



Clinical trial results:

A Randomized, Open-Label Study to Evaluate the Efficacy and Safety of ABT-450/Ritonavir/ABT-267 and ABT-333 Co-administered with and without Ribavirin Compared to Telaprevir Co-administered with Pegylated Interferon -2a and Ribavirin in Treatment-Naïve Adults with Chronic Hepatitis C Genotype 1 Virus Infection (MALACHITE I)

Summary

EudraCT number	2012-003754-84
Trial protocol	HU FI SK PL
Global end of trial date	16 July 2015

Results information

Result version number	v1 (current)
This version publication date	24 July 2016
First version publication date	24 July 2016

Trial information

Trial identification

Sponsor protocol code	M13-774
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01854697
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 4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Yan Luo, AbbVie, Yan.Luo@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	16 July 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study to evaluate the efficacy and safety of three experimental drugs compared with telaprevir (a licensed product) in people with hepatitis C virus infection who have not had treatment before.

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	28 March 2013
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	Argentina: 12
Country: Number of subjects enrolled	Australia: 36
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	Chile: 29
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	Hungary: 32
Country: Number of subjects enrolled	Norway: 16
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Romania: 83
Country: Number of subjects enrolled	Slovakia: 5
Worldwide total number of subjects	311
EEA total number of subjects	183

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)	308
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a Screening Period of up to 35 days.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: 3-DAA + RBV in GT1a

Arm description:

ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a)

Arm type	Experimental
Investigational medicinal product name	ABT-450/r/ABT-267
Investigational medicinal product code	
Other name	Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267)
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

Arm title	Arm B: TPV/PR in GT1a
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Arm description:

Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and

weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a)

Arm type	Active comparator
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	INCIVO®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

TPV 375 mg film-coated tablets, to be taken orally as 2 tablets every 8 hours, which corresponds to 750 mg TPV dose every 8 hours. Alternative dosing schedules for TPV (1,125 mg every 12 hours) were allowed per the prescribing information and only if approved by AbbVie.

Investigational medicinal product name	Peginterferon alfa-2a
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegylated interferon α-2a in kits of 1 prefilled syringe with 180 µg/0.5 mL per syringe. PegIFN was administered as an SC injection once per week.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

Arm title	Arm C: 3-DAA + RBV in GT1b
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Arm description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b)

Arm type	Experimental
Investigational medicinal product name	ABT-450/r/ABT-267
Investigational medicinal product code	
Other name	Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267)
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

Arm title	Arm D: 3-DAA in GT1b
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Arm description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b)

Arm type	Experimental
Investigational medicinal product name	ABT-450/r/ABT-267
Investigational medicinal product code	
Other name	Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267)
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

Arm title	Arm E: TPV/PR in GT1b
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Arm description:

Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b)

Arm type	Active comparator
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	INCIVO®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

TPV 375 mg film-coated tablets, to be taken orally as 2 tablets every 8 hours, which corresponds to 750 mg TPV dose every 8 hours. Alternative dosing schedules for TPV (1,125 mg every 12 hours) were allowed per the prescribing information and only if approved by AbbVie.

Investigational medicinal product name	Peginterferon alfa-2a
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegylated interferon α-2a in kits of 1 prefilled syringe with 180 µg/0.5 mL per syringe. PegIFN was

administered as an SC injection once per week.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

Number of subjects in period 1	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b
Started	69	34	84
Completed	63	31	82
Not completed	6	3	2
Withdrew Consent	-	1	-
To enter another AbbVie study	1	-	-
Not Specified	-	1	1
Adverse event	1	-	-
Lost to follow-up	4	1	1

Number of subjects in period 1	Arm D: 3-DAA in GT1b	Arm E: TPV/PR in GT1b
Started	83	41
Completed	80	39
Not completed	3	2
Withdrew Consent	1	-
To enter another AbbVie study	-	1
Not Specified	-	-
Adverse event	-	1
Lost to follow-up	2	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A: 3-DAA + RBV in GT1a
Reporting group description: ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a)	
Reporting group title	Arm B: TPV/PR in GT1a
Reporting group description: Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a)	
Reporting group title	Arm C: 3-DAA + RBV in GT1b
Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b)	
Reporting group title	Arm D: 3-DAA in GT1b
Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b)	
Reporting group title	Arm E: TPV/PR in GT1b
Reporting group description: Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b)	

Reporting group values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b
Number of subjects	69	34	84
Age, Customized Units: participants			
< 55 years	46	23	59
>= 55 years	23	11	25
Age Continuous Units: years			
arithmetic mean	46.1	44.5	46.2
standard deviation	± 12.25	± 14.1	± 11.34
Gender, Male/Female Units: participants			
Female	21	17	46
Male	48	17	38

Reporting group values	Arm D: 3-DAA in GT1b	Arm E: TPV/PR in GT1b	Total
Number of subjects	83	41	311
Age, Customized Units: participants			
< 55 years	60	31	219
>= 55 years	23	10	92

Age Continuous Units: years arithmetic mean standard deviation	47.1 ± 11.33	45.9 ± 10.78	-
Gender, Male/Female Units: participants			
Female	43	24	151
Male	40	17	160

End points

End points reporting groups

Reporting group title	Arm A: 3-DAA + RBV in GT1a
Reporting group description: ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a)	
Reporting group title	Arm B: TPV/PR in GT1a
Reporting group description: Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a)	
Reporting group title	Arm C: 3-DAA + RBV in GT1b
Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b)	
Reporting group title	Arm D: 3-DAA in GT1b
Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b)	
Reporting group title	Arm E: TPV/PR in GT1b
Reporting group description: Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b)	

Primary: Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment (SVR12) - Primary Efficacy Analyses

End point title	Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment (SVR12) - Primary Efficacy Analyses
End point description: The percentage of subjects with sustained virologic response (plasma Hepatitis C virus ribonucleic acid [HCV RNA] level less than the lower limit of quantitation [$< \text{LLOQ}$]) 12 weeks after the last dose of study drug.	
End point type	Primary
End point timeframe: 12 weeks after the last actual dose of active study drug	

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	34	84	83
Units: percentage of subjects				
number (not applicable)	97.1	82.4	98.8	97.6

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	78			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Difference
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	32.6

Notes:

[1] - The primary endpoint assessment comparison was made within each of the 2 HCV genotypes (GT1a and GT1b). Within HCV GT1a, the 3-DAA + RBV and TPV/PR arms were compared. Within HCV GT1b, the 3-DAA and TPV/PR arms were compared. The test treatment arm was considered noninferior to the TPV/PR arm in the respective HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm B: TPV/PR in GT1a v Arm A: 3-DAA + RBV in GT1a
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Parameter estimate	Difference
Point estimate	14.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	28.2

Notes:

[2] - The primary endpoint assessment comparison was made within each of the 2 HCV genotypes (GT1a and GT1b). Within HCV GT1a, the 3-DAA + RBV and TPV/PR arms were compared. Within HCV GT1b, the 3-DAA and TPV/PR arms were compared. The test treatment arm was considered noninferior to the TPV/PR arm in the respective HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Secondary: Mean Change From Baseline to the Final Treatment Visit in Short-Form 36 Version 2 Health Status Survey (SF-36V2) Mental Component Summary (MCS)

End point title	Mean Change From Baseline to the Final Treatment Visit in Short-Form 36 Version 2 Health Status Survey (SF-36V2) Mental Component Summary (MCS)
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End point description:

SF-36V2 is a generic 36-item questionnaire measuring health-related quality of life (HRQoL) covering 2 summary measures: physical component summary (PCS) and MCS; it consists of 8 subscales. The MCS is represented by 4 subscales: vitality, social function, role limitations due to emotional problems, and mental health. Subjects self-report on items in a subscale that have choices per item. Scoring is done for both MCS subscale scores and summary scores; for each, the range is 0 (worst HRQoL) to 100 (best HRQoL).

End point type	Secondary
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End point timeframe:

From Day 1 of treatment up to 12 weeks for Arms A, C and D and up to 24 or 48 weeks for Arms B and E

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	32	84	83
Units: units on a scale				
arithmetic mean (standard deviation)	-4.2 (± 10.59)	-5.8 (± 12.18)	-0.3 (± 8.89)	-0.1 (± 7.73)

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)	-6.4 (± 11.78)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.351
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.39
upper limit	6.65
Variability estimate	Standard error of the mean
Dispersion value	2.28

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Least Squares Mean of Difference
Point estimate	5.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.19
upper limit	9.47
Variability estimate	Standard error of the mean
Dispersion value	1.84

Statistical analysis title	Statistical Analysis 3
Comparison groups	Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Least Squares Mean of Difference
Point estimate	5.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	8.54
Variability estimate	Standard error of the mean
Dispersion value	1.65

Secondary: Mean Change From Baseline to the Final Treatment Visit in SF-36V2 Physical Component Summary (PCS)

End point title	Mean Change From Baseline to the Final Treatment Visit in SF-36V2 Physical Component Summary (PCS)
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End point description:

SF-36V2 is a generic 36-item questionnaire measuring HRQoL covering 2 summary measures: PCS and MCS; it consists of 8 subscales. The PCS is represented by 4 subscales: physical function, role limitations due to physical problems, bodily pain, and general health perception. Subjects self-report on items in a subscale that have choices per item. Scoring is done for both PCS subscale scores and summary scores; for each, the range is 0 (worst HRQoL) to 100 (best HRQoL).

End point type	Secondary
End point timeframe:	
From Day 1 of treatment up to 12 weeks for Arms A, C and D and up to 24 or 48 weeks for Arms B and E	

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	32	84	83
Units: units on a scale				
arithmetic mean (standard deviation)	0.5 (± 8.63)	-5.5 (± 8.26)	0.4 (± 5.8)	2.2 (± 4.34)

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)	-5.5 (± 11.46)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	6.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.72
upper limit	9.44
Variability estimate	Standard error of the mean
Dispersion value	1.69

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	6.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.36
upper limit	9.37
Variability estimate	Standard error of the mean
Dispersion value	1.27

Statistical analysis title	Statistical Analysis 3
Comparison groups	Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.55
upper limit	8.85
Variability estimate	Standard error of the mean
Dispersion value	1.34

Secondary: Percentage of Subjects With SVR12 - Secondary Efficacy Analyses

End point title	Percentage of Subjects With SVR12 - Secondary Efficacy Analyses
End point description: The percentage of subjects with sustained virologic response (plasma HCV RNA level < LLOQ) 12 weeks after the last dose of study drug.	
End point type	Secondary
End point timeframe: 12 weeks after the last actual dose of active study drug	

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	34	84	83
Units: percentage of subjects				
number (not applicable)	97.1	82.4	98.8	97.6

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	78			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	38

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Difference
Point estimate	20.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.9
upper limit	33.6

Notes:

[3] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	241.1

Statistical analysis title	Statistical Analysis 4
Comparison groups	Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Cochran-Mantel-Haenszel
Confidence interval	
sides	2-sided

Secondary: Percentage of Subjects with Virologic Failure During Treatment

End point title	Percentage of Subjects with Virologic Failure During Treatment
End point description:	
Subjects in Arms A, C or D demonstrating any of the following were considered virologic failures and discontinued therapy:	
• Confirmed increase from nadir in HCV RNA (defined as 2 consecutive HCV RNA measurements of >1 log₁₀ IU/mL above nadir) at any time point during treatment • Failure to achieve HCV RNA < LLOQ by Week 6 or • Confirmed HCV RNA ≥ LLOQ (defined as 2 consecutive HCV RNA measurements ≥ LLOQ) at any point after HCV RNA < LLOQ during treatment after HCV RNA < LLOQ.	
Subjects in Arms B and E followed virologic stopping criteria described in the TPV Summary of Product Characteristics; they were considered virologic failures and discontinued therapy as follows:	
• HCV RNA > 1000 IU/mL at Week 4 to Week 12, discontinue TPV and pegIFN and RBV • HCV RNA > 1000 IU/mL at Week 12, discontinue pegIFN and RBV • Confirmed HCV RNA > lower limit of detection (LLOD) at Week 24, discontinue pegIFN and RBV • Confirmed HCV RNA > LLOD at Week 36, discontinue pegIFN and RBV.	
End point type	Secondary
End point timeframe:	
12 weeks for Arms A, C and D and 24 weeks or 48 weeks for Arms B and E	

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	34	84	83
Units: percentage of subjects				
number (not applicable)	2.9	5.9	0	1.2

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	12.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Post-treatment Relapse

End point title	Percentage of Subjects with Post-treatment Relapse
End point description: Hepatitis C virus (HCV) ribonucleic acid (RNA) confirmed greater than or equal to the lower limit of quantification (LLOQ) between the end of treatment and 24 weeks post treatment among subjects completing treatment and with HCV RNA less than the LLOQ at the end of treatment.	
End point type	Secondary
End point timeframe: Within 24 weeks post treatment	

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66 ^[4]	28 ^[5]	84 ^[6]	81 ^[7]
Units: percentage of subjects				
number (not applicable)	0	0	1.2	0

Notes:

[4] - subjects with sustained virologic response at Week 24 (SVR24)

[5] - subjects with sustained virologic response at Week 24 (SVR24)

[6] - subjects with sustained virologic response at Week 24 (SVR24)

[7] - subjects with sustained virologic response at Week 24 (SVR24)81

End point values	Arm E: TPV/PR in GT1b			
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Subject group type	Reporting group			
Number of subjects analysed	32 ^[8]			
Units: percentage of subjects				
number (not applicable)	6.3			

Notes:

[8] - subjects with sustained virologic response at Week 24 (SVR24)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response 24 Weeks After Treatment (SVR24)

End point title	Percentage of Subjects With Sustained Virologic Response 24 Weeks After Treatment (SVR24)
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End point description:

The percentage of subjects with sustained virologic response (plasma HCV RNA level < LLOQ) 24 weeks after the last dose of study drug.

End point type	Secondary
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End point timeframe:

24 weeks after the last actual dose of active study drug

End point values	Arm A: 3-DAA + RBV in GT1a	Arm B: TPV/PR in GT1a	Arm C: 3-DAA + RBV in GT1b	Arm D: 3-DAA in GT1b
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	34	84	83
Units: percentage of subjects				
number (not applicable)	95.7	82.4	97.6	97.6

End point values	Arm E: TPV/PR in GT1b			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of subjects				
number (not applicable)	78			

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[9]
Parameter estimate	Difference
Point estimate	13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	27

Notes:

[9] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1a HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[10]
Parameter estimate	Difference
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	32.6

Notes:

[10] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[11]
Parameter estimate	Difference
Point estimate	19.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.5
upper limit	32.7

Notes:

[11] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) collected from time of study drug administration until 30 days following discontinuation or completion of study drug administration, up to 96 weeks. Serious AEs collected from signing of informed consent until study completion.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	3 DAA + RBV
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Reporting group description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks

Reporting group title	TPV + PEGIFN + RBV
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Reporting group description:

TPV 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir

Reporting group title	3 DAA
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Reporting group description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks

Serious adverse events	3 DAA + RBV	TPV + PEGIFN + RBV	3 DAA
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 153 (0.65%)	9 / 75 (12.00%)	0 / 83 (0.00%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
PROSTATE CANCER			
subjects affected / exposed	1 / 153 (0.65%)	0 / 75 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	0 / 153 (0.00%)	2 / 75 (2.67%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
Eye disorders			
RETINOPATHY			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
Gastrointestinal disorders			
HAEMATOCHESIA			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
Skin and subcutaneous tissue disorders			
TOXIC SKIN ERUPTION			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABSCESS LIMB			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (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
CELLULITIS			

subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	3 DAA + RBV	TPV + PEGIFN + RBV	3 DAA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 153 (65.36%)	74 / 75 (98.67%)	29 / 83 (34.94%)
Nervous system disorders			
DYSGEUSIA			
subjects affected / exposed	2 / 153 (1.31%)	6 / 75 (8.00%)	0 / 83 (0.00%)
occurrences (all)	2	6	0
DIZZINESS			
subjects affected / exposed	7 / 153 (4.58%)	13 / 75 (17.33%)	2 / 83 (2.41%)
occurrences (all)	7	14	2
HEADACHE			
subjects affected / exposed	41 / 153 (26.80%)	23 / 75 (30.67%)	16 / 83 (19.28%)
occurrences (all)	48	30	17
LETHARGY			
subjects affected / exposed	6 / 153 (3.92%)	4 / 75 (5.33%)	0 / 83 (0.00%)
occurrences (all)	6	4	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	10 / 153 (6.54%)	32 / 75 (42.67%)	1 / 83 (1.20%)
occurrences (all)	12	47	1
LEUKOPENIA			
subjects affected / exposed	0 / 153 (0.00%)	4 / 75 (5.33%)	0 / 83 (0.00%)
occurrences (all)	0	4	0
NEUTROPENIA			
subjects affected / exposed	0 / 153 (0.00%)	14 / 75 (18.67%)	0 / 83 (0.00%)
occurrences (all)	0	17	0
General disorders and administration site conditions			
ASTHENIA			

subjects affected / exposed occurrences (all)	11 / 153 (7.19%) 16	15 / 75 (20.00%) 18	2 / 83 (2.41%) 2
CHILLS			
subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	7 / 75 (9.33%) 7	3 / 83 (3.61%) 3
FATIGUE			
subjects affected / exposed occurrences (all)	21 / 153 (13.73%) 21	23 / 75 (30.67%) 25	4 / 83 (4.82%) 5
INFLUENZA LIKE ILLNESS			
subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	7 / 75 (9.33%) 7	1 / 83 (1.20%) 1
INJECTION SITE ERYTHEMA			
subjects affected / exposed occurrences (all)	0 / 153 (0.00%) 0	5 / 75 (6.67%) 5	0 / 83 (0.00%) 0
PYREXIA			
subjects affected / exposed occurrences (all)	4 / 153 (2.61%) 5	16 / 75 (21.33%) 17	2 / 83 (2.41%) 2
Eye disorders			
VISION BLURRED			
subjects affected / exposed occurrences (all)	0 / 153 (0.00%) 0	5 / 75 (6.67%) 5	1 / 83 (1.20%) 1
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	6 / 75 (8.00%) 7	1 / 83 (1.20%) 1
ANAL PRURITUS			
subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	10 / 75 (13.33%) 11	0 / 83 (0.00%) 0
ANORECTAL DISCOMFORT			
subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	4 / 75 (5.33%) 8	0 / 83 (0.00%) 0
DIARRHOEA			
subjects affected / exposed occurrences (all)	15 / 153 (9.80%) 19	12 / 75 (16.00%) 12	7 / 83 (8.43%) 8
DRY MOUTH			

subjects affected / exposed occurrences (all)	5 / 153 (3.27%) 5	4 / 75 (5.33%) 4	0 / 83 (0.00%) 0
HAEMORRHOIDS			
subjects affected / exposed occurrences (all)	0 / 153 (0.00%) 0	4 / 75 (5.33%) 4	0 / 83 (0.00%) 0
NAUSEA			
subjects affected / exposed occurrences (all)	32 / 153 (20.92%) 37	30 / 75 (40.00%) 33	7 / 83 (8.43%) 7
VOMITING			
subjects affected / exposed occurrences (all)	11 / 153 (7.19%) 12	14 / 75 (18.67%) 17	1 / 83 (1.20%) 1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed occurrences (all)	11 / 153 (7.19%) 11	8 / 75 (10.67%) 8	1 / 83 (1.20%) 1
DYSPNOEA			
subjects affected / exposed occurrences (all)	7 / 153 (4.58%) 7	5 / 75 (6.67%) 5	0 / 83 (0.00%) 0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	10 / 75 (13.33%) 10	1 / 83 (1.20%) 1
DRY SKIN			
subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	4 / 75 (5.33%) 5	1 / 83 (1.20%) 1
ECZEMA			
subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	4 / 75 (5.33%) 5	0 / 83 (0.00%) 0
ERYTHEMA			
subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	4 / 75 (5.33%) 4	0 / 83 (0.00%) 0
PRURITUS			
subjects affected / exposed occurrences (all)	19 / 153 (12.42%) 22	26 / 75 (34.67%) 30	5 / 83 (6.02%) 5
RASH			

subjects affected / exposed occurrences (all)	12 / 153 (7.84%) 13	17 / 75 (22.67%) 25	0 / 83 (0.00%) 0
RASH PRURITIC subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	7 / 75 (9.33%) 11	0 / 83 (0.00%) 0
Psychiatric disorders DEPRESSION subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	7 / 75 (9.33%) 7	0 / 83 (0.00%) 0
INSOMNIA subjects affected / exposed occurrences (all)	14 / 153 (9.15%) 14	7 / 75 (9.33%) 7	0 / 83 (0.00%) 0
IRRITABILITY subjects affected / exposed occurrences (all)	11 / 153 (7.19%) 11	7 / 75 (9.33%) 7	0 / 83 (0.00%) 0
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	6 / 75 (8.00%) 6	2 / 83 (2.41%) 2
BACK PAIN subjects affected / exposed occurrences (all)	4 / 153 (2.61%) 4	4 / 75 (5.33%) 5	1 / 83 (1.20%) 1
MYALGIA subjects affected / exposed occurrences (all)	7 / 153 (4.58%) 10	12 / 75 (16.00%) 17	2 / 83 (2.41%) 2
Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all)	13 / 153 (8.50%) 14	7 / 75 (9.33%) 8	4 / 83 (4.82%) 5
UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	10 / 153 (6.54%) 10	3 / 75 (4.00%) 3	1 / 83 (1.20%) 1
URINARY TRACT INFECTION subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 2	5 / 75 (6.67%) 5	1 / 83 (1.20%) 1
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	6 / 153 (3.92%)	17 / 75 (22.67%)	1 / 83 (1.20%)
occurrences (all)	7	17	1
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 153 (0.00%)	4 / 75 (5.33%)	0 / 83 (0.00%)
occurrences (all)	0	5	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 153 (0.65%)	5 / 75 (6.67%)	0 / 83 (0.00%)
occurrences (all)	1	5	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	1 / 153 (0.65%)	4 / 75 (5.33%)	0 / 83 (0.00%)
occurrences (all)	1	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2013	The purpose of this amendment was to: • prohibit the use of hormonal contraceptives during study drug administration.
18 June 2013	The purpose of this amendment was to: • specify screening criteria that should remain stable did not need to be re-tested if rescreening occurred within the initial 35-day screening window; • allow for additional rescreening if screening failure related to an eligibility criterion that was subsequently amended; • update Inclusion Criterion No. 3 to allow enrollment of subjects with a borderline pregnancy test result under certain circumstances; • amend Exclusion Criterion No. 9 to allow appropriate use of over-the-counter and prescription medication; • make minor language edits to clarify the eligibility criteria; • allow informed consent for optional samples to be performed at the Baseline Visit; • clarify language relating to pill-count requirements; • clarify that the IRT system should be used for drug accountability; • update the pregnancy section to be consistent with current AbbVie HCV safety language relating to pregnancy; • update addresses and contact details; • make minor edits for consistency and clarity throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported