Clinical trial results:
A Randomized, Open-Label, Active-Controlled, Multicenter Study to Compare Efficacy and Safety of ABT-493/ABT-530 to Sofosbuvir Co-Administered with Daclatasvir in Adults with Chronic Hepatitis C Virus Genotype 3 Infection (ENDURANCE-3)

Summary

EudraCT number	2015-002272-24
Trial protocol	DE GB SE
Global end of trial date	06 February 2017

Results information

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

Trial information

Trial identification

Sponsor protocol code	M13-594

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02640157
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	06 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate non-inferiority in the percentage of subjects achieving a 12-week sustained virologic response (SVR12) after 12 weeks of treatment with ABT-493/ABT-530 to 12 weeks of treatment with Sofosbuvir and Daclatasvir; to demonstrate non-inferiority of 8 weeks of treatment with ABT-493/ABT-530 to 12 weeks of treatment with ABT-493/ABT-530; and to assess safety of ABT-493/ABT-530 compared to Sofosbuvir and Daclatasvir in treatment-naïve adults with chronic hepatitis C virus (HCV) genotype 3 (GT3) infection.

Protection of trial subjects:

The investigator or his/her representative explained the nature of the study to the subject, and answered all questions regarding this study. Prior to any study-related screening procedures being performed on the subject, the informed consent statement was reviewed, signed, and dated by the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 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	Sweden: 20
Country: Number of subjects enrolled	United Kingdom: 82
Country: Number of subjects enrolled	France: 46
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Australia: 70
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	United States: 146
Country: Number of subjects enrolled	Switzerland: 41
Country: Number of subjects enrolled	New Zealand: 44
Worldwide total number of subjects	506
EEA total number of subjects	175

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)	488
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects must have been HCV treatment-naïve (i.e., subject had never received any anti-HCV treatment) prior to enrolling in the study.

Pre-assignment

Screening details:

A total of 506 participants were randomized and 505 received ≥ 1 dose of study drug. One participant in Arm B was randomized in error and never dispensed study drug. This study included a 42-day screening period.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

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:

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

Arm title	Arm B

Arm description:

Sofosbuvir 400 mg once daily (QD) co-administered with daclatasvir 60 mg QD for 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg once daily for 12 weeks.

Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	
Other name	Daklinza
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg once daily for 12 weeks.

Arm title	Arm C

Arm description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (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:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily for 8 weeks.

Number of subjects in period 1[1]	Arm A	Arm B	Arm C
Started	233	115	157
Received study drug	233	115	157
Completed study drug	225	112	154
Discontinued study drug	8 [2]	3 [3]	3 [4]
Completed	220	111	147
Not completed	13	4	10
Consent withdrawn by subject	2	-	2
Adverse event, non-fatal	2	2	1
Lost to follow-up	9	2	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 506 participants were enrolled; 1 subject (Arm B) was enrolled in error, was never dispensed study drug, and is excluded from the analysis.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number refers to study drug disposition and not overall study disposition.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number refers to study drug disposition and not overall study disposition.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number refers to study drug disposition and not overall study disposition.

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.	
Reporting group title	Arm B
Reporting group description:	
Sofosbuvir 400 mg once daily (QD) co-administered with daclatasvir 60 mg QD for 12 weeks.	
Reporting group title	Arm C
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 8 weeks.	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	233	115	157
Age categorical Units: Subjects			

Age continuous			
Safety population: All participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	47.18	47.06	45.43
standard deviation	± 10.68	± 11.31	± 12.19
Gender categorical Units: Subjects			
Female	112	63	64
Male	121	52	93

Reporting group values	Total		
Number of subjects	505		
Age categorical Units: Subjects			

Age continuous			
Safety population: All participants who received at least one dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	239		
Male	266		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.	
Reporting group title	Arm B
Reporting group description:	
Sofosbuvir 400 mg once daily (QD) co-administered with daclatasvir 60 mg QD for 12 weeks.	
Reporting group title	Arm C
Reporting group description:	
ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 8 weeks.	

Primary: Percentage of Participants With Sustained Virologic Response 12 weeks Post-treatment (SVR12): Noninferiority of Arm A to Arm B

End point title	Percentage of Participants With Sustained Virologic Response 12 weeks Post-treatment (SVR12): Noninferiority of Arm A to Arm B[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. The primary efficacy endpoint was noninferiority in the percentage of participants achieving SVR12 of the 12-week regimen (Arm A) to the standard of care (Arm B: 12 weeks of treatment with sofosbuvir [SOF] + daclatasvir [DCV]), defined as: a) the lower bound of the 95% confidence interval (CI) for the difference was above the non-inferiority margin of –6% and the lower bound of the 95% CI for the SVR12 rate within Arm A was greater than 92%; OR b) the lower bound of the 95% CI for the difference was below the non-inferiority margin of –6% and the lower bound of the 97.5% CI for the SVR12 rate within Arm A was greater than 92%; OR c) the lower bound of the 97.5% CI for the difference was above the non-inferiority margin of –6% and the lower bound of the 95% CI for the SVR12 rate within Arm A was below 92%.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy endpoint was noninferiority in the percentage of participants achieving SVR12 of the 12-week regimen (Arm A) to the standard of care (Arm B: 12 weeks of treatment with sofosbuvir + daclatasvir). For Arm A, the percentage of subjects (97.5% CI) is 95.3% (92.2, 98.4). See noninferiority criteria a) and c) in Statistical Analyses sections below.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233[2]	115[3]		
Units: Percentage of participants				
number (confidence interval 95%)	95.3 (92.6 to 98.0)	96.5 (93.2 to 99.9)		

Notes:

[2] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

[3] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

Statistical analyses

Statistical analysis title	Difference in SVR12 rates (Arm A - Arm B)

Statistical analysis description:

Noninferiority: a) the lower bound (LB) of the 95%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm A was >92%; or b) the LB of the 95%CI for the difference was below the non-inferiority margin of -6% and the LB of the 97.5%CI for the SVR12 rate within Arm A was >92%; or c) the LB of the 97.5%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm A was below 92%.

Comparison groups	Arm A v Arm B
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in percentage of participants
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	3.1

Notes:

[4] - Noninferiority criterion a)

Statistical analysis title	Difference in SVR12 rates (Arm A - Arm B)

Statistical analysis description:

Noninferiority: a) the lower bound (LB) of the 95%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm A was >92%; or b) the LB of the 95%CI for the difference was below the non-inferiority margin of -6% and the LB of the 97.5%CI for the SVR12 rate within Arm A was >92%; or c) the LB of the 97.5%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm A was below 92%.

Comparison groups	Arm A v Arm B
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in percentage of participants
Point estimate	-1.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-6.2
upper limit	3.7

Notes:

[5] - Noninferiority criterion c)

Primary: Percentage of Participants With Sustained Virologic Response 12 weeks Post-treatment (SVR12): Noninferiority of Arm C to Arm A

End point title	Percentage of Participants With Sustained Virologic Response 12 weeks Post-treatment (SVR12): Noninferiority of Arm C to Arm A[6]

End point description:

SVR12 was defined as plasma HCV RNA level <LLOQ 12 weeks after the last dose of study drug. If the first primary efficacy objective (noninferiority of Arm A to Arm B) was achieved, then the second primary efficacy objective, noninferiority in the percentage of participants achieving SVR12 of the 8-week regimen (Arm C) to the 12-week regimen (Arm A) was to be tested. Noninferiority was defined as: a) the lower bound of the 95% CI for the difference was above the noninferiority margin of –6% and the lower bound of the 95% CI for the SVR12 rate within Arm C was greater than 92%, OR b) the lower bound of the 95% CI for the difference was below the noninferiority margin of –6% and the lower bound

of the 97.5% CI for the SVR12 rate within Arm C was greater than 92%, OR c) the lower bound of the 97.5% CI for the difference was above the noninferiority margin of –6% and the lower bound of the 95% CI for the SVR12 rate within Arm C was below 92%.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: If the first primary efficacy objective (noninferiority of Arm A to Arm B) was achieved, then the second primary efficacy objective, noninferiority in the percentage of participants achieving SVR12 of the 8-week regimen (Arm C) to the 12-week regimen (Arm A) was to be tested. For Arm C, the percentage of subjects (97.5% CI) is 94.9% (91.0, 98.8). See noninferiority criteria a) and c) in Statistical Analyses sections below.

End point values	Arm A	Arm C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233[7]	157[8]		
Units: percentage of participants				
number (confidence interval 95%)	95.3 (92.6 to 98.0)	94.9 (91.5 to 98.3)		

Notes:

[7] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

[8] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

Statistical analyses

Statistical analysis title	Difference in SVR12 rates (Arm C - Arm A)

Statistical analysis description:

Noninferiority: a) the lower bound (LB) of the 95%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm C was >92%; or b) the LB of the 95%CI for the difference was below the non-inferiority margin of -6% and the LB of the 97.5%CI for the SVR12 rate within Arm C was >92%; or c) the LB of the 97.5%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm C was below 92%.

Comparison groups	Arm A v Arm C
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Difference in percentage of participants
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	4

Notes:

[9] - Noninferiority criterion a)

Statistical analysis title	Noninferiority of Arm C to Arm A

Statistical analysis description:

Noninferiority: a) the lower bound (LB) of the 95%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm C was >92%; or b) the LB of the 95%CI for the difference was below the non-inferiority margin of -6% and the LB of the 97.5%CI for the SVR12 rate within Arm C was >92%; or c) the LB of the 97.5%CI for the difference was above the non-inferiority margin of -6% and the LB of the 95%CI for the SVR12 rate within Arm C was below 92%.

Comparison groups	Arm A v Arm C

Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Difference in percentage of participants
Point estimate	-0.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-5.4
upper limit	4.6

Notes:

[10] - Noninferiority criterion c)

Secondary: Percentage of Participants With Sustained Virologic Response 12 weeks post-treatment (SVR12): Superiority of Arm A to Arm B

End point title	Percentage of Participants With Sustained Virologic Response 12 weeks post-treatment (SVR12): Superiority of Arm A to Arm B[11]

End point description:

SVR12 was defined as plasma HCV RNA level <LLOQ 12 weeks after the last dose of study drug. Per statistical analysis plan to adjust for multiplicity among the primary and first secondary hypothesis tests, the test for superiority of Arm A to Arm B was not conducted.

End point type	Secondary

End point timeframe:

12 weeks after the last actual dose of study drug

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was defined as superiority of the 12-week regimen (Arm A) to the standard of care (Arm B: 12 weeks of treatment with sofosbuvir + daclatasvir).

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233[12]	115[13]		
Units: percentage of participants				
number (confidence interval 95%)	95.3 (92.6 to 98.0)	96.5 (93.2 to 99.9)		

Notes:

[12] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

[13] - ITT: subjects rcvd ≥ 1 dose of Tx; missing data after backwards imputation = nonresponders

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 in 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 (end of treatment for Arm C), and 12 (end of treatment for Arms A and B) or premature discontinuation from treatment

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	233[14]	115[15]	157[16]	
Units: percentage of participants				
number (confidence interval 95%)	0.4 (0.1 to 2.4)	0 (0.0 to 3.2)	0.6 (0.1 to 3.5)	

Notes:

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

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

[16] - 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	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	222[17]	114[18]	150[19]	
Units: percentage of participants				
number (confidence interval 95%)	1.4 (0.5 to 3.9)	0.9 (0.2 to 4.8)	3.3 (1.4 to 7.6)	

Notes:

[17] - Subjects rcvd ≥ 1 dose of Tx, completed Tx, and had HCV RNA <LLOQ at the final treatment visit

[18] - Subjects rcvd ≥ 1 dose of Tx, completed Tx, and had HCV RNA <LLOQ at the final treatment visit

[19] - Subjects rcvd ≥ 1 dose of Tx, completed Tx, 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 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/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

Reporting group title	Arm B

Reporting group description:

Sofosbuvir 400 mg once daily (QD) co-administered with daclatasvir 60 mg QD for 12 weeks.

Reporting group title	Arm C

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 8 weeks.

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 233 (2.15%)	2 / 115 (1.74%)	3 / 157 (1.91%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Paranasal sinus and nasal cavity malignant neoplasm recurrent			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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			
Accidental overdose			
subjects affected / exposed	0 / 233 (0.00%)	0 / 115 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Limb injury			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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
Poisoning			
subjects affected / exposed	0 / 233 (0.00%)	0 / 115 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	0 / 233 (0.00%)	0 / 115 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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
Hypoxia			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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
Psychiatric disorders			
Dependence			
subjects affected / exposed	0 / 233 (0.00%)	0 / 115 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance-induced psychotic disorder			

subjects affected / exposed	0 / 233 (0.00%)	1 / 115 (0.87%)	0 / 157 (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
Infections and infestations			
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 233 (0.00%)	0 / 115 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 233 (0.43%)	0 / 115 (0.00%)	0 / 157 (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
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 233 (0.00%)	1 / 115 (0.87%)	0 / 157 (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

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	126 / 233 (54.08%)	53 / 115 (46.09%)	64 / 157 (40.76%)
Nervous system disorders			
Headache			
subjects affected / exposed	60 / 233 (25.75%)	21 / 115 (18.26%)	31 / 157 (19.75%)
occurrences (all)	64	22	31
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 233 (1.72%)	7 / 115 (6.09%)	3 / 157 (1.91%)
occurrences (all)	4	9	4
Fatigue			
subjects affected / exposed	44 / 233 (18.88%)	16 / 115 (13.91%)	20 / 157 (12.74%)
occurrences (all)	45	16	20
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	15 / 233 (6.44%)	4 / 115 (3.48%)	18 / 157 (11.46%)
occurrences (all)	15	5	19
Nausea			
subjects affected / exposed	32 / 233 (13.73%)	15 / 115 (13.04%)	19 / 157 (12.10%)
occurrences (all)	32	15	20
Vomiting			
subjects affected / exposed	10 / 233 (4.29%)	5 / 115 (4.35%)	9 / 157 (5.73%)
occurrences (all)	12	5	9
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 233 (3.86%)	6 / 115 (5.22%)	0 / 157 (0.00%)
occurrences (all)	9	6	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 233 (5.15%)	6 / 115 (5.22%)	4 / 157 (2.55%)
occurrences (all)	13	6	4
Upper respiratory tract infection			
subjects affected / exposed	15 / 233 (6.44%)	4 / 115 (3.48%)	2 / 157 (1.27%)
occurrences (all)	15	4	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2015	- Changed the comparator arm regimen from SOF 400 mg QD + RBV 1,000 or 1,200 mg (weight-based total daily dose) for 24 weeks to SOF 400 mg QD + DCV 60 mg QD for 12 weeks. - Made necessary updates throughout the protocol to reflect the change from RBV to DCV in the comparator arm. - Increased the number of subjects to be enrolled from approximately 300 to approximately 345 due to modification of the noninferiority margin as a result of the change in active comparator. - Specified the reflex assay used for determination of HCV genotype/subtype. - Revised Inclusion Criteria 2 and 3 to list birth control options for females of childbearing potential (both female subjects or female partners of male subjects) removed pregnancy precautions due to absence of RBV in the comparator arm. - Updated SAE reporting requirements to include all SAEs that occurred during the Post-Treatment Period regardless of relatedness to study drug. - Revised the analytical method, including decreasing the noninferiority margin for the primary efficacy analysis due to the change of the active comparator. - Revised the key secondary efficacy analysis due to the changes made to the primary efficacy analysis.
01 October 2015	- Changed the primary analysis population for the between-arm comparison of efficacy from the per protocol population to the ITT population. - Updated Inclusion Criteria 2 and 3 to require at least 1 effective form of birth control for female subjects of childbearing potential (both female subjects and female partners of male subjects) starting at screening and for 30 days after the last dose of study drug. - Added Appendix C to list effective forms of birth control that were allowed during the study.
09 October 2015	- Updated Inclusion Criterion 2 to clarify that female participants in Arm B were to follow contraceptive precautions as per local SOF and DCV labels. - Added a statement to Appendix C to denote highly effective methods of contraception and instances in their use per Clinical Trial Facilitation Group guidance.
29 January 2016	- Added an 8-week ABT-493/ABT-530 treatment duration arm. - Added a primary efficacy analysis for the 8-week comparison due to the addition of an 8-week treatment arm. - Added efficacy analysis details specific to the added 8-week treatment arm. - Added baseline creatinine clearance and estimated glomerular filtration rate (eGFR) to the list of efficacy subgroup variables. - Modified the sample size due to the addition of the 8-week treatment arm. - The PRO analysis on the cumulative number of subjects who have ever experienced an increase from baseline was updated to align across the ABT-493/ABT-530 program.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported