Clinical trial results:
An Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Combination With Sofosbuvir and Ribavirin in Chronic Hepatitis C (HCV) Infected Subjects Who Have Experienced Virologic Failure in AbbVie HCV Clinical Studies (MAGELLAN-3)

Summary

EudraCT number	2016-002491-26
Trial protocol	GB SE ES DE
Global end of trial date	30 July 2021

Results information

Result version number	v1 (current)
This version publication date	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	M15-942

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02939989
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@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	30 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to assess the efficacy by evaluating the percentage of subjects achieving sustained virologic response 12 weeks postdosing (SVR12) in each treatment arm and safety of glecaprevir/pibrentasvir (GLE/PIB) plus sofosbuvir (SOF) and ribavirin (RBV) in adults or adolescents with chronic HCV genotype 1-6 infection who previously failed HCV treatment in an AbbVie HCV Parent Study.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2016
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: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	China: 4
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	33
EEA total number of subjects	4

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)	26
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with hepatitis C virus (HCV) genotypes (GT) 1–6 infection who had virologic failure while participating in an AbbVie HCV Parent Study were enrolled at 26 sites in 12 countries.

Pre-assignment

Screening details:

Participants were allocated to 1 of 2 treatment arms based on HCV GT, cirrhosis status, and treatment experience with protease inhibitor (PI) and/or nonstructural viral protein 5A protease inhibitor (NS5Ai)-containing regimens prior to enrolling in the AbbVie HCV Parent 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	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks

Arm description:

Participants without cirrhosis who had non-genotype 3 infection and were naïve to PI and NS5Ai prior to participation in AbbVie HCV parent study received daily treatment with glecaprevir/pibrentasvir (GLE/PIB) 300 mg/120 mg plus sofosbuvir (SOF) 400 mg plus twice-daily weight-based ribavirin (RBV) 600 mg - 1200 mg daily total for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Glecaprevir/Pibrentasvir
Investigational medicinal product code	ABT-493/ABT-530
Other name	MAVYRET, MAVIRET
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Glecaprevir/pibrentasvir co-formulated film-coated tablets taken orally once a day for a total daily dose of 300 mg/120 mg.

Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOVALDI
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sofosbuvir 400 mg film-coated tablet taken orally once a day.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin film-coated tablets taken orally twice a day for a total daily dose of 600 mg to 1200 mg based on the participant's age and body weight at Baseline.

Arm title	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks

Arm description:

Participants with genotype 3, and/or compensated cirrhosis, and/or experience with PI and/or NS5Ai

prior to participation in Abbvie HCV parent study received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Glecaprevir/Pibrentasvir
Investigational medicinal product code	ABT-493/ABT-530
Other name	MAVYRET, MAVIRET
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Glecaprevir/pibrentasvir co-formulated film-coated tablets taken orally once a day for a total daily dose of 300 mg/120 mg.

Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	SOVALDI
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sofosbuvir 400 mg film-coated tablet taken orally once a day.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin film-coated tablets taken orally twice a day for a total daily dose of 600 mg to 1200 mg based on the participant's age and body weight at Baseline.

Number of subjects in period 1	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks
Started	5	28
Completed	5	28

Baseline characteristics

Reporting groups	
Reporting group title	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks
Reporting group description:	
Participants without cirrhosis who had non-genotype 3 infection and were naïve to PI and NS5Ai prior to participation in AbbVie HCV parent study received daily treatment with glecaprevir/pibrentasvir (GLE/PIB) 300 mg/120 mg plus sofosbuvir (SOF) 400 mg plus twice-daily weight-based ribavirin (RBV) 600 mg - 1200 mg daily total for 12 weeks.	
Reporting group title	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks
Reporting group description:	
Participants with genotype 3, and/or compensated cirrhosis, and/or experience with PI and/or NS5Ai prior to participation in Abbvie HCV parent study received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 16 weeks.	

Reporting group values	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks	Total
Number of subjects	5	28	33
Age categorical Units: Subjects			
< 65 years old	3	23	26
≥ 65 years old	2	5	7
Age continuous Units: years			
arithmetic mean	59.6	54.3	
standard deviation	± 8.08	± 9.35	-
Gender categorical Units: Subjects			
Female	1	4	5
Male	4	24	28
Race Units: Subjects			
White	3	22	25
Black or African American	0	1	1
Asian	2	5	7
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	5	26	31
HCV Genotype Units: Subjects			
Genotype 1	1	7	8
Genotype 2	4	0	4
Genotype 3	0	19	19
Genotype 4	0	1	1
Genotype 5	0	0	0
Genotype 6	0	1	1

Treatment Regimen Received in AbbVie HCV Parent Study			
GLE/PIB = glecaprevir/pibrentasvir; OBV/PTV/RTV + DSV + RBV = ombitasvir/paritaprevir/ritonavir + dasabuvir (VIEKIRAX and EXVIERA) + ribavirin			
Units: Subjects			
GLE/PIB	4	28	32
OBV/PTV/RTV + DSV + RBV	1	0	1
Treatment Response for AbbVie HCV Parent Study Units: Subjects			
On-treatment non-responder	0	10	10
Breakthrough	0	0	0
Post-treatment relapse	5	18	23
HCV Ribonucleic Acid (RNA) Level Units: log10 IU/mL			
arithmetic mean	6.79	6.23	
standard deviation	± 0.217	± 0.958	-

End points

End points reporting groups

Reporting group title	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks

Reporting group description:

Participants without cirrhosis who had non-genotype 3 infection and were naïve to PI and NS5Ai prior to participation in AbbVie HCV parent study received daily treatment with glecaprevir/pibrentasvir (GLE/PIB) 300 mg/120 mg plus sofosbuvir (SOF) 400 mg plus twice-daily weight-based ribavirin (RBV) 600 mg - 1200 mg daily total for 12 weeks.

Reporting group title	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks

Reporting group description:

Participants with genotype 3, and/or compensated cirrhosis, and/or experience with PI and/or NS5Ai prior to participation in Abbvie HCV parent study received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 16 weeks.

Subject analysis set title	Total
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 12 or 16 weeks.

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 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification (LLOQ; 15 IU/mL) 12 weeks after the last dose of study drug.
Assessed in the intention-to-treat (ITT) population, which included all patients who received at least 1 dose of study drugs. A backward imputation method was used to impute missing responses. Participants with missing data after backward imputation were counted as non-responders.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug, Week 24 or Week 28 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, and comparisons between treatment groups were not planned or conducted.

End point values	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks	Total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	28	33	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (56.6 to 100.0)	96.4 (82.3 to 99.4)	97.0 (84.7 to 99.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment Virologic Failure

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

End point description:

On-treatment virologic failure was defined as meeting one of the following:
• 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
• confirmed HCV RNA greater than or equal to 100 IU/mL after HCV RNA < 15 IU/mL during the treatment period, or
• HCV RNA ≥ 15 IU/mL at end of treatment with at least 6 weeks of treatment.

End point type	Secondary

End point timeframe:

12 or 16 weeks depending on the treatment regimen

End point values	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks	Total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	28	33	
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 43.4)	0 (0.0 to 12.1)	0 (0.0 to 10.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Post-treatment Relapse

End point title	Percentage of Participants With Post-treatment Relapse

End point description:

Post-treatment relapse was defined as confirmed HCV RNA greater than or equal to 15 IU/mL between the end of treatment and 12 weeks after the last dose of study drug among participants who completed treatment with HCV RNA levels < 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.

End point type	Secondary

End point timeframe:

From the end of treatment (Week 12 or 16) through 12 weeks after the last dose of study drug (Weeks 24 or 28 depending on the treatment regimen).

End point values	Glecaprevir/Pibrentasvir + SOF + RBV for 12 weeks	Glecaprevir/Pibrentasvir + SOF + RBV for 16 weeks	Total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	28	33	
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 43.4)	3.6 (0.6 to 17.7)	3.0 (0.5 to 15.3)	

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 up to 30 days after last dose; up to 20 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	GLE/PIB + SOF + RBV for 12 weeks

Reporting group description:

Participants without cirrhosis who had non-genotype 3 infection and were naïve to PI and NS5Ai prior to participation in AbbVie HCV parent study received daily treatment with glecaprevir/pibrentasvir (GLE/PIB) 300 mg/120 mg plus sofosbuvir (SOF) 400 mg plus twice-daily weight-based ribavirin (RBV) 600 mg - 1200 mg daily total for 12 weeks.

Reporting group title	GLE/PIB + SOF + RBV for 16 weeks

Reporting group description:

Participants with genotype 3, and/or compensated cirrhosis, and/or experience with PI and/or NS5Ai prior to participation in Abbvie HCV parent study received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 16 weeks.

Reporting group title	Total

Reporting group description:

Participants received daily treatment with GLE/PIB 300 mg/120 mg plus SOF 400 mg plus twice-daily weight-based RBV 600 mg - 1200 mg daily total for 12 or 16 weeks.

Serious adverse events	GLE/PIB + SOF + RBV for 12 weeks	GLE/PIB + SOF + RBV for 16 weeks	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	2 / 28 (7.14%)	3 / 33 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

CHRONIC GASTRITIS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	0 / 5 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
BRONCHIECTASIS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 5 (0.00%)	1 / 28 (3.57%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	GLE/PIB + SOF + RBV for 12 weeks	GLE/PIB + SOF + RBV for 16 weeks	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	21 / 28 (75.00%)	26 / 33 (78.79%)
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
HAEMATOCRIT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
MEAN CELL VOLUME INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
RED BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
WEIGHT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 5 (20.00%)	4 / 28 (14.29%)	5 / 33 (15.15%)
occurrences (all)	1	4	5
HEADACHE			

subjects affected / exposed	1 / 5 (20.00%)	5 / 28 (17.86%)	6 / 33 (18.18%)
occurrences (all)	1	6	7
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 5 (0.00%)	3 / 28 (10.71%)	3 / 33 (9.09%)
occurrences (all)	0	3	3
FATIGUE			
subjects affected / exposed	1 / 5 (20.00%)	3 / 28 (10.71%)	4 / 33 (12.12%)
occurrences (all)	1	3	4
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
MALAISE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 5 (0.00%)	2 / 28 (7.14%)	2 / 33 (6.06%)
occurrences (all)	0	2	2
DRY MOUTH			
subjects affected / exposed	0 / 5 (0.00%)	2 / 28 (7.14%)	2 / 33 (6.06%)
occurrences (all)	0	2	2
GASTRITIS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 5 (20.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
NAUSEA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
VOMITING			

subjects affected / exposed	0 / 5 (0.00%)	2 / 28 (7.14%)	2 / 33 (6.06%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 5 (0.00%)	3 / 28 (10.71%)	3 / 33 (9.09%)
occurrences (all)	0	3	3
LARYNGEAL PAIN			
subjects affected / exposed	1 / 5 (20.00%)	0 / 28 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	1 / 5 (20.00%)	6 / 28 (21.43%)	7 / 33 (21.21%)
occurrences (all)	2	6	8
RASH			
subjects affected / exposed	1 / 5 (20.00%)	1 / 28 (3.57%)	2 / 33 (6.06%)
occurrences (all)	1	2	3
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 5 (20.00%)	3 / 28 (10.71%)	4 / 33 (12.12%)
occurrences (all)	1	3	4
IRRITABILITY			
subjects affected / exposed	0 / 5 (0.00%)	4 / 28 (14.29%)	4 / 33 (12.12%)
occurrences (all)	0	4	4
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	4 / 28 (14.29%)	4 / 33 (12.12%)
occurrences (all)	0	4	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2016	Key changes included: • Added the definition of AbbVie HCV Parent Study. • Updated results from clinical studies. • Added language to enroll certain subjects at AbbVie's discretion. • Added language regarding subject enrollment and the number of subjects to be enrolled in each treatment arm. • Removed text regarding collection of samples for intensive pharmacokinetic (PK) analysis. • Updated the contraception language for male and female subjects • Revised contraception recommendations. • Updated language for pregnancy testing and liver diagnostic testing. • Added language for the HIV-1 antiretroviral (ARV) Regimen Dosing Card and the Study Drug Dosing Card. • Updated Medications and Supplements Prohibited with GLE/PIB Administration Table. • Updated contact information for AE reporting and protocol deviations. • Clarified text for toxicity management of laboratory abnormalities. • Revised sensitivity analysis language to include both Wilson score interval and normal approximation to binomial distribution for the modified intention-to-treat populations. • Revised subgroup analysis. • Updated references. • Updated collection of pregnancy testing and dosing card. • Deleted Post-Treatment Weeks 2 and 8 visits from the Post-Treatment Study Activities Table.

06 November 2017	• Added a 24-hour emergency number. • Incorporated recent approval of GLE/PIB and updated text to refer to the Investigator's Brochure. • Updated study design to allow patients with virologic failures from AbbVie's Phase 3b/4 GLE/PIB studies. • Included RBV dosing guidelines for adolescents based on baseline age and weight. • Clarified which arm subjects with mixed and unknown HCV genotypes would be enrolled. • Removed collection of dosing information for HIV ARV and collection/analysis of HIV ARV PK samples. • Updated statistical analyses to include subjects infected with more than one HCV genotype. • Clarified that the more restrictive approach to contraception between the local RBV label and the protocol should be used. • Updated list of AIDS-Defining Conditions. • Added exclusion for subjects who had documented HCV reinfection in the parent AbbVie study. • Updated guidance for medications taken during the treatment and post-treatment period. • Provided guidance for prohibited medications or supplements administered with GLE/PIB, added ethinyl estradiol. • Added progestogen to prohibited therapies section. • Updated to ensure all cirrhotic subjects had a protocol required liver ultrasound at the last post-treatment visit. • Clarified that PK samples were not to be collected on Day 1. • Clarified HCV virologic failure criteria. • Clarified when dosing was to be administered at site and use of commercial supplies. • Deleted irrelevant information regarding rationale for dose selection. • Specified minimum requirements for alanine aminotransferase (ALT) elevations and criteria for study drug discontinuation. • Replaced anti-hepatitis A virus immunoglobulin test with anti-hepatitis A virus total test. • Specified that an interim analysis may be conducted. • Specified that for high SVR12 rates less than 100%, the Wilson score test was used for calculating the 95% confidence interval in the primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported