Clinical trial results:
A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Adults with Chronic Hepatitis C Virus (HCV) Genotypes 1-6 Infection and Human Immunodeficiency Virus-1 (HIV-1) Co-infection (EXPEDITION-2)

Summary

EudraCT number	2015-005577-20
Trial protocol	GB DE PL
Global end of trial date	07 June 2017

Results information

Result version number	v1 (current)
This version publication date	12 April 2018
First version publication date	12 April 2018

Trial information

Trial identification

Sponsor protocol code	M14-730

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02738138
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	EU Clinical Trials Helpdesk, 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	27 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 June 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 efficacy and safety of ABT-493/ABT-530 in adults with chronic hepatitis C virus genotype 1-6 infection and human immunodeficiency virus-1 co-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	17 May 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	Poland: 15
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belarus: 4
Country: Number of subjects enrolled	Puerto Rico: 14
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	United States: 44
Worldwide total number of subjects	153
EEA total number of subjects	65

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)	151
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a 35-day screening period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: ABT-493/ABT-530 for 8 weeks

Arm description:

HCV Genotype (GT)1-6/HIV-1 co-infected non-cirrhotic subjects treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 8 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 administered orally

Arm title	Arm B: ABT-493/ABT-530 for 12 Weeks

Arm description:

HCV GT1-6/HIV-1 coinfected subjects with compensated cirrhosis treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (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 administered orally

Number of subjects in period 1	Arm A: ABT-493/ABT-530 for 8 weeks	Arm B: ABT-493/ABT-530 for 12 Weeks
Started	137	16
Completed	134	15
Not completed	3	1
Adverse event, non-fatal	-	1
Lost to follow-up	2	-
Not further specified	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: ABT-493/ABT-530 for 8 weeks
Reporting group description:	
HCV Genotype (GT)1-6/HIV-1 co-infected non-cirrhotic subjects treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 8 weeks	
Reporting group title	Arm B: ABT-493/ABT-530 for 12 Weeks
Reporting group description:	
HCV GT1-6/HIV-1 coinfected subjects with compensated cirrhosis treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 12 weeks	

Reporting group values	Arm A: ABT-493/ABT-530 for 8 weeks	Arm B: ABT-493/ABT-530 for 12 Weeks	Total
Number of subjects	137	16	153
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	45.00	50.00	
standard deviation	± 10.22	± 8.36	-
Gender categorical Units: Subjects			
Female	24	1	25
Male	113	15	128

End points

End points reporting groups

Reporting group title	Arm A: ABT-493/ABT-530 for 8 weeks
Reporting group description:	
HCV Genotype (GT)1-6/HIV-1 co-infected non-cirrhotic subjects treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 8 weeks	
Reporting group title	Arm B: ABT-493/ABT-530 for 12 Weeks
Reporting group description:	
HCV GT1-6/HIV-1 coinfected subjects with compensated cirrhosis treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 12 weeks	
Subject analysis set title	Intention-to-treat (ITT) Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Per protocol, all efficacy analyses were performed using the intention-to-treat (ITT) population (all enrolled participants who received at least 1 dose of study drug); in addition, efficacy analyses were performed overall, combining Treatment Arms A and B.	

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 active study drug.	
End point type	Primary
End point timeframe:	
12 weeks after last 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	Intention-to-treat (ITT) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	153			
Units: participants				
number (confidence interval 95%)	98.0 (95.8 to 100.0)			

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 ≥ 100 IU/mL 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 at end of treatment with at least 6	

weeks of treatment.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Intention-to-treat (ITT) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	153			
Units: participants				
number (confidence interval 95%)	0.7 (0.1 to 3.6)			

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	Intention-to-treat (ITT) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	151[2]			
Units: participants				
number (confidence interval 95%)	0 (0.0 to 2.5)			

Notes:

[2] - Per protocol, ITT population including only those with post-treatment data, excluding reinfection.

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).

Adverse event reporting additional description:

TEAEs and SAEs are defined as any AE or SAE from the first dose of study drug to 30 days after the last dose of study drug (up to 16 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Arm A: ABT-493/ABT-530 for 8 weeks

Reporting group description:

HCV Genotype (GT)1-6/HIV-1 co-infected non-cirrhotic subjects treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 8 weeks

Reporting group title	Arm B: ABT-493/ABT-530 for 12 Weeks

Reporting group description:

HCV GT1-6/HIV-1 coinfected subjects with compensated cirrhosis treated with ABT-493/ABT-530 300 mg/120 mg coformulated tablet administered orally once a day (QD) for 12 weeks

Serious adverse events	Arm A: ABT-493/ABT-530 for 8 weeks	Arm B: ABT-493/ABT-530 for 12 Weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 137 (2.19%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 137 (0.73%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A: ABT-493/ABT-530 for 8 weeks	Arm B: ABT-493/ABT-530 for 12 Weeks	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 137 (36.50%)	7 / 16 (43.75%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 137 (2.19%)	1 / 16 (6.25%)	
occurrences (all)	3	1	
Headache			
subjects affected / exposed	12 / 137 (8.76%)	0 / 16 (0.00%)	
occurrences (all)	13	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	18 / 137 (13.14%)	0 / 16 (0.00%)	
occurrences (all)	18	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	2 / 137 (1.46%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	1 / 137 (0.73%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Dental caries			
subjects affected / exposed	1 / 137 (0.73%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	12 / 137 (8.76%)	1 / 16 (6.25%)	
occurrences (all)	13	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 137 (1.46%)	1 / 16 (6.25%)	
occurrences (all)	2	2	
Sinus congestion			
subjects affected / exposed	1 / 137 (0.73%)	1 / 16 (6.25%)	
occurrences (all)	1	2	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 137 (2.19%)	1 / 16 (6.25%)	
occurrences (all)	3	1	
Rash			
subjects affected / exposed	5 / 137 (3.65%)	1 / 16 (6.25%)	
occurrences (all)	5	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 137 (1.46%)	1 / 16 (6.25%)	
occurrences (all)	2	2	

Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Sinusitis bacterial			
subjects affected / exposed	0 / 137 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	12 / 137 (8.76%)	0 / 16 (0.00%)	
occurrences (all)	13	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2016	The purpose of this amendment was to update text throughout the protocol to remove all instances of glecaprevir/ pibrentasvir (GLE/PIB) dose of 200 mg/80 mg once daily dosing as well as the related treatment Arms B and D and to reflect that the 300 mg/120 mg dose of GLE/PIB was the only dose investigated in this study. In addition, this amendment included an update to text that revised permissive HIV-1 antiretrovirals based on completed drug interaction studies, and those HIV-1 antiretrovirals where no significant interaction was predicted based on metabolic and transporter pathways. An inclusion criterion was updated to clarify the qualifying HIV-1 antiretrovial treatment (ART) regimen. Finally, text was edited to clarify prohibited hormonal contraceptives/replacement therapy containing ethinyl estradiol.
21 March 2016	The purpose of this amendment was to revise the primary and secondary objectives to incorporate a comparison of the overall sustained virologic response 12 weeks post dosing (SVR12) rate with a historical threshold and to modify the population for the primary objective to the intent-to-treat (ITT) population. Edited text also included a description of how the historical threshold for the primary efficacy analysis was calculated, provided the rationale for selection of a 6% noninferiority margin, and updated sample size to describe the power to demonstrate noninferiority to the historical control SVR12 rate. Finally, this amendment included edits throughout to include Efficacy Treatment Adjustment Criteria Rationale to ensure optimal efficacy in the noncirrhotic population by incorporating the ability to extend treatment from 8 weeks to 12 weeks for Arm A based on a pre-specified evaluation of the number of subjects experiencing post-treatment HCV relapse.
12 July 2016	The purpose of this amendment was to update text throughout the protocol for the following reasons: to revise permissive Human Immunodeficiency Virus (HIV)-1 antiretrovirals based on either completed drug interaction studies, and/or those HIV-1 antiretrovirals for which no significant interaction was predicted based on metabolic and transporter pathways; to increase the overall sample size to allow for enrollment of additional HCV GT1 subjects; to edit inclusion criteria to clarify the qualifying HIV-1 ART regimen; and to clarify cirrhotic subjects who were receiving DRV and LPV were not eligible for the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported.

Notes: