Clinical trial results:
A Single Arm, Open-label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Adults with Chronic Hepatitis C Virus Genotype 1, 2, 4, 5 or 6 Infection and Compensated Cirrhosis (EXPEDITION-1)

Summary

EudraCT number	2015-003797-32
Trial protocol	DE BE ES
Global end of trial date	10 February 2017

Results information

Result version number	v1 (current)
This version publication date	15 December 2017
First version publication date	15 December 2017

Trial information

Trial identification

Sponsor protocol code	M14-172

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02642432
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, Abbvie, 001 800-633-9110,
Scientific contact	Joaquin Valdes, Abbvie, joaquin.m.valdes@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	10 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of ABT-493/ABT-530 following 12 weeks of treatment in adults with chronic Hepatitis C Virus Infection genotype 1, 2, 4, 5 or 6 infection and 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	07 December 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	Canada: 29
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	United States: 69
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Germany: 16
Worldwide total number of subjects	146
EEA total number of subjects	45

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)	105
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a 35-day screening period.

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	ABT-493/ABT-530

Arm description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-493 coformulated with ABT-530

Number of subjects in period 1	ABT-493/ABT-530
Started	146
Completed	138
Not completed	8
Not specified	3
Adverse event	2
Withdrew consent	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	ABT-493/ABT-530
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.	

Reporting group values	ABT-493/ABT-530	Total	
Number of subjects	146	146	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 60.12 ± 10.43	 -	
Gender categorical Units: Subjects			
Female	56	56	
Male	90	90	

End points

End points reporting groups

Reporting group title	ABT-493/ABT-530

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 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]) 12 weeks after the last dose of study drug. Participants with missing data after backwards 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: Descriptive data are summarized for this end point per protocol.

End point values	ABT-493/ABT-530			
Subject group type	Reporting group			
Number of subjects analysed	146[2]			
Units: percentage of participants				
number (confidence interval 95%)	99.3 (98.0 to 100.0)			

Notes:

[2] - Intent-to-treat (ITT) population: all participants who received at least 1 dose of study drug

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 increase of > 1 log(subscript)10(subscript) IU/mL above the lowest value post-baseline HCV RNA during treatment; confirmed HCV RNA ≥ 100 IU/mL after HCV RNA < LLOQ during treatment, or HCV RNA ≥ LLOQ at end of treatment with at least 6 weeks of treatment.

End point type	Secondary

End point timeframe:

Treatment Weeks 1, 2, 4, 8, and 12 (end of treatment) or premature discontinuation from treatment

End point values	ABT-493/ABT-530			
Subject group type	Reporting group			
Number of subjects analysed	146[3]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 2.6)			

Notes:

[3] - All participants who received at least 1 dose of study drug (ITT population).

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, excluding reinfection.

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	ABT-493/ABT-530			
Subject group type	Reporting group			
Number of subjects analysed	144[4]			
Units: percentage of participants				
number (confidence interval 95%)	0.7 (0.1 to 3.8)			

Notes:

[4] - ITT population who completed treatment and had HCV RNA <LLOQ at the final treatment visit.

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 the time of study drug administration until 30 days after the last dose of study drug (up to 16 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any AE or SAE event with an onset date that is after the first dose of study drug until 30 days after the last dose of study drug and were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	ABT-493/ABT-530

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

Serious adverse events	ABT-493/ABT-530		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 146 (7.53%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Investigations			
Tumour marker increased			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	2 / 146 (1.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Gastric ulcer			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Rectal abscess			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endophthalmitis			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 146 (0.68%)		
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	ABT-493/ABT-530		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 146 (43.15%)		
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 146 (13.70%)		
occurrences (all)	20		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	27 / 146 (18.49%)		
occurrences (all)	27		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 146 (8.22%)		
occurrences (all)	12		
Nausea			
subjects affected / exposed	13 / 146 (8.90%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	14 / 146 (9.59%)		
occurrences (all)	14		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	9 / 146 (6.16%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2015	The main purpose of this amendment was to update the introduction with safety and efficacy data in cirrhotic subjects; update inclusion (clarify contraception use during the study, expand the categories of treatment-experienced subjects allowed [SOF plus RBV with or without pegIFN treatment failures]) and update the protocol to align with the addition of this subject population); and clarify the period of AE collection after completion of study treatment.
23 November 2015	The main purpose of this amendment was to update the introduction and benefit/risk sections with newly available safety and efficacy information; increase the number of genotype (GT) 5 and GT6 subjects to approximately 30 and the overall total number of subjects to approximately 175; update inclusion criteria (clarify contraception use during the study); and clarify that the primary analysis was to be conducted in the intent-to-treat (ITT) population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported