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 4, 5, or 6 Infection (ENDURANCE-4)

Summary

EudraCT number	2015-002349-80
Trial protocol	PT BE GB ES IT
Global end of trial date	09 January 2017

Results information

Result version number	v1 (current)
This version publication date	13 December 2017
First version publication date	13 December 2017

Trial information

Trial identification

Sponsor protocol code	M13-583

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02636595
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	Neddie Zadeikis, Abbvie, neddie.zadeikis@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	09 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 January 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 evaluate the effect of response to treatment by evaluating the percentage of subjects achieving a 12-week sustained virologic response (SVR12) after 12 weeks of treatment with ABT-493/ABT-530 and to evaluate the safety of the regimen in participants with chronic hepatitis C virus (HCV) genotype (GT) 4, 5, or 6 infection.

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	30 October 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	Portugal: 11
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	South Africa: 11
Worldwide total number of subjects	121
EEA total number of subjects	100

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)	108
From 65 to 84 years	13
85 years and over	0

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	121
Completed	119
Not completed	2
Not specified	1
Lost to follow-up	1

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	121	121	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 52.66 ± 10.95	 -	
Gender categorical Units: Subjects			
Female	44	44	
Male	77	77	

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	121[2]			
Units: percentage of participants				
number (confidence interval 95%)	99.2 (97.6 to 100)			

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	121[3]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 3.1)			

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	118[4]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 3.2)			

Notes:

[4] - ITT population who completed treatment and had HCV RNA <LLLOQ 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 with an onset date 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	1 / 121 (0.83%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 121 (0.83%)		
occurrences causally related to treatment / all	2 / 2		
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	59 / 121 (48.76%)		
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 121 (20.66%)		
occurrences (all)	29		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	11 / 121 (9.09%) 11 21 / 121 (17.36%) 21		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	8 / 121 (6.61%) 8 12 / 121 (9.92%) 13		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	9 / 121 (7.44%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2015	The purpose of this amendment was to expand the definition of treatment-experienced to include sofosbuvir plus ribavirin with or without pegylated interferon failure; increase the number of subjects to be enrolled from 120 to 130; and clarify contraception requirements and study procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported