Clinical trial results:
A Randomized, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Co-Administration of ABT-493 and ABT-530 (or ABT-493/ABT-530) With and Without Ribavirin in Adults With Chronic Hepatitis C Virus (HCV) Infection who Failed a Prior Direct-Acting Antiviral Agent (DAA)-Containing Therapy

Summary

EudraCT number	2015-002350-13
Trial protocol	ES GB
Global end of trial date	23 January 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	M15-410

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02446717
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	Armen Asatryan, Abbvie, armen.asatryan@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	23 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 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 assess the efficacy and safety of ABT-493 and ABT-530 with or without ribavirin (RBV) in participants with chronic hepatitis C virus, (HCV)-infection who previously failed treatment with a direct acting antiviral (DAA)-containing regimen.

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	23 April 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	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Australia: 24
Country: Number of subjects enrolled	Puerto Rico: 3
Country: Number of subjects enrolled	United States: 94
Worldwide total number of subjects	141
EEA total number of subjects	20

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)	126
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a 42-day screening period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

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, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (tablet) dosed with ABT-530 (tablet)

Arm title	ARM B

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

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, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (tablet) dosed with ABT-530 (tablet)

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

Dosage and administration details:

Tablet

Arm title	ARM C

Arm description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
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, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
ABT-493 (tablet) dosed with ABT-530 (tablet)	
Arm title	ARM D
Arm description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.	
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	
Arm title	ARM E
Arm description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis.	
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	Arm A	ARM B	ARM C
Started	6	22	22
Completed	6	21	20
Not completed	0	1	2
Adverse event	-	-	1
Lost to follow-up	-	1	1
Withdrew consent	-	-	-

Number of subjects in period 1	ARM D	ARM E
Started	44	47
Completed	43	46
Not completed	1	1
Adverse event	-	-
Lost to follow-up	-	1
Withdrew consent	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM B
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM C
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM D
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.	
Reporting group title	ARM E
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis.	

Reporting group values	Arm A	ARM B	ARM C
Number of subjects	6	22	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.5	55.2	58.5
standard deviation	± 9.16	± 6.29	± 6.56
Gender categorical Units: Subjects			
Female	3	2	4
Male	3	20	18

Reporting group values	ARM D	ARM E	Total
Number of subjects	44	47	141
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	55.6	55.6	
standard deviation	± 8.57	± 8.31	-
Gender categorical Units: Subjects			
Female	13	14	36

Male	31	33	105

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM B
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM C
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.	
Reporting group title	ARM D
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.	
Reporting group title	ARM E
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without 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 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	Arm A	ARM B	ARM C	ARM D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[2]	22[3]	22[4]	44[5]
Units: percentage of participants				
number (confidence interval 95%)	100 (61.0 to 100)	95.5 (78.2 to 99.2)	86.4 (66.7 to 95.3)	88.6 (76.0 to 95.0)

Notes:

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

[3] - Intent-to-treat population: all participants who received at least 1 dose of study drug

[4] - Intent-to-treat population: all participants who received at least 1 dose of study drug

[5] - Intent-to-treat population: all participants who received at least 1 dose of study drug

End point values	ARM E			
Subject group type	Reporting group			
Number of subjects analysed	47[6]			
Units: percentage of participants				
number (confidence interval 95%)	91.5 (80.1 to 96.6)			

Notes:

[6] - Intent-to-treat 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 Sustained Virologic Response 4 Weeks Post-treatment (SVR4)

End point title	Percentage of Participants With Sustained Virologic Response 4 Weeks Post-treatment (SVR4)

End point description:

SVR4 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 4 weeks after the last dose of study drug. Participants with missing data after backwards imputation were imputed as nonresponders.

End point type	Secondary

End point timeframe:

4 weeks after the last actual dose of study drug

End point values	Arm A	ARM B	ARM C	ARM D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[7]	22[8]	22[9]	44[10]
Units: percentage of participants				
number (confidence interval 95%)	100.0 (61.0 to 100.0)	95.5 (78.2 to 99.2)	95.5 (78.2 to 99.2)	90.9 (78.8 to 96.4)

Notes:

[7] - ITT population

[8] - ITT population

[9] - ITT population

[10] - ITT population

End point values	ARM E			
Subject group type	Reporting group			
Number of subjects analysed	47[11]			
Units: percentage of participants				
number (confidence interval 95%)	91.5 (80.1 to 96.6)			

Notes:

[11] - ITT population

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 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:

Day 3, Treatment Weeks 1, 2, 4, 6, 8, 10, 12 (end of treatment for 12-week treatment arms), and 16 (end of treatment for 16-week treatment arm) or premature discontinuation from treatment

End point values	Arm A	ARM B	ARM C	ARM D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[12]	22[13]	22[14]	44[15]
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 39.0)	0.0 (0.0 to 14.9)	4.5 (0.8 to 21.8)	2.3 (0.4 to 11.8)

Notes:

[12] - ITT population

[13] - ITT population

[14] - ITT population

[15] - ITT population

End point values	ARM E			
Subject group type	Reporting group			
Number of subjects analysed	47[16]			
Units: percentage of participants				
number (confidence interval 95%)	8.5 (3.4 to 19.9)			

Notes:

[16] - 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 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	Arm A	ARM B	ARM C	ARM D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[17]	21[18]	21[19]	43[20]
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 39.0)	4.8 (0.8 to 22.7)	0.0 (0.0 to 15.5)	9.3 (3.7 to 21.6)

Notes:

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

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

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

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

End point values	ARM E			
Subject group type	Reporting group			
Number of subjects analysed	43[21]			
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 8.2)			

Notes:

[21] - 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 20 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any AE or SAE 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	Arm A

Reporting group description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

Reporting group title	ARM B

Reporting group description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

Reporting group title	ARM C

Reporting group description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

Reporting group title	ARM D

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.

Reporting group title	ARM E

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis.

Serious adverse events	Arm A	ARM B	ARM C
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 22 (4.55%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 6 (16.67%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ARM D	ARM E	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			

subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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	ARM B	ARM C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	17 / 22 (77.27%)	16 / 22 (72.73%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	5 / 22 (22.73%)	8 / 22 (36.36%)
occurrences (all)	1	7	9
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed	1 / 6 (16.67%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	8 / 22 (36.36%)	4 / 22 (18.18%)
occurrences (all)	1	8	4
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 6 (16.67%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	1	2	1
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	1	2	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	6 / 22 (27.27%)	3 / 22 (13.64%)
occurrences (all)	1	6	4
Toothache			

subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	1 / 22 (4.55%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	6 / 22 (27.27%)	0 / 22 (0.00%)
occurrences (all)	0	6	0
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 22 (0.00%)	4 / 22 (18.18%)
occurrences (all)	0	0	5
Musculoskeletal stiffness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	0 / 6 (0.00%)	3 / 22 (13.64%)	1 / 22 (4.55%)
occurrences (all)	0	3	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	ARM D	ARM E	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 44 (52.27%)	27 / 47 (57.45%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 44 (13.64%)	11 / 47 (23.40%)	
occurrences (all)	8	11	
Hypoaesthesia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Lethargy			
subjects affected / exposed	3 / 44 (6.82%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Somnolence			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 44 (2.27%)	3 / 47 (6.38%)	
occurrences (all)	1	6	
Fatigue			
subjects affected / exposed	3 / 44 (6.82%)	5 / 47 (10.64%)	
occurrences (all)	3	5	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 44 (0.00%)	4 / 47 (8.51%)	
occurrences (all)	0	4	
Diarrhoea			
subjects affected / exposed	2 / 44 (4.55%)	2 / 47 (4.26%)	
occurrences (all)	2	2	
Dyspepsia			
subjects affected / exposed	2 / 44 (4.55%)	4 / 47 (8.51%)	
occurrences (all)	2	4	
Faeces discoloured			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 44 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	4 / 44 (9.09%)	3 / 47 (6.38%)	
occurrences (all)	5	4	
Toothache			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 44 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 44 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 47 (4.26%)	
occurrences (all)	2	2	
Irritability			
subjects affected / exposed	0 / 44 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 44 (2.27%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 44 (2.27%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 44 (2.27%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 47 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2015	The main purpose of this amendment was to update the dosage strength of ABT-530 from 120 mg QD to 80 mg QD in treatment Arm A and of ABT-493 from 200 mg QD to 300 mg QD in treatment Arm B; clarify inclusion criterion (permitted prior direct acting antiviral agent [DAA] treatment); clarify the definition of on-treatment failure in DAA-experienced subjects; and revise treatment extension (from additional 4 weeks [total duration of 16 weeks] to 12 weeks [total duration of 24 weeks], add ribavirin and sofosbuvir to the treatment regimen for the subjects to whom treatment extension criteria are applied, and classify NS3/4A/NS5A-experienced subjects as NS3/4A-experienced/NS5A-naïve for the purpose of treatment extension).
24 April 2015	The main purpose of this amendment was to update the definitions of on-treatment failure and post-treatment failure; clarify inclusion criteria (provide examples of prior DAA-containing therapies); update secondary objective to include evaluation of 2 dose levels of ABT-530; and clarify treatment extension criteria.
16 June 2015	The main purpose of this amendment was to clarify inclusion criteria (definition of true abstinence, clarify when additional assessments for liver cirrhosis need to be made based on the initial test results); stop enrollment in Arm A; update virologic stopping criterion (remove "Failure to achieve hepatitis C virus [HCV] ribonucleic acid [RNA] < LLOQ by Week 6"); and clarify adverse event (AE) collection period.
10 September 2015	The main purpose of this amendment was to add Part 2 of the study based upon meeting pre specified efficacy and safety criteria; include use of ABT-493/ABT-530 co-formulated tablet for Part 2; clarify rescreening for Part 2; update inclusion criteria (remove upper age limit for inclusion in Part 2; allow enrollment of GT4, 5, and 6 in Part 2; specify acceptable methods of contraception in Parts 1 and 2; clarify the accepted definitions of chronic HCV; specify eligible prior DAA regimens in Part 2; remove the upper BMI limit in Part 2; clarify accepted criteria of defining absence of cirrhosis and include criteria for defining presence of compensated cirrhosis in Part 2; exclude subjects with hepatocellular carcinoma [HCC] in Part 2) and exclusion criteria (exclude subjects with HCV RNA load of < 1000 IU/mL in Part 2); update prohibited therapy; clarify timing of study procedures; and clarify AE collection period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported