Clinical trial results:
An Open-Label, Single-Arm Study to Evaluate the Safety and Efficacy of Ombitasvir/ABT-450/Ritonavir and Dasabuvir in Adults with Genotype 1b Chronic Hepatitis C Virus (HCV) Infection and Cirrhosis (TURQUOISE-III)

Summary

EudraCT number	2014-001953-18
Trial protocol	BE
Global end of trial date	06 November 2015

Results information

Result version number	v1 (current)
This version publication date	05 August 2016
First version publication date	05 August 2016

Trial information

Trial identification

Sponsor protocol code	M14-490

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02219503
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Roger Trinh, AbbVie, roger.trinh@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	06 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 June 2015
Global end of trial reached?	Yes
Global end of trial date	06 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of ombitasvir/ paritaprevir/ ritonavir and dasabuvir in adults with genotype 1b chronic hepatitis C virus (HCV) infection and cirrhosis.

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	15 September 2014
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	Belgium: 18
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	60
EEA total number of subjects	18

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)	45
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 60 subjects were enrolled and all the subjects completed the study. All 60 subjects were analyzed for both efficacy (included all subjects who received at least 1 dose of study drug (ITT)) and safety.

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	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir

Arm description:

Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir/Paritaprevir/Ritonavir
Investigational medicinal product code	
Other name	ABT-267 also know as ombitasvir, ABT-450 also know as paritaprevir, Ritonavir also known as norvir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ombitasvir/Paritaprevir/Ritonavir 25/150/100 mg milligram(s), administered for oral use.

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	
Other name	ABT-333
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Dasabuvir 500 mg milligram(s), administered for oral use

Number of subjects in period 1	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir
Started	60
Completed	60

Baseline characteristics

Reporting groups	
Reporting group title	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir
Reporting group description:	
Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.	

Reporting group values	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	45	45	
From 65-84 years	15	15	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	59.5		
standard deviation	± 9.53	-	
Gender, Male/Female Units: participants			
Female	23	23	
Male	37	37	
Interleukin 28B (IL28B) Genotype Units: Subjects			
CC	10	10	
CT	36	36	
TT	14	14	
Missing	0	0	

End points

End points reporting groups

Reporting group title	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir

Reporting group description:

Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.

Primary: Percentage of Subjects With Sustained Virologic Response 12 Weeks (SVR12) Post-treatment

End point title	Percentage of Subjects With Sustained Virologic Response 12 Weeks (SVR12) Post-treatment[1]

End point description:

Sustained Virologic Response 12 (SVR12) is defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) less than the lower limit of quantification (< LLOQ; < 25 IU/mL) 12 weeks after the last dose of study drug.

End point type	Primary

End point timeframe:

Post-treatment Day 1 to Post-treatment Week 12

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 percentage of subjects (95% CI, calculated using Wilson score method) from post-treatment day 1 to post-treatment week 12 was 100 (94.0 to 100.0). Non-inferiority was to be declared if the lower confidence bound was greater than 72.7% and superiority was to be declared if the lower confidence bound was greater than 83.2%.

End point values	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percentage of participants				
number (confidence interval 95%)	100 (94 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with On-Treatment Virologic Failure

End point title	Percentage of Subjects with On-Treatment Virologic Failure

End point description:

On-Treatment Virologic Failure is defined as confirmed HCV RNA >= LLOQ after HCV RNA < LLOQ during treatment, or confirmed increase from nadir (local minimum value) in HCV RNA [2 consecutive HCV RNA measurements > 1 log10 IU/mL above nadir] at any time point during treatment, or failure to suppress during treatment [all on-treatment values of HCV RNA >= LLOQ] with at least 6 weeks [defined as active study drug duration ≥ 36 days] of treatment.

End point type	Secondary

End point timeframe:

Day 1 through Week 12

End point values	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Post-Treatment Relapse

End point title	Percentage of Subjects with Post-Treatment Relapse

End point description:

Post- Treatment Relapse is defined as confirmed HCV RNA >= LLOQ between end of treatment and 12 weeks after last actual dose of active study drug [up to and including the SVR12 assessment time point] for a subject with HCV RNA < LLOQ at Final Treatment Visit who completes treatment.

End point type	Secondary

End point timeframe:

Post-treatment Day 1 to Post-treatment Week 12

End point values	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from the time of study drug administration to 30 days after last dose of study drug (12 weeks); SAEs were also collected from the time that informed consent was obtained until the end of the study (up to 42 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	18.0
Dictionary version	18.0

Reporting groups

Reporting group title	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir

Reporting group description:

Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.

Serious adverse events	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 60 (1.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
SYNCOPE			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 60 (65.00%)		

Vascular disorders HYPERTENSION subjects affected / exposed occurrences (all)	 3 / 60 (5.00%) 3		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all) HEADACHE subjects affected / exposed occurrences (all)	 6 / 60 (10.00%) 7 11 / 60 (18.33%) 11		
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)	 13 / 60 (21.67%) 13		
Gastrointestinal disorders ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all) DYSPEPSIA subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all)	 3 / 60 (5.00%) 3 12 / 60 (20.00%) 13 4 / 60 (6.67%) 4 4 / 60 (6.67%) 5		
Respiratory, thoracic and mediastinal disorders COUGH subjects affected / exposed occurrences (all)	 4 / 60 (6.67%) 4		
Skin and subcutaneous tissue disorders PRURITUS subjects affected / exposed occurrences (all) PRURITUS GENERALISED	 6 / 60 (10.00%) 6 		

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Psychiatric disorders INSOMNIA subjects affected / exposed occurrences (all)	 6 / 60 (10.00%) 6		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) MYALGIA subjects affected / exposed occurrences (all)	 6 / 60 (10.00%) 6 4 / 60 (6.67%) 4		
Infections and infestations INFLUENZA subjects affected / exposed occurrences (all) NASOPHARYNGITIS subjects affected / exposed occurrences (all)	 4 / 60 (6.67%) 4 4 / 60 (6.67%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2014	The purpose of this amendment was to update inclusion/exclusion criteria and language related to hormonal contraceptives for female subjects of childbearing potential; update the way the date and time of the second-to-last dose and the date and time of last dose before each pharmacokinetic visit will be recorded; and to update Investigator Brochures version numbers for ombitasvir, paritaprevir, and dasabuvir in Reference section.
17 September 2014	The purpose of this amendment was to update the primary objective and primary endpoints to include comparison of the SVR12 rate of the ombitasvir/paritaprevir/r and dasabuvir treated subjects to a threshold based on the historical SVR12 rates of sofosbuvir plus pegIFN/RBV in the same patient population; to show the derivation of the thresholds on which the primary endpoints are based; to exclude sofosbuvir treatment-experienced patients; and to update determination of the sample size, to show the power of the study for the comparisons to the threshold based on the SVR12 rate of sofosbuvir plus pegIFN/RBV.
02 March 2015	The purpose of this amendment was to update the approximate number of subjects to be enrolled into the study; to align with the current product label; and to update exclusion criteria to clarify subject exclusion based on current or past clinical evidence of Child-Pugh B or C classification or clinical history of liver decompensation at time of screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported