Clinical trial results:
An Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Co-Administration of ABT-493 and ABT-530 With and Without Ribavirin in Subjects with Chronic Hepatitis C Virus (HCV) Genotype 1, 4, 5, and 6 Infection (SURVEYOR-I)

Summary

EudraCT number	2014-002925-36
Trial protocol	GB
Global end of trial date	19 February 2016

Results information

Result version number	v1 (current)
This version publication date	08 March 2017
First version publication date	08 March 2017

Trial information

Trial identification

Sponsor protocol code	M14-867

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02243280
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, MD, 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	19 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this Phase 2, open-label, 2-part, multicenter study was to evaluate the efficacy, safety, and pharmacokinetics of co-administration of ABT-493 and ABT-530 with and without ribavirin (RBV) at different doses in chronic Hepatitis C virus (HCV) Genotype 1 (GT1), Genotype 4 (GT4), Genotype 5 (GT5), and Genotype 6 (GT6) infection with compensated cirrhosis (GT1 only) or without cirrhosis (GT1, GT4, GT5, or GT6). Although RBV was initially planned in the protocol, it was not administered in any of the study arms.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2014
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	Australia: 6
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	New Zealand: 14
Country: Number of subjects enrolled	Puerto Rico: 16
Country: Number of subjects enrolled	United States: 129
Worldwide total number of subjects	174
EEA total number of subjects	0

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	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Inclusion Criteria: Male or female 18 -70 years; Screening laboratory result of HCV GT1, GT4, GT5, or GT6 infection; Chronic HCV infection; Subject either HCV treatment-naïve or combination of pegylated-interferon ribavirin experienced; Subjects must be documented as non-cirrhotic or cirrhotic.

Pre-assignment

Screening details:

Exclusion criteria: History of severe, life-threatening or other significant sensitivity to any drug; Positive test result at Screening for hepatitis B surface antigen (HBsAg) or anti-human immunodeficiency virus antibody (HIV Ab); Co-infection with more than one HCV genotype; Any cause of liver disease other than chronic HCV infection.

Period 1

Period 1 title	Enrolled
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Arm title	Arm B

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1- infected participants without cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg once daily (QD)

Arm title	Arm F

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1- infected participants with compensated cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Arm title	Arm I

Arm description:

ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Arm title	Arm K

Arm description:

ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1- infected participants without cirrhosis

Arm type	Experimental

Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Number of subjects in period 1	Arm A	Arm B	Arm F
Started	40	39	27
Completed	40	39	27

Number of subjects in period 1	Arm I	Arm K
Started	34	34
Completed	34	34

Period 2

Period 2 title	Treated
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis

Two subjects in Arm I received the incorrect dose of study drug (ABT-493 200 mg instead of 300 mg) and included in Arm A instead of Arm I in the safety population.

Arm type	Experimental

Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Arm title	Arm B

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1- infected participants without cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg once daily (QD)

Arm title	Arm F

Arm description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1- infected participants with compensated cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg once daily (QD)

Arm title	Arm I
Arm description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis	
Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300 mg once daily (QD)	
Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
120 mg once daily (QD)	
Arm title	Arm K
Arm description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1- infected participants without cirrhosis	
Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300 mg once daily (QD)	
Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
120 mg once daily (QD)	

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Two subjects in Arm I received the incorrect dose of study drug (ABT-493 200 mg instead of 300 mg) and are included in Arm A instead of Arm I.

Number of subjects in period 2	Arm A	Arm B	Arm F
Started	42	39	27
Completed treatment	42	38 [2]	27
Completed	41	39	27
Not completed	1	0	0
Adverse event, serious fatal	1	-	-
Lost to follow-up	-	-	-

Number of subjects in period 2	Arm I	Arm K
Started	32	34
Completed treatment	32	33
Completed	31	31
Not completed	1	3
Adverse event, serious fatal	-	1
Lost to follow-up	1	2

Notes:

[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: One subject discontinued study drug on Day 42 due to noncompliance.

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis Two subjects in Arm I received the incorrect dose of study drug (ABT-493 200 mg instead of 300 mg) and included in Arm A instead of Arm I in the safety population.	
Reporting group title	Arm B
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1- infected participants without cirrhosis	
Reporting group title	Arm F
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1- infected participants with compensated cirrhosis	
Reporting group title	Arm I
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis	
Reporting group title	Arm K
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1- infected participants without cirrhosis	

Reporting group values	Arm A	Arm B	Arm F
Number of subjects	42	39	27
Age categorical Units: Subjects			
Age Continuous			
Safety population: all participants who received at least 1 dose of study drug. Two participants assigned to Arm I received the incorrect dose of study drug throughout their participation in the study (ABT-493 200 mg QD instead of 300 mg) and are therefore included in Arm A instead of Arm I in the safety population.			
Units: years			
arithmetic mean	52.4	52.5	58.9
standard deviation	± 10.01	± 10.41	± 5.47
Gender categorical Units: Subjects			
Female	17	21	7
Male	25	18	20

Reporting group values	Arm I	Arm K	Total
Number of subjects	32	34	174
Age categorical Units: Subjects			

Age Continuous			
Safety population: all participants who received at least 1 dose of study drug. Two participants assigned to Arm I received the incorrect dose of study drug throughout their participation in the study (ABT-493 200 mg QD instead of 300 mg) and are therefore included in Arm A instead of Arm I in the safety population.			
Units: years			
arithmetic mean	55	53.5	
standard deviation	± 11.13	± 10.34	-
Gender categorical			
Units: Subjects			
Female	16	15	76
Male	16	19	98

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis	
Reporting group title	Arm B
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1- infected participants without cirrhosis	
Reporting group title	Arm F
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1- infected participants with compensated cirrhosis	
Reporting group title	Arm I
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis	
Reporting group title	Arm K
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1- infected participants without cirrhosis	
Reporting group title	Arm A
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis Two subjects in Arm I received the incorrect dose of study drug (ABT-493 200 mg instead of 300 mg) and included in Arm A instead of Arm I in the safety population.	
Reporting group title	Arm B
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1- infected participants without cirrhosis	
Reporting group title	Arm F
Reporting group description:	
ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1- infected participants with compensated cirrhosis	
Reporting group title	Arm I
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis	
Reporting group title	Arm K
Reporting group description:	
ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1- infected participants without cirrhosis	

Primary: Percentage of participants with sustained virologic response (SVR) 12 weeks post-treatment

End point title	Percentage of participants with sustained virologic response (SVR) 12 weeks post-treatment[1]
End point description:	
The percentage of participants with sustained virologic response (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.

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: The primary efficacy endpoint was the percentage of subjects who achieved SVR12 (HCV RNA < LLOQ 12 weeks after the last actual dose of study drug). For each treatment arm, the number and percentage of subjects achieving SVR12 was summarized along with a 95% confidence interval using Wilson score interval. No further statistical analyses were performed.

End point values	Arm A	Arm B	Arm F	Arm I
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[2]	39[3]	27[4]	34[5]
Units: percentage of participants				
number (confidence interval 95%)	100 (91.2 to 100)	97.4 (86.8 to 99.5)	96.3 (81.7 to 99.3)	100 (89.8 to 100)

Notes:

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

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

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

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

End point values	Arm K			
Subject group type	Reporting group			
Number of subjects analysed	34[6]			
Units: percentage of participants				
number (confidence interval 95%)	97.1 (85.1 to 99.5)			

Notes:

[6] - Intention-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 (SVR) 4 weeks post-treatment

End point title	Percentage of participants with sustained virologic response (SVR) 4 weeks post-treatment

End point description:

The percentage of participants with sustained virologic response (plasma hepatitis C virus ribonucleic acid [HCV RNA] less than the lower limit of quantification [<LLOQ]) 4 weeks after the last dose of study drug.

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 F	Arm I
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[7]	39[8]	27[9]	34[10]
Units: percentage of participants				
number (confidence interval 95%)	100 (91.2 to 100)	97.4 (86.8 to 99.5)	96.3 (81.7 to 99.3)	100 (89.8 to 100)

Notes:

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

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

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

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

End point values	Arm K			
Subject group type	Reporting group			
Number of subjects analysed	34[11]			
Units: percentage of participants				
number (confidence interval 95%)	100 (89.8 to 100)			

Notes:

[11] - Intention-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 on-treatment virologic failure

End point title	Percentage of participants with on-treatment virologic failure

End point description:

The percentage of participants with on-treatment virologic failure (defined as confirmed hepatitis C virus ribonucleic acid (HCV RNA) greater than or equal to the lower limit of quantitation [≥ LLOQ] 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:

Screening, Day 1, Day 3, treatment weeks 1, 2, 4, 6, 8, 10, and 12 or premature discontinuation from treatment

End point values	Arm A	Arm B	Arm F	Arm I
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[12]	39[13]	27[14]	34[15]
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 8.8)	0 (0 to 9)	0 (0 to 12.5)	0 (0 to 10.2)

Notes:

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

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

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

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

End point values	Arm K			
Subject group type	Reporting group			
Number of subjects analysed	34[16]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 10.2)			

Notes:

[16] - Intention-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 post-treatment relapse

End point title	Percentage of participants with post-treatment relapse

End point description:

Post-treatment relapse was defined as confirmed hepatitis C virus ribonucleic acid (HCV RNA) greater than or equal to the lower limit of quantitation (≥ 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	Arm A	Arm B	Arm F	Arm I
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40[17]	38[18]	27[19]	34[20]
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 8.8)	2.6 (0.5 to 13.5)	3.7 (0.7 to 18.3)	0 (0 to 10.2)

Notes:

[17] - Participants who rcvd ≥ 1 dose of study drug, completed trt, and had HCV RNA <LLOQ at last trt visit

[18] - Participants who rcvd ≥ 1 dose of study drug, completed trt, and had HCV RNA <LLOQ at last trt visit

[19] - Participants who rcvd ≥ 1 dose of study drug, completed trt, and had HCV RNA <LLOQ at last trt visit

[20] - Participants who rcvd ≥ 1 dose of study drug, completed trt, and had HCV RNA <LLOQ at last trt visit

End point values	Arm K			
Subject group type	Reporting group			
Number of subjects analysed	33[21]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 10.4)			

Notes:

[21] - Participants who rcvd ≥ 1 dose of study drug, completed trt, and had HCV RNA <LLOQ at last trt 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) 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:

Serious adverse events were collected starting after the study-specific informed consent was signed and continuing until 30 days after the last dose of study drug, up to 23 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Arm A

Reporting group description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis. Two subjects in Arm I received the incorrect dose of study drug (ABT-493 200 mg instead of 300 mg) and included in Arm A instead of Arm I in the safety population.

Reporting group title	Arm B

Reporting group description:

ABT-493 200 mg once daily (QD) + ABT-530 40 mg QD for 12 weeks in HCV genotype 1-infected participants without cirrhosis

Reporting group title	Arm F

Reporting group description:

ABT-493 200 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 1-infected participants with compensated cirrhosis

Reporting group title	Arm I

Reporting group description:

ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 12 weeks in HCV genotype 4-, 5-, and 6-infected participants without cirrhosis

Reporting group title	Arm K

Reporting group description:

ABT-493 300 mg once daily (QD) + ABT-530 120 mg QD for 8 weeks in HCV genotype 1-infected participants without cirrhosis

Serious adverse events	Arm A	Arm B	Arm F
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)	0 / 39 (0.00%)	1 / 27 (3.70%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	0 / 27 (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

Prostate cancer metastatic			
subjects affected / exposed	1 / 42 (2.38%)	0 / 39 (0.00%)	0 / 27 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm I	Arm K	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	1 / 34 (2.94%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 32 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer metastatic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 32 (0.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Arm B	Arm F
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 42 (52.38%)	22 / 39 (56.41%)	9 / 27 (33.33%)
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 42 (4.76%)	2 / 39 (5.13%)	0 / 27 (0.00%)
occurrences (all)	2	2	0
Headache			
subjects affected / exposed	5 / 42 (11.90%)	8 / 39 (20.51%)	3 / 27 (11.11%)
occurrences (all)	6	10	3
Memory impairment			
subjects affected / exposed	0 / 42 (0.00%)	2 / 39 (5.13%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 39 (5.13%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 42 (23.81%)	5 / 39 (12.82%)	3 / 27 (11.11%)
occurrences (all)	10	6	3
Pain			
subjects affected / exposed	1 / 42 (2.38%)	1 / 39 (2.56%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 39 (2.56%)	0 / 27 (0.00%)
occurrences (all)	3	1	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 42 (0.00%)	1 / 39 (2.56%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)	3 / 39 (7.69%)	1 / 27 (3.70%)
occurrences (all)	3	3	1
Dry mouth			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	3 / 42 (7.14%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	5 / 42 (11.90%)	8 / 39 (20.51%)	0 / 27 (0.00%)
occurrences (all)	5	8	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 42 (4.76%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Paranasal sinus discomfort			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 39 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 39 (2.56%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 42 (4.76%)	3 / 39 (7.69%)	0 / 27 (0.00%)
occurrences (all)	2	3	0
Depression			
subjects affected / exposed	2 / 42 (4.76%)	0 / 39 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1

Insomnia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 39 (7.69%)	0 / 27 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 39 (2.56%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 42 (2.38%)	1 / 39 (2.56%)	1 / 27 (3.70%)
occurrences (all)	1	1	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 42 (4.76%)	1 / 39 (2.56%)	2 / 27 (7.41%)
occurrences (all)	2	1	2
Urinary tract infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 39 (2.56%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 42 (0.00%)	0 / 39 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1

Non-serious adverse events	Arm I	Arm K	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 32 (62.50%)	19 / 34 (55.88%)	
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 32 (6.25%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Headache			
subjects affected / exposed	8 / 32 (25.00%)	1 / 34 (2.94%)	
occurrences (all)	8	1	
Memory impairment			

subjects affected / exposed	0 / 32 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 32 (9.38%)	6 / 34 (17.65%)	
occurrences (all)	3	6	
Pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 34 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 32 (6.25%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 32 (3.13%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	5 / 32 (15.63%)	3 / 34 (8.82%)	
occurrences (all)	5	3	
Dry mouth			
subjects affected / exposed	2 / 32 (6.25%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Flatulence			
subjects affected / exposed	2 / 32 (6.25%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	3 / 32 (9.38%)	3 / 34 (8.82%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 32 (3.13%)	3 / 34 (8.82%)	
occurrences (all)	1	3	
Paranasal sinus discomfort			
subjects affected / exposed	0 / 32 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	3	
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 32 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	2 / 32 (6.25%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 34 (2.94%)	
occurrences (all)	3	1	
Back pain			
subjects affected / exposed	0 / 32 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Urinary tract infection			

subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	3 / 34 (8.82%) 3	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1	 2 / 34 (5.88%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2014	Amendment 1 (multinational) Added treatment Arm B to include alternate dose of ABT-530. Extended Screening Period duration from 35 to 42 days. Revised the time period for contraception use in inclusion criteria.
02 December 2014	Amendment 1.01 (multinational) Added Part 2 including chronic HCV GT1-infected subjects without cirrhosis (8-week treatment duration), HCV GT1-infected subjects with compensated cirrhosis (12-week treatment duration), and HCV GT4-, GT5-, and GT6-infected subjects without cirrhosis (12-week treatment duration), based on the safety and efficacy results from the initial two arms (Part 1, Arms A and B) of the study. Updated Inclusion Criteria 10 and 11 to enhance the criteria for defining absence of cirrhosis based on FibroTest and aminotransferase/platelet ratio index (APRI) scores. Updated Resistance Analyses to include phylogenetic analysis of viral subtypes to determine/confirm subtypes of HCV GT4, 5, or 6, so that treatment efficacy could be compared across different subtypes.
23 February 2015	Amendment 1.02 (US/Puerto Rico) Added Arm K. Added a potential method (deep sequencing) to sequence HCV samples.
12 March 2015	Amendment 1.03 (UK) Clarified the definition of total abstinence. Specified all contraceptive methods. Clarified period of AE collection after completion of study treatment.
06 April 2015	Amendment 1.01.01 (multinational) Replaced dose of ABT-493 200 mg with 300 mg in Arm I. Updated the randomization methods of the population of subjects with compensated cirrhosis in the event that less than 4 arms were opened for enrollment. Included subjects who were on stable chronic opioid maintenance therapy. Updated the Toxicity Management section. Updated results for Part 1 of the study with preliminary safety and efficacy data that would be utilized for the enablement criteria for Part 2. Clarified that any past historical liver biopsy demonstrating cirrhosis was acceptable, and no further testing was necessary at a later time.
06 April 2015	Amendment 1.02.01 (US/Puerto Rico) Implemented the same changes from multinational Amendment 1.01.01 into the US/Puerto Rico-only protocol (Amendment 1.02)
06 April 2015	Amendment 1.03.01 (UK) Implemented the same changes from multinational Amendment 1.01.01 into the UK-only protocol (Amendment 1.03).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported