------------------------------------

End point description:

SVR12 is defined as hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification (LLOQ; less than 15 IU/mL) 12 weeks after the last actual dose of study drug. The analysis was conducted in all enrolled participants who received at least one dose of study drug. Backward imputation, where applicable, was used to impute missing data. Participants with missing data after backward imputation were counted as non-responders.

End point type	Primary
----------------	---------

End point timeframe:

12 weeks after last dose of study drug (week 20 or 24 depending on the treatment regimen)

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 formal hypothesis was tested in this study.

End point values	Genotype 5-infected	Genotype 6-infected		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	61		
Units: percentage of participants				
number (confidence interval 95%)	95.7 (79.0 to 99.2)	98.4 (91.3 to 99.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment HCV Virologic Failure

End point title	Percentage of Participants With On-treatment HCV Virologic Failure
-----------------	--------------------------------------------------------------------

End point description:

HCV virologic failure was defined as one of the following conditions:

- confirmed HCV RNA ≥ 100 IU/mL after HCV RNA < 15 IU/mL during the Treatment Period; or confirmed increase from nadir in HCV RNA (two consecutive HCV RNA measurements > 1 log₁₀ IU/mL above nadir) at any time point during the Treatment Period; or
- HCV RNA ≥ 15 IU/mL at end of treatment with at least 6 weeks of treatment, where the HCV RNA value must be collected on or after Study Drug Day 36 and study drug duration ≥ 36 days.

The analysis was conducted in all enrolled participants who received at least one dose of study drug.

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

End point timeframe:

8 or 12 weeks (depending on the treatment regimen)

End point values	Genotype 5- infected	Genotype 6- infected		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	61		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 14.3)	1.6 (0.3 to 8.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Relapse

End point title	Percentage of Participants With Relapse
-----------------	-----------------------------------------

End point description:

Relapse was defined as confirmed HCV RNA ≥ 15 IU/mL between the end of treatment and 12 weeks after the last dose of study drug among participants who completed treatment as planned with HCV RNA < 15 IU/mL at the end of treatment and had post-treatment HCV RNA data; participants who had been shown to be re-infected were not considered to have relapsed.

The analysis was conducted in all enrolled participants who received at least one dose of study drug, with HCV RNA < 15 IU/mL at the end of treatment, at least one post-treatment HCV RNA value, and who completed the assigned treatment.

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

End point timeframe:

End of treatment (week 8 or 12 depending on the treatment regimen) through 12 weeks after the end of treatment.

End point values	Genotype 5- infected	Genotype 6- infected		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	60		
Units: percentage of participants				
number (confidence interval 95%)	4.3 (0.8 to 21.0)	0.0 (0.0 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 30 days after the last dose of study drug; 12 or 16 weeks depending on the treatment regimen.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Glecaprevir/Pibrentasvir
-----------------------	--------------------------

Reporting group description:

Participants received oral glecaprevir/pibrentasvir 300 mg/120 mg once daily for 8 or 12 weeks.

Serious adverse events	Glecaprevir/Pibrentasvir		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 84 (5.95%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
MAJOR DEPRESSION			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
ESCHERICHIA PYELONEPHRITIS			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER HELICOBACTER			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GIARDIASIS			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY TUBERCULOSIS			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIRAL INFECTION			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Glecaprevir/Pibrentasvir		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 84 (30.95%)		
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	6		
HEADACHE			
subjects affected / exposed	11 / 84 (13.10%)		
occurrences (all)	11		
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	11 / 84 (13.10%)		
occurrences (all)	11		
Gastrointestinal disorders			

NAUSEA subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		
Psychiatric disorders INSOMNIA subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 July 2017	<ul style="list-style-type: none">- Update Protocol Section 5.2.3.3, Prohibited Therapy, Table 1, Prohibited Medications and Supplements, deleting "Any herbal supplements (including milk thistle)" and allowing the investigator to reintroduce medications prohibited by the protocol 14 or more days following the last dose of study drug, instead of 30 days or more as specified in the original protocol.- Alpha fetoprotein for HCC screening was deleted from the protocol, because the protocol-required HCC screening incorporated more sensitive and specific imaging exams (ultrasound, MRI, positron emission tomography scan), making determination of alpha fetoprotein levels unnecessary. HCC screening liver ultrasound was added at PT Week 24 to assess if the subject did or did not develop HCC during the course of the trial.-Based on regulatory authority feedback, the method to calculate the CIs for the primary efficacy endpoints was changed to the Wilson score method if the number of SVR12 non-responders was less than 5 or, otherwise, normal approximation to the binomial distribution.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported