Clinical trial results:
Open-label Study to Evaluate the Safety and Efficacy of the Combination of Ombitasvir, Paritaprevir/r ± Dasabuvir with Ribavirin (RBV) in Adult Patients with GT1 or GT4 Chronic HCV Infection and Response to Prior Treatment of Early Stage Hepatocellular Carcinoma

Summary

EudraCT number	2015-001049-10
Trial protocol	ES
Global end of trial date	29 December 2016

Results information

Result version number	v2 (current)
This version publication date	05 April 2018
First version publication date	14 October 2017
Version creation reason	• Correction of full data set Correction in secondary outcome measure time frame.

Trial information

Trial identification

Sponsor protocol code	M14-726

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02504099
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Marisol Martinez, MD, AbbVie, Marisol.Martinez@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 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir (OBV/PTV/r), with or without dasabuvir (DSV) coadministered with or without ribavirin (RBV) for 12 or 24 weeks in adult patients with genotype 1 or genotype 4 chronic HCV infection and treated early stage Hepatocellular Carcinoma with compensated cirrhosis.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
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: 3
Worldwide total number of subjects	3
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)	0
Adults (18-64 years)	2
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was stopped due to low enrollment.

Period 1

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

Arms

Arm title	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks

Arm description:

OBV/PTV/r (ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) with or without dasabuvir (250 mg twice daily) with or without weight-based ribavirin (± RBV; dosed 1,000 or 1,200 mg daily divided twice a day) for 12 or 24 weeks, dosed as per label based on HCV genotype/subtype and presence of cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ombitasvir/paritaprevir/ritonavir
Investigational medicinal product code	
Other name	Viekirax, paritaprevir also known as ABT-450, ombitasvir also known as ABT-267
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ombitasvir coformulated with paritaprevir and ritonavir

Investigational medicinal product name	dasabuvir
Investigational medicinal product code	
Other name	Exviera, dasabuvir also known as ABT-333
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet

Investigational medicinal product name	ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet

Number of subjects in period 1	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks

Reporting group description:

OBV/PTV/r (ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) with or without dasabuvir (250 mg twice daily) with or without weight-based ribavirin (± RBV; dosed 1,000 or 1,200 mg daily divided twice a day) for 12 or 24 weeks, dosed as per label based on HCV genotype/subtype and presence of cirrhosis.

Reporting group values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks	Total	
Number of subjects	3	3	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 64.3 ± 1.53	 -	
Gender categorical Units: Subjects			
Female	1	1	
Male	2	2	

End points

End points reporting groups

Reporting group title	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks

Reporting group description:

OBV/PTV/r (ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) with or without dasabuvir (250 mg twice daily) with or without weight-based ribavirin (± RBV; dosed 1,000 or 1,200 mg daily divided twice a day) for 12 or 24 weeks, dosed as per label based on HCV genotype/subtype and presence of cirrhosis.

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]) 12 weeks after the last dose of study drug. Participants with missing data after flanking imputation were imputed as nonresponders.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug

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: The study was stopped due to low enrollment; analyses of efficacy end points were not performed.

End point values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: percentage of participants				
number (not applicable)				

Notes:

[2] - The study was stopped due to low enrollment; analyses of efficacy end points were not performed.

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 confirmed HCV RNA ≥ LLOQ after HCV RNA < LLOQ during treatment; confirmed increase of > 1 log(subscript)10(subscript) IU/mL above the lowest value post-baseline in HCV RNA during treatment; or HCV RNA ≥ LLOQ throughout treatment with at least 6 weeks of treatment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Treatment Weeks 2, 4, 8, 12 (end of treatment for 12-week treatment), 16, 20 and 24 (end of treatment for 24-week treatment)

End point values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: percentage of participants				
number (not applicable)				

Notes:

[3] - The study was stopped due to low enrollment; analyses of efficacy end points were not performed

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 ≥ LLOQ between the end of treatment and 12 weeks after the last dose of study drug among participants who completed treatment with HCV RNA levels < LLOQ at the end of treatment.

End point type	Secondary

End point timeframe:

From the end of treatment through 12 weeks after the last dose of study drug

End point values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: percentage of participants				
number (not applicable)				

Notes:

[4] - The study was stopped due to low enrollment; analyses of efficacy end points were not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Long Term Clinical Outcomes

End point title	Percentage of Participants With Long Term Clinical Outcomes

End point description:

The percentage of participants with long term clinical outcomes (de novo hepatocellular carcinoma (HCC) lesions, liver decompensation, unexpected liver transplant, liver related death, or any of the above) from first dose of study drug through 24 weeks post-treatment follow-up.

End point type	Secondary

End point timeframe:

up to 48 weeks

End point values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: percentage of participants				
number (not applicable)				

Notes:

[5] - The study was stopped due to low enrollment; analyses of efficacy end points were not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Recurrent HCV Infection Post Liver Transplant

End point title	Percentage of Participants With Recurrent HCV Infection Post Liver Transplant

End point description:

The percentage of participants with recurrent HCV infection post liver transplant out of all participants with liver transplant during the study.

End point type	Secondary

End point timeframe:

from liver transplant to 24 weeks post-treatment (up to 48 weeks)

End point values	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: percentage of participants				
number (not applicable)				

Notes:

[6] - The study was stopped due to low enrollment; analyses of efficacy end points were not performed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 30 days after the last dose of study drug (up to 16 weeks for 12-week treatment and up to 28 weeks for 24-week treatment)

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event that begins or worsens in severity after initiation of study drug until 30 days after the last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks

Reporting group description:

OBV/PTV/r (ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) with or without dasabuvir (250 mg twice daily) with or without weight-based ribavirin (± RBV; dosed 1,000 or 1,200 mg daily divided twice a day) for 12 or 24 weeks, dosed as per label based on HCV genotype/subtype and presence of cirrhosis.

Serious adverse events	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Lymphopenia			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Portal hypertensive gastropathy			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Irritability			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue			

disorders Back pain subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2015	The main purpose of this amendment was to add hepatitis C virus (HCV) RNA assessments at Weeks 8 and 16; update inclusion criteria (to allow enrollment of subject who have previously been exposed to sofosbuvir [SOF] but no other HCV direct-acting antiviral agents [DAAs]l clarify definition of compensated cirrhosis); update study rationale and justification; clarify study procedures; and permit subjects with HCV subgenotype 1b (HCV GT1b) to be treated with a ribavirin-free regimen.
24 February 2016	The purpose of this amendment was to reduce enrollment from 60 subjects to 3 subjects and to reduce the duration of study from 168 weeks to 24 weeks post-treatment due to study closure for low enrolment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported