Clinical trial results:
A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Coadministration of ABT-450 with Ritonavir (ABT-450/r) and ABT-267 in Adults with Chronic Hepatitis C Virus Infection (PEARL-I)

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-005762-38
Trial protocol	ES HU IT
Global end of trial date	17 February 2015
Results information	
Result version number	v1 (current)
This version publication date	18 May 2016
First version publication date	18 May 2016

Trial information

Trial identification	
Sponsor protocol code	M13-393
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01685203
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire , United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, +001 800-633-9110,
Scientific contact	Nilou Mobashery, MD, AbbVie, nilou.mobashery@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	17 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of co-administration of ABT-450 (also known as paritaprevir) with ritonavir (ABT-450/r) and ABT-267 (also known as ombitasvir) in adults with chronic hepatitis C virus infection.

Protection of trial subjects:

Participants read and understood information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Spain: 60
Country: Number of subjects enrolled	France: 74
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Romania: 49
Country: Number of subjects enrolled	Turkey: 9
Country: Number of subjects enrolled	United States: 63
Worldwide total number of subjects	316
EEA total number of subjects	244

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)	291
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Group 5 (Genotype 4 (GT4) treatment-experienced, ABT-450 150 mg + ritonavir 100 mg + ABT-267 25 mg (2-DAA) regimen for 12 weeks) was not open to enrollment, based on a protocol-specified interim review of results from the treatment-naïve GT4 Groups 1 and 4 that indicated higher SVR rates among subjects receiving the 2-DAA regimen with ribavirin.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4-infected participants

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 12 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 12 weeks

Arm title	Group 2

Arm description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve HCV GT1b-infected participants

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 12 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 12 weeks

Arm title	Group 3

Arm description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, HCV GT1b-infected, pegylated-interferon/ribavirin (pegIFN/RBV) treatment null responder participants

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 12 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 12 weeks

Arm title	Group 4

Arm description:

ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4 -infected participants

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 12 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 12 weeks

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

Dosage and administration details:

1,000 mg/day if body weight < 75 kg or 1,200 mg/day if body weight ≥ 75 kg, divided twice daily, for 12 weeks

Arm title	Group 6

Arm description:

ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, HCV GT4-infected, pegylated-interferon/RBV (pegIFN/RBV) treatment-experienced participants

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 12 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 12 weeks

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

Dosage and administration details:

1,000 mg/day if body weight < 75 kg or 1,200 mg/day if body weight ≥ 75 kg, divided twice daily, for 12 weeks

Arm title	Group 7

Arm description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, treatment-naïve participants with compensated cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 24 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 24 weeks

Arm title	Group 8

Arm description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, pegylated-interferon/RBV(pegIFN/RBV) treatment-experienced participants with compensated cirrhosis

Arm type	Experimental
Investigational medicinal product name	ABT-450/ritonavir
Investigational medicinal product code	
Other name	ABT-450 also known as paritaprevir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet; ABT-450; Capsule; ritonavir
ABT-450 150 mg/ritonavir 100 mg once daily for 24 weeks

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	ABT-267 also known as ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg once daily for 24 weeks

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	44	42	40
Completed study drug	42	40	39 [1]
Completed	40	39	40
Not completed	4	3	0
Adverse event, non-fatal	-	-	-
Adverse event and withdrew consent	1	-	-
Patient's decision	-	-	-
Lost to follow-up	3	3	-

Number of subjects in period 1	Group 4	Group 6	Group 7
Started	42	49	47
Completed study drug	42	49	43 [2]
Completed	41	49	44
Not completed	1	0	3
Adverse event, non-fatal	-	-	2
Adverse event and withdrew consent	-	-	-

Patient's decision	-	-	1
Lost to follow-up	1	-	-

Number of subjects in period 1	Group 8
Started	52
Completed study drug	52
Completed	52
Not completed	0
Adverse event, non-fatal	-
Adverse event and withdrew consent	-
Patient's decision	-
Lost to follow-up	-

Notes:

[1] - 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 but continued the study in the post-treatment period.

[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 but continued the study in the post-treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4-infected participants	
Reporting group title	Group 2
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve HCV GT1b-infected participants	
Reporting group title	Group 3
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, HCV GT1b-infected, pegylated-interferon/ribavirin (pegIFN/RBV) treatment null responder participants	
Reporting group title	Group 4
Reporting group description:	
ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4 -infected participants	
Reporting group title	Group 6
Reporting group description:	
ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, HCV GT4-infected, pegylated-interferon/RBV (pegIFN/RBV) treatment-experienced participants	
Reporting group title	Group 7
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, treatment-naïve participants with compensated cirrhosis	
Reporting group title	Group 8
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, pegylated-interferon/RBV(pegIFN/RBV) treatment-experienced participants with compensated cirrhosis	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	44	42	40
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	42	36
From 65-84 years	2	0	4
85 years and over	0	0	0

Age continuous			
Units: years			
arithmetic mean	48.9	55.8	54.2
standard deviation	± 10.03	± 6.88	± 9.61
Gender categorical			
Units: Subjects			
Female	20	17	25
Male	24	25	15

Reporting group values	Group 4	Group 6	Group 7
Number of subjects	42	49	47
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	48	40
From 65-84 years	1	1	7
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44.2	50.9	57.8
standard deviation	± 12.67	± 10.13	± 7.12
Gender categorical			
Units: Subjects			
Female	14	13	24
Male	28	36	23

Reporting group values	Group 8	Total	
Number of subjects	52	316	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	42	291	
From 65-84 years	10	25	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	57.1		
standard deviation	± 6.02	-	

Gender categorical Units: Subjects			
Female	19	132	
Male	33	184	

Subject analysis sets

Subject analysis set title	Overall study
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who received at least 1 dose of study drug.

Reporting group values	Overall study		
Number of subjects	316		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	291		
From 65-84 years	25		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	52.8		
standard deviation	± 10.1		
Gender categorical Units: Subjects			
Female	132		
Male	184		

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4-infected participants	

Reporting group title	Group 2
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve HCV GT1b-infected participants	

Reporting group title	Group 3
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, HCV GT1b-infected, pegylated-interferon/ribavirin (pegIFN/RBV) treatment null responder participants	

Reporting group title	Group 4
Reporting group description:	
ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4 -infected participants	

Reporting group title	Group 6
Reporting group description:	
ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, HCV GT4-infected, pegylated-interferon/RBV (pegIFN/RBV) treatment-experienced participants	

Reporting group title	Group 7
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, treatment-naïve participants with compensated cirrhosis	

Reporting group title	Group 8
Reporting group description:	
ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, pegylated-interferon/RBV(pegIFN/RBV) treatment-experienced participants with compensated cirrhosis	

Subject analysis set title	Overall study
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants who received at least 1 dose of study drug.	

Primary: Percentage of participants in each treatment group with sustained virologic response 12 weeks post-treatment

End point title	Percentage of participants in each treatment group with sustained virologic response 12 weeks post-treatment
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 quantitation [<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	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44[1]	42[2]	40[3]	42[4]
Units: Percentage of participants				
number (confidence interval 95%)	90.9 (78.3 to 97.5)	95.2 (83.8 to 99.4)	90 (76.3 to 97.2)	100 (91.6 to 100)

Notes:

[1] - All randomized participants who received at least 1 dose of study drug.

[2] - All participants who received at least 1 dose of study drug.

[3] - All participants who received at least 1 dose of study drug.

[4] - All randomized participants who received at least 1 dose of study drug.

End point values	Group 6	Group 7	Group 8	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[5]	47[6]	52[7]	
Units: Percentage of participants				
number (confidence interval 95%)	100 (92.7 to 100)	97.9 (88.7 to 99.9)	98.1 (89.7 to 100)	

Notes:

[5] - All participants who received at least 1 dose of study drug.

[6] - All participants who received at least 1 dose of study drug.

[7] - All participants who received at least 1 dose of study drug.

Statistical analyses

Statistical analysis title	Pairwise comparison between Groups 2 and 3
Comparison groups	Group 2 v Group 3
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.381 [8]
Method	Regression, Logistic

Notes:

[8] - Treatment group, baseline log(subscript)10(subscript) HCV RNA level and Interleukin-28B (IL28B) genotype (CC or non-CC) were used as predictors

Statistical analysis title	Additional comparison, Group 1 vs Group 4
Comparison groups	Group 1 v Group 4
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.086 [9]
Method	Stratum-adjusted Mantel-Haenszel

Notes:

[9] - Difference in rates after adjusting for Interleukin-28 (IL28) genotype (CC or Non-CC) using stratum-adjusted Mantel-Haenszel proportions and continuity-corrected variances.

Secondary: Percentage of Participants in Each Treatment Group With Sustained Virologic Response 24 Weeks Post-treatment

End point title	Percentage of Participants in Each Treatment Group With Sustained Virologic Response 24 Weeks Post-treatment

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 quantitation [<LLOQ]) 24 weeks after the last dose of

study drug.

End point type	Secondary

End point timeframe:

24 weeks after the last actual dose of study drug

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44[10]	42[11]	40[12]	42[13]
Units: Percentage of participants				
number (confidence interval 95%)	86.4 (72.6 to 94.8)	92.9 (80.5 to 98.5)	90 (76.3 to 97.2)	100 (91.6 to 100)

Notes:

[10] - All randomized participants who received at least 1 dose of study drug.

[11] - All participants who received at least 1 dose of study drug.

[12] - All participants who received at least 1 dose of study drug.

[13] - All randomized participants who received at least 1 dose of study drug.

End point values	Group 6	Group 7	Group 8	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[14]	47[15]	52[16]	
Units: Percentage of participants				
number (confidence interval 95%)	100 (92.7 to 100)	97.9 (88.7 to 99.9)	98.1 (89.7 to 100)	

Notes:

[14] - All participants who received at least 1 dose of study drug.

[15] - All participants who received at least 1 dose of study drug.

[16] - All participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Each Treatment Group With On-treatment Virologic Failure

End point title	Percentage of Participants in Each Treatment Group With On-treatment Virologic Failure

End point description:

Virologic failure during treatment was defined as rebound (confirmed HCV RNA greater than or equal to the lower limit of quantitation [≥ LLOQ] after HCV RNA < LLOQ during treatment, or confirmed increase from the lowest value post baseline in HCV RNA [2 consecutive HCV RNA measurements > 1 log(subscript)10(subscript) IU/mL above the lowest value post baseline] at any time point during treatment), or failure to suppress (HCV RNA ≥ LLOQ persistently during treatment with at least 6 weeks [≥ 36 days] of treatment).

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 3, and Treatment Weeks 1, 2 ,3 ,4, 6, 8, 10, and 12 for all participants and Treatment Weeks 16, 20 and 24 for Groups 7 and 8

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44[17]	42[18]	40[19]	42[20]
Units: Percentage of participants				
number (confidence interval 95%)	2.3 (0.1 to 12)	0 (0 to 8.4)	2.5 (0.1 to 13.2)	0 (0 to 8.4)

Notes:

[17] - All randomized participants who received at least 1 dose of study drug.

[18] - All participants who received at least 1 dose of study drug.

[19] - All participants who received at least 1 dose of study drug.

[20] - All randomized participants who received at least 1 dose of study drug.

End point values	Group 6	Group 7	Group 8	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[21]	47[22]	52[23]	
Units: Percentage of participants				
number (confidence interval 95%)	0 (0 to 7.3)	0 (0 to 7.5)	0 (0 to 6.8)	

Notes:

[21] - All participants who received at least 1 dose of study drug.

[22] - All participants who received at least 1 dose of study drug.

[23] - All participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Each Treatment Group With Post-treatment Virologic Relapse.

End point title	Percentage of Participants in Each Treatment Group With Post-treatment Virologic Relapse.

End point description:

Participants were considered to have virologic relapse after treatment if they had confirmed quantifiable plasma Hepatitis C virus ribonucleic acid (HCV RNA) ≥ lower limit of quantification (LLOQ) between the end of treatment and 12 weeks after the last dose of study drug among participants who completed treatment with HCV RNA < LLOQ at the end of treatment.

End point type	Secondary

End point timeframe:

Within 12 weeks after the last dose of study drug

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42[24]	40[25]	39[26]	42[27]
Units: Percentage of participants				
number (confidence interval 95%)	4.8 (0.6 to 16.2)	0 (0 to 8.8)	7.7 (1.6 to 20.9)	0 (0 to 8.4)

Notes:

[24] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit

[25] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit

[26] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit
[27] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit

End point values	Group 6	Group 7	Group 8	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[28]	44[29]	52[30]	
Units: Percentage of participants				
number (confidence interval 95%)	0 (0 to 7.3)	0 (0 to 8)	1.9 (0 to 10.3)	

Notes:
[28] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit
[29] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit
[30] - Subjects who rcvd at least 1 dose of study drug and ended Tx with HCV RNA <LLOQ at the last Tx visit

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each treatment group with treatment-emergent adverse events

End point title	Percentage of participants in each treatment group with treatment-emergent adverse events

End point description:
Treatment-emergent adverse events were defined as any event that began or worsened in severity after initiation of study drug through 30 days after the last dose of study drug.

End point type	Secondary

End point timeframe:
From the time of study drug administration until 30 days after the last dose, up to 16 weeks for Groups 1, 2, 3, 4, and 6, and up to 28 weeks for Groups 7 and 8

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44[31]	42[32]	40[33]	42[34]
Units: Percentage of participants				
number (not applicable)	77.3	73.8	80	88.1

Notes:
[31] - All randomized participants who received at least one dose of study drug.
[32] - All participants who received at least one dose of study drug.
[33] - All participants who received at least one dose of study drug.
[34] - All randomized participants who received at least one dose of study drug.

End point values	Group 6	Group 7	Group 8	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[35]	47[36]	52[37]	
Units: Percentage of participants				
number (not applicable)	85.7	85.1	71.2	

Notes:
[35] - All participants who received at least one dose of study drug.
[36] - All participants who received at least one dose of study drug.
[37] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from study drug administration until 30 days after the last dose, up to 16 wks for Groups 1-4, & 6, and up to 28 wks for Groups 7 & 8. Serious AEs were collected from informed consent until the end of the study, up to 65 wks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Group 1

Reporting group description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4-infected participants

Reporting group title	Group 2

Reporting group description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, treatment-naïve HCV GT1b-infected participants

Reporting group title	Group 3

Reporting group description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 12 weeks to adult noncirrhotic, HCV GT1b-infected, pegylated-interferon/ribavirin (pegIFN/RBV) treatment null responder participants

Reporting group title	Group 4

Reporting group description:

ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, treatment-naïve, HCV GT4 -infected participants

Reporting group title	Group 6

Reporting group description:

ABT-450 150 mg/ r 100 mg, ABT-267 25 mg , once daily and weight-based ribavirin (RBV; 1,000 mg/day if < 75 kg or 1,200 mg/day if ≥ 75 kg, divided twice daily) for 12 weeks to adult noncirrhotic, HCV GT4-infected, pegylated-interferon/RBV (pegIFN/RBV) treatment-experienced participants

Reporting group title	Group 7

Reporting group description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, treatment-naïve participants with compensated cirrhosis

Reporting group title	Group 8

Reporting group description:

ABT-450 150 mg/ r 100 mg, and ABT-267 25 mg once daily for 24 weeks to adult, HCV GT1b-infected, pegylated-interferon/RBV(pegIFN/RBV) treatment-experienced participants with compensated cirrhosis

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 44 (4.55%)	1 / 42 (2.38%)	1 / 40 (2.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic neoplasm			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (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
Humerus fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Road traffic accident			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (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
Vascular disorders			
Peripheral artery aneurysm			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Partial seizures			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
General disorders and administration site conditions			
Device extrusion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (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

Serious adverse events	Group 4	Group 6	Group 7
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic neoplasm			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Humerus fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Road traffic accident			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Vascular disorders			
Peripheral artery aneurysm			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Nervous system disorders			

Partial seizures			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
General disorders and administration site conditions			
Device extrusion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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
Gastrointestinal disorders			
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (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	Group 8		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 52 (3.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic neoplasm			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral artery aneurysm			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Partial seizures			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Device extrusion			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 44 (68.18%)	24 / 42 (57.14%)	26 / 40 (65.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 44 (25.00%)	3 / 42 (7.14%)	2 / 40 (5.00%)
occurrences (all)	12	6	2
Fatigue			
subjects affected / exposed	3 / 44 (6.82%)	6 / 42 (14.29%)	0 / 40 (0.00%)
occurrences (all)	4	6	0
Influenza like illness			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
Irritability			

subjects affected / exposed	3 / 44 (6.82%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	1 / 44 (2.27%)	3 / 42 (7.14%)	0 / 40 (0.00%)
occurrences (all)	1	3	0
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	2 / 40 (5.00%)
occurrences (all)	0	2	2
Dyspnoea exertional			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 44 (4.55%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	2 / 44 (4.55%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Depression			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	3 / 40 (7.50%)
occurrences (all)	1	1	3
Headache			
subjects affected / exposed	13 / 44 (29.55%)	14 / 42 (33.33%)	10 / 40 (25.00%)
occurrences (all)	16	16	11
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 44 (2.27%)	3 / 42 (7.14%)	1 / 40 (2.50%)
occurrences (all)	1	4	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	2 / 44 (4.55%)	6 / 42 (14.29%)	0 / 40 (0.00%)
occurrences (all)	2	6	0
Dyspepsia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	4 / 44 (9.09%)	8 / 42 (19.05%)	0 / 40 (0.00%)
occurrences (all)	4	9	0
Vomiting			
subjects affected / exposed	0 / 44 (0.00%)	3 / 42 (7.14%)	0 / 40 (0.00%)
occurrences (all)	0	4	0
Skin and subcutaneous tissue disorders			

Dry skin			
subjects affected / exposed	0 / 44 (0.00%)	7 / 42 (16.67%)	0 / 40 (0.00%)
occurrences (all)	0	7	0
Pruritus			
subjects affected / exposed	2 / 44 (4.55%)	6 / 42 (14.29%)	0 / 40 (0.00%)
occurrences (all)	2	8	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	3 / 44 (6.82%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	2 / 40 (5.00%)
occurrences (all)	0	2	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Nasopharyngitis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 42 (2.38%)	2 / 40 (5.00%)
occurrences (all)	2	1	3
Rhinitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	3 / 44 (6.82%)	2 / 42 (4.76%)	2 / 40 (5.00%)
occurrences (all)	3	2	2
Gastroenteritis			

subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 42 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Increased appetite			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	0 / 40 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Group 4	Group 6	Group 7
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 42 (76.19%)	38 / 49 (77.55%)	34 / 47 (72.34%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 42 (2.38%)	1 / 49 (2.04%)	7 / 47 (14.89%)
occurrences (all)	1	2	7
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 42 (23.81%)	16 / 49 (32.65%)	10 / 47 (21.28%)
occurrences (all)	14	21	12
Fatigue			
subjects affected / exposed	5 / 42 (11.90%)	9 / 49 (18.37%)	4 / 47 (8.51%)
occurrences (all)	7	11	4
Influenza like illness			
subjects affected / exposed	0 / 42 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	6 / 42 (14.29%)	2 / 49 (4.08%)	1 / 47 (2.13%)
occurrences (all)	6	2	1
Oedema peripheral			
subjects affected / exposed	1 / 42 (2.38%)	2 / 49 (4.08%)	2 / 47 (4.26%)
occurrences (all)	1	2	2
Pyrexia			

subjects affected / exposed	1 / 42 (2.38%)	3 / 49 (6.12%)	1 / 47 (2.13%)
occurrences (all)	1	3	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 42 (4.76%)	4 / 49 (8.16%)	3 / 47 (6.38%)
occurrences (all)	2	4	3
Dyspnoea exertional			
subjects affected / exposed	2 / 42 (4.76%)	3 / 49 (6.12%)	0 / 47 (0.00%)
occurrences (all)	2	5	0
Epistaxis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 42 (9.52%)	2 / 49 (4.08%)	1 / 47 (2.13%)
occurrences (all)	4	2	1
Insomnia			
subjects affected / exposed	4 / 42 (9.52%)	8 / 49 (16.33%)	3 / 47 (6.38%)
occurrences (all)	4	8	4
Depression			
subjects affected / exposed	1 / 42 (2.38%)	3 / 49 (6.12%)	1 / 47 (2.13%)
occurrences (all)	1	3	1
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 42 (0.00%)	3 / 49 (6.12%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Headache			
subjects affected / exposed	14 / 42 (33.33%)	14 / 49 (28.57%)	9 / 47 (19.15%)
occurrences (all)	18	16	11
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 42 (4.76%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	2	1	3
Abdominal pain upper			
subjects affected / exposed	1 / 42 (2.38%)	1 / 49 (2.04%)	1 / 47 (2.13%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	6 / 42 (14.29%)	3 / 49 (6.12%)	7 / 47 (14.89%)
occurrences (all)	7	4	8
Dyspepsia			
subjects affected / exposed	2 / 42 (4.76%)	4 / 49 (8.16%)	0 / 47 (0.00%)
occurrences (all)	2	4	0
Flatulence			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	7 / 42 (16.67%)	6 / 49 (12.24%)	5 / 47 (10.64%)
occurrences (all)	9	7	5
Vomiting			
subjects affected / exposed	2 / 42 (4.76%)	0 / 49 (0.00%)	2 / 47 (4.26%)
occurrences (all)	6	0	2
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 42 (0.00%)	3 / 49 (6.12%)	1 / 47 (2.13%)
occurrences (all)	0	5	1
Pruritus			

subjects affected / exposed	1 / 42 (2.38%)	5 / 49 (10.20%)	8 / 47 (17.02%)
occurrences (all)	1	7	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 49 (2.04%)	4 / 47 (8.51%)
occurrences (all)	2	1	4
Back pain			
subjects affected / exposed	2 / 42 (4.76%)	4 / 49 (8.16%)	6 / 47 (12.77%)
occurrences (all)	2	4	6
Myalgia			
subjects affected / exposed	0 / 42 (0.00%)	5 / 49 (10.20%)	3 / 47 (6.38%)
occurrences (all)	0	5	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 49 (4.08%)	3 / 47 (6.38%)
occurrences (all)	1	2	5
Influenza			
subjects affected / exposed	0 / 42 (0.00%)	2 / 49 (4.08%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Nasopharyngitis			
subjects affected / exposed	2 / 42 (4.76%)	6 / 49 (12.24%)	4 / 47 (8.51%)
occurrences (all)	2	6	4
Rhinitis			
subjects affected / exposed	0 / 42 (0.00%)	3 / 49 (6.12%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 42 (4.76%)	1 / 49 (2.04%)	2 / 47 (4.26%)
occurrences (all)	2	1	2
Urinary tract infection			
subjects affected / exposed	1 / 42 (2.38%)	2 / 49 (4.08%)	2 / 47 (4.26%)
occurrences (all)	1	3	3
Gastroenteritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	1 / 42 (2.38%)	3 / 49 (6.12%)	2 / 47 (4.26%)
occurrences (all)	1	3	2
Hyperglycaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3

Non-serious adverse events	Group 8		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 52 (63.46%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	9		
Fatigue			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	6		
Influenza like illness			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Irritability			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal			

disorders Cough subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	5 / 52 (9.62%) 6 0 / 52 (0.00%) 0 1 / 52 (1.92%) 1 3 / 52 (5.77%) 3		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2 4 / 52 (7.69%) 4 1 / 52 (1.92%) 1		
Investigations Blood pressure increased subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache	1 / 52 (1.92%) 1		

subjects affected / exposed occurrences (all)	10 / 52 (19.23%) 11		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 52 (1.92%) 1 4 / 52 (7.69%) 4 7 / 52 (13.46%) 8 0 / 52 (0.00%) 0 3 / 52 (5.77%) 3 5 / 52 (9.62%) 6 1 / 52 (1.92%) 1		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0 9 / 52 (17.31%) 9		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	5 / 52 (9.62%) 5		
Myalgia subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2		
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Influenza subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 4		
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4		
Rhinitis subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Hyperglycaemia			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Increased appetite			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2012	Protocol Amendment No. 1 was dated 27 June 2012, and 86 subjects were enrolled into the study under this amendment. The purpose of Amendment No. 1 is summarized as follows: ● Modify the study design, by removing the HCV GT1a 8-week treatment group. ● Revise the study objectives based on the modified study design. ● Revise the efficacy variables based on the modified study design. ● Revise the efficacy endpoints based on the modified study design. ● Revise how study enrollment would occur. ● Update the data required for review prior to opening Group 1 and/or Group 4. ● Clarify post study treatment information. ● Clarify the efficacy stopping criteria. ● Include the collection of optional mRNA study samples. ● Incorporate Administrative Change 1. ● Address any inconsistencies throughout the protocol.
21 January 2013	Protocol Amendment No. 2 was dated 21 January 2013, and 127 subjects were enrolled into the study under this amendment. The purpose of Amendment No. 2 is summarized as follows: ● Modify the study design by: Removing the HCV GT1a 12-week treatment group. Removing the HCV GT1b 8-week treatment group. Adding 2 GT4 treatment-naïve treatment arms (Groups 1 and 4). Adding 2 GT4 treatment-experienced treatment arms (Groups 5 and 6). Adding GT1b treatment-naïve and treatment-experienced subjects with compensated cirrhosis (Groups 7 and 8). ● Revise the study objectives based on the modified study design. ● Revise the efficacy variables based on the modified study design. ● Revise the statistical analyses based on the modified study design. ● Revise how study enrollment will occur. ● Add the data required for review prior to opening Groups 5 – 8. ● Clarify the efficacy stopping criteria. ● Change the primary Study Designated Physician. ● Incorporate Administrative Change 2. ● Update Section 1.0 – Title Page. ● Update Section 1.2 – Synopsis, Section 1.3 – List of Abbreviations and Definition of Terms, and Section 2.0 – Table of Contents. ● Update Section 3.0 – Introduction, Section 4.0 – Study Objectives, Section 5.0 – Investigational Plan, and Section 6.0 – Adverse Events and all subsections under each of these sections. ● Update Section 8.0 – Statistical Methods and Determination of Sample Size and all subsections under this section. ● Update Section 15.0 – Reference List. ● Added Appendix C – Clinical Toxicity Grades. ● Address any inconsistencies throughout the protocol.
08 April 2013	Protocol Amendment No. 3 was dated 08 April 2013, and 95 subjects were enrolled into the study under this amendment. The purpose of Amendment No. 3 is summarized as follows: ● Prohibit the use of hormonal contraceptives during study drug administration.

13 August 2013	Protocol Amendment No. 4 was dated 13 August 2013, and 6 subjects were enrolled into the study under this amendment. The purpose of Amendment No. 4 is summarized as follows: ● Address inconsistencies throughout the protocol. ● Modify Inclusion Criterion No. 2 and corresponding contraception language throughout the protocol to specify contraindication of hormone eluting IUDs. ● Modify Inclusion Criterion No. 11 to include FibroTest/APRI. ● Modify Exclusion Criterion No. 8 to allow for rescreening of subjects who test positive for alcohol on their initial drug/alcohol screening. ● Modify Exclusion Criterion No. 20 to exclude an Absolute Neutrophil Count (ANC) < 1200 cells/µL for subjects of African descent who are black. ● Modify Section 5.1.1.1 Rescreening language. ● Remove language prohibiting the use of inhibitors of CYP2C8 from Section 5.2.3.3 Prohibited Therapy. ● Add a laboratory collection at Post-Treatment Week 12 visit in Table 2 for subjects participating in Substudy 2. ● Remove requirement that sites maintain a MEMS cap accountability form provided by AbbVie. ● Modify Section 5.3.2.3 Disposition of Samples to remove "An inventory of the samples included will accompany the package." ● Modify Section 5.5.7 Drug Accountability language. ● Modify Section 6.7.3 to include additional language regarding the management of bilirubin elevations. ● Modify definition of on-treatment virologic failure. ● Add footnotes for Ascites to Table 4. ● Modify Section 8.1.3.2 Secondary Efficacy Endpoints.
17 October 2013	Amendment No. 5 was dated 17 October 2013, and 2 subjects were enrolled under this amendment. The purpose of Amendment No. 5 is summarized as follows: ● Modify the text to reflect the decision to extend the treatment period for Groups 7 and 8 subjects to 24 weeks. ● Modify study design to reflect the decision to open enrollment for Group 6 (the HCV GT4 treatment-experienced group to be treated with the 2-DAA regimen plus RBV) but not Group 5 (the HCV GT4 treatment-experienced group to be treated with the 2-DAA regimen without RBV). ● Remove the interim analyses for all subjects who have completed treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Not applicable

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25837829

http://www.ncbi.nlm.nih.gov/pubmed/26170136