Clinical trial results:
A Randomized, Open-Label, Multicenter Study to Evaluate the Antiviral Activity, Safety, and Pharmacokinetics, of ABT-450 with Ritonavir (ABT-450/r) in Combination with ABT-267 and/or ABT-333 With and Without Ribavirin (RBV) for 8, 12 or 24 Weeks in Treatment-Naïve and Null Responder Subjects with Genotype 1 Chronic Hepatitis C Virus Infection

Summary

EudraCT number	2010-022455-31
Trial protocol	GB ES
Global end of trial date	19 September 2013

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	13 June 2015

Trial information

Trial identification

Sponsor protocol code	M11-652

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01464827
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, 011 800-633-9110,
Scientific contact	Daniel Cohen, MD, AbbVie , daniel.cohen@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the safety of all treatment regimens and the percentage of subjects achieving 24-week sustained virologic response (SVR24; hepatitis C virus [HCV] ribonucleic acid [RNA] less than the lower limit of quantitation [LLOQ] at post-treatment Week 24) following treatment for 8 weeks versus 12 weeks with 3 direct-acting antiviral agents (DAA) and ribavirin (RBV) in HCV genotype 1-infected treatment-naïve adults.

Protection of trial subjects:

The study was conducted in accordance with the protocol, ICH guidelines, applicable regulations and guidelines governing clinical study conduct, and the ethical principles that have their origin in the Declaration of Helsinki. All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	03 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	France: 58
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United States: 400
Country: Number of subjects enrolled	Canada: 5
Worldwide total number of subjects	580
EEA total number of subjects	166

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)	548
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects underwent screening procedures within 35 days prior to enrollment. HCV genotype 1-infected adult male and female subjects who were either treatment-naïve or previous null responders to pegylated interferon (pegIFN) and RBV were eligible to participate.

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	Group A

Arm description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

Arm title	Group B

Arm description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group C

Arm description:

Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group D

Arm description:

Treatment-naïve participants received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:	
100 mg capsules	

Arm title	Group E
Arm description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ABT-333 400 mg twice daily for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 mg tablets	
Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use
Dosage and administration details:	
400 mg tablets	
Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
100 mg capsules	
Arm title	Group F
Arm description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 mg tablets	

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group G

Arm description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100 mg capsules	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).	
Arm title	Group H
Arm description: Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50 mg tablets	
Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use
Dosage and administration details: 400 mg tablets	
Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100 mg capsules	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group I

Arm description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group J

Arm description:

Participants who were null-responders to previous HCV treatment received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group K

Arm description:

Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet

Routes of administration	Oral use
Dosage and administration details: 25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100 mg capsules	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).	
Arm title	Group L
Arm description: Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50 mg tablets	
Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use
Dosage and administration details: 400 mg tablets	
Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100 mg capsules	

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group M

Arm description:

Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg tablets

Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

400 mg tablets

Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg tablets

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg capsules

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

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Arm title	Group N

Arm description:

Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin

dosed by weight, twice daily, for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	ABT-450
Investigational medicinal product code	
Other name	Paritaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50 mg tablets	
Investigational medicinal product name	ABT-333
Investigational medicinal product code	
Other name	Dasabuvir
Pharmaceutical forms	Tablet
Routes of administration	Other use
Dosage and administration details: 400 mg tablets	
Investigational medicinal product name	ABT-267
Investigational medicinal product code	
Other name	Ombitasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25 mg tablets	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100 mg capsules	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin tablets administered at a weight-based dose, between 1,000 to 1,200 mg daily (divided).

Number of subjects in period 1	Group A	Group B	Group C
Started	80	43	39
Treated	80	41	39
Completed	77	36	39
Not completed	3	7	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Other	2	3	-

Lost to follow-up	-	2	-
Not treated	-	2	-

Number of subjects in period 1	Group D	Group E	Group F
Started	40	80	39
Treated	40	79	39
Completed	36	72	38
Not completed	4	8	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Other	2	3	-
Lost to follow-up	2	3	1
Not treated	-	1	-

Number of subjects in period 1	Group G	Group H	Group I
Started	41	40	40
Treated	40	40	40
Completed	37	37	37
Not completed	4	3	3
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Other	1	-	3
Lost to follow-up	2	2	-
Not treated	1	-	-

Number of subjects in period 1	Group J	Group K	Group L
Started	47	23	23
Treated	45	23	22
Completed	44	21	21
Not completed	3	2	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Other	1	2	-
Lost to follow-up	-	-	1
Not treated	2	-	1

Number of subjects in period 1	Group M	Group N
Started	23	22
Treated	23	20
Completed	21	19
Not completed	2	3
Consent withdrawn by subject	-	-

Adverse event, non-fatal	1	-
Other	1	-
Lost to follow-up	-	1
Not treated	-	2

Baseline characteristics

Reporting groups

Reporting group title	Group A
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 8 weeks.	
Reporting group title	Group B
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group C
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group D
Reporting group description:	
Treatment-naïve participants received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group E
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ABT-333 400 mg twice daily for 12 weeks.	
Reporting group title	Group F
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group G
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group H
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.	
Reporting group title	Group I
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.	
Reporting group title	Group J
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group K
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group L
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group M

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Reporting group title	Group N

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Reporting group values	Group A	Group B	Group C
Number of subjects	80	43	39
Age categorical Units: Subjects			

Age continuous			
Data are provided for the safety population (participants who received at least 1 dose of direct-acting antiviral agent).			
Units: years			
arithmetic mean	50.1	50.8	51.1
standard deviation	± 9.99	± 9.84	± 8.07
Gender categorical Units: Subjects			
Female	34	24	14
Male	46	19	25

Reporting group values	Group D	Group E	Group F
Number of subjects	40	80	39
Age categorical Units: Subjects			

Age continuous			
Data are provided for the safety population (participants who received at least 1 dose of direct-acting antiviral agent).			
Units: years			
arithmetic mean	49	48.3	49.4
standard deviation	± 10.59	± 10.53	± 9.72
Gender categorical Units: Subjects			
Female	20	34	19
Male	20	46	20

Reporting group values	Group G	Group H	Group I
Number of subjects	41	40	40
Age categorical Units: Subjects			

Age continuous			
Data are provided for the safety population (participants who received at least 1 dose of direct-acting antiviral agent).			
Units: years			

arithmetic mean	51	51.5	51.5
standard deviation	± 11.08	± 11.95	± 9.78

Gender categorical Units: Subjects			
Female	16	22	24
Male	25	18	16

Reporting group values	Group J	Group K	Group L
Number of subjects	47	23	23
Age categorical Units: Subjects			

Age continuous			
Data are provided for the safety population (participants who received at least 1 dose of direct-acting antiviral agent).			
Units: years			
arithmetic mean	50.6	48.5	51.2
standard deviation	± 11.19	± 12.91	± 12.07
Gender categorical Units: Subjects			
Female	19	7	10
Male	28	16	13

Reporting group values	Group M	Group N	Total
Number of subjects	23	22	580
Age categorical Units: Subjects			

Age continuous			
Data are provided for the safety population (participants who received at least 1 dose of direct-acting antiviral agent).			
Units: years			
arithmetic mean	51.5	54.6	
standard deviation	± 9.06	± 11.78	-
Gender categorical Units: Subjects			
Female	8	9	260
Male	15	13	320

End points reporting groups

Reporting group title	Group A
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 8 weeks.	
Reporting group title	Group B
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group C
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group D
Reporting group description:	
Treatment-naïve participants received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group E
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ABT-333 400 mg twice daily for 12 weeks.	
Reporting group title	Group F
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.	
Reporting group title	Group G
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group H
Reporting group description:	
Treatment-naïve participants received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.	
Reporting group title	Group I
Reporting group description:	
Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.	
Reporting group title	Group J
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group K
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group L
Reporting group description:	
Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.	
Reporting group title	Group M

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 100 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Reporting group title	Group N

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Subject analysis set title	Group A
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 8 weeks.

Subject analysis set title	Group B
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.

Subject analysis set title	Group C + D
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 (100 mg or 200 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Group E
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ABT-333 400 mg twice daily for 12 weeks.

Subject analysis set title	Group F + G
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Group H + I
Subject analysis set type	Safety analysis

Subject analysis set description:

Treatment-naïve participants received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Subject analysis set title	Group J
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were null-responders to previous HCV treatment received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Group K + L
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were null-responders to previous HCV treatment received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Group M + N
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were null-responders to previous HCV treatment received ABT-450 (100 mg or 150

mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Subject analysis set title	Groups F + G + K + L
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants (treatment-naïve and null-responders) received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Groups H + I + M + N
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants (treatment-naïve and null-responders) received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Subject analysis set title	Groups C + D + J
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants (treatment-naïve and null-responders) received ABT-450 (100 mg or 200 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Subject analysis set title	Groups F + G + H + I
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Treatment-naïve participants received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 or 24 weeks.

Subject analysis set title	Groups K + L + M + N
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who were null-responders to previous HCV treatment received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 or 24 weeks.

Primary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)[1]

End point description:

An adverse event was defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and that did not necessarily have a causal relationship with this treatment.
The investigator assessed the relationship of each AE to the use of direct-acting antiviral agents (DAAs) and to ribavirin, and rated the severity of each event as either:
Mild: The AE was transient and easily tolerated by the participant; Moderate: The AE caused the participant discomfort and interrupted usual activities; Severe: The AE caused considerable interference with the participant's usual activities and could have been incapacitating or life-threatening.
A serious adverse event was any event that resulted in death, was life-threatening, resulted in or prolonged hospitalization, resulted in a congenital anomaly or persistent or significant disability or was any other important medical event requiring medical or surgical intervention.

End point type	Primary

End point timeframe:

From the time of study drug administration until 30 days following discontinuation of study drug administration (up to 28 weeks).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety was assessed by summarizing the incidence of adverse events.

End point values	Group A	Group B	Group C + D	Group E
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	41	79	79
Units: participants				
Any adverse event	67	36	71	68
Any adverse event at least possibly DAArelated	58	29	53	51
Any severe adverse event	3	0	3	5
Any serious adverse event	0	0	2	2
Any AE leading to discontinuation of study drug	1	0	0	0
Any AE leading to interruption of study drug	0	1	2	1
Any AE leading to ribavirin dose modification	2	2	4	0
Any fatal adverse events	0	0	0	0

End point values	Group F + G	Group H + I	Group J	Group K + L
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	80	45	45
Units: participants				
Any adverse event	71	77	42	39
Any adverse event at least possibly DAArelated	57	68	35	30
Any severe adverse event	3	3	1	1
Any serious adverse event	1	1	0	0
Any AE leading to discontinuation of study drug	3	3	1	0
Any AE leading to interruption of study drug	0	1	0	0
Any AE leading to ribavirin dose modification	9	10	3	1
Any fatal adverse events	0	0	0	0

End point values	Group M + N			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: participants				
Any adverse event	37			
Any adverse event at least possibly DAArelated	28			
Any severe adverse event	1			
Any serious adverse event	2			
Any AE leading to discontinuation of study drug	1			
Any AE leading to interruption of study drug	0			
Any AE leading to ribavirin dose modification	3			

Any fatal adverse events	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose for 8 Weeks Versus 12 Weeks of Treatment With 3 DAAs and Ribavirin

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose for 8 Weeks Versus 12 Weeks of Treatment With 3 DAAs and Ribavirin

End point description:

The percentage of participants achieving sustained virologic response 24 weeks after the last dose of study drug (SVR24), defined as hepatitis C virus (HCV) ribonucleic acid (RNA) less than the lower limit of quantitation (LLOQ), without any confirmed quantifiable (≥ LLOQ) post-treatment value before that time point. HCV RNA levels were measured from plasma by a central laboratory. The LLOQ for the assay was 25 IU/mL.
The primary efficacy endpoint was the comparison between treatment-naïve participants following 8 weeks of treatment with 3 DAAs and ribavirin and those with 12 weeks of treatment with 3 DAAs and ribavirin (Group A versus Group G).
Participants with missing data were counted as non-responders.

End point type	Primary

End point timeframe:

Post Treatment Week 24

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	41	39	40
Units: percentage of participants				
number (not applicable)	87.5	82.9	84.6	92.5

End point values	Group E	Group F	Group G	Group H
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	39	40	40
Units: percentage of participants				
number (not applicable)	88.6	97.4	95	92.5

End point values	Group I	Group J	Group K	Group L
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	45	23	22
Units: percentage of participants				

number (not applicable)	90	88.9	91.3	95.5

End point values	Group M	Group N		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	20		
Units: percentage of participants				
number (not applicable)	91.3	100		

Statistical analyses

Statistical analysis title	Primary analysis

Statistical analysis description:

The primary efficacy endpoint was the comparison of the percentage of treatment-naïve participants with SVR24 after treatment with 3 DAAs (at the 150 mg ABT-450 dose) and ribavirin for 8 weeks (Group A) versus 12 weeks (Group G).

Comparison groups	Group G v Group A
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.406 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	2.61

Notes:

[2] - Pre-specified 2-sided significance level of 0.05.

[3] - Logistic regression with baseline log10 HCV RNA level, treatment group, Interleukin 28B genotype (CC or non-CC), HCV subgenotype (1a or non-1a), and geographic region (US or non-US) as predictors. No adjustment for multiple comparison.

Secondary: Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment of Different Durations With 3 Direct-acting Antiviral Agents (DAAs) and Ribavirin

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment of Different Durations With 3 Direct-acting Antiviral Agents (DAAs) and Ribavirin

End point description:

This endpoint compares the percentage of participants achieving sustained virologic response 24 weeks after the last dose of study drug (HCV RNA < LLOQ at post-treatment Week 24) following treatment with 3 DAAs (ABT-450/ritonavir, ABT-267, and ABT-333) and ribavirin in both treatment naïve and null-responder participants for 8 weeks (Group A) versus 12 weeks (Groups F + G + K + L) versus 24 weeks (Groups H + I + M + N).
Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Post-Treatment Week 24

End point values	Group A	Groups F + G + K + L	Groups H + I + M + N	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	80	124	123	
Units: percentage of participants				
number (not applicable)	87.5	95.2	92.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The percentage of participants with SVR24 after treatment for 8 weeks versus 12 weeks was compared using logistic regression with treatment group, baseline log10 HCV RNA level, HCV subgenotype (1a or non-1a), geographic region (US or non-US), Interleukin 28B genotype (CC or non-CC), and ABT-450/ritonavir dose and population (treatment-naïve or null-responders) as predictors.

Comparison groups	Group A v Groups F + G + K + L
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.266 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	2.02

Notes:

[4] - Pre-specified 2-sided significance level of 0.05.

[5] - No adjustment for multiple comparison.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The percentage of participants with SVR24 after treatment for 8 weeks versus 24 weeks was compared using logistic regression with treatment group, baseline log10 HCV RNA level, HCV subgenotype (1a or non-1a), geographic region (US or non-US), Interleukin 28B genotype (CC or non-CC), ABT-450/ritonavir dose and population (treatment-naïve or null-responders) as predictors.

Comparison groups	Group A v Groups H + I + M + N
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.525 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	2.4

Notes:

[6] - Pre-specified 2-sided significance level of 0.05.

[7] - No adjustment for multiple comparison.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The percentage of participants with SVR24 after treatment for 12 weeks versus 24 weeks was compared using logistic regression with treatment group, baseline log10 HCV RNA level, HCV subgenotype (1a or non-1a), geographic region (US or non-US), Interleukin 28B genotype (CC or non-CC), ABT-450/ritonavir dose and population (treatment-naïve or null-responders) as predictors.

Comparison groups	Groups F + G + K + L v Groups H + I + M + N
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.375 [9]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	4.92

Notes:

[8] - Pre-specified 2-sided significance level of 0.05.

[9] - No adjustment for multiple comparison.

Secondary: Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment for 12 Weeks With 2 DAAs and Ribavirin Versus 3 DAAs and Ribavirin

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment for 12 Weeks With 2 DAAs and Ribavirin Versus 3 DAAs and Ribavirin

End point description:

This endpoint compares the percentage of participants achieving sustained virologic response 24 weeks post-dose (HCV RNA < LLOQ at post-treatment Week 24) following treatment with 2 DAAs (ABT-450/ritonavir plus ABT-333 [Group B] or ABT-450/ritonavir plus ABT-267 [Groups C + D + J]) and ribavirin versus 3 DAAs (ABT-450/ritonavir plus ABT-333 and ABT-267) and ribavirin (Groups F + G + K + L).
Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Post-Treatment Week 24

End point values	Group B	Groups F + G + K + L	Groups C + D + J	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	124	124	
Units: percentage of participants				
number (not applicable)	82.9	95.2	88.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The percentage of participants with SVR24 after treatment with 2 DAAs and ribavirin versus 3 DAAs and ribavirin was compared using stratum-adjusted Mantel-Haenszel (MH) method with Interleukin 28B genotype (CC or non-CC) and HCV subgenotype (1a or non-1a).

Comparison groups	Group B v Groups F + G + K + L
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.068 [11]
Method	Mantel-Haenszel
Parameter estimate	Difference (Group B - Groups F + G + K)
Point estimate	-12.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.2
upper limit	0.88

Notes:

[10] - Pre-specified 2-sided significance level of 0.05.

[11] - The Mantel-Haenszel method was used because logistic regression failed due to separation or quasi-separation. There was no adjustment for multiple comparison.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The percentage of participants with SVR24 after treatment with 2 DAAs and ribavirin versus 3 DAAs and ribavirin was compared using stratum-adjusted Mantel-Haenszel (MH) method with Interleukin 28B genotype (CC or non-CC) and HCV subgenotype (1a or non-1a).

Comparison groups	Groups F + G + K + L v Groups C + D + J
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.065 [13]
Method	Mantel-Haenszel
Parameter estimate	Difference (Group C+D+J - Group F+G+K+L)
Point estimate	-6.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.93
upper limit	0.43

Notes:

[12] - Pre-specified 2-sided significance level of 0.05.

[13] - The Mantel-Haenszel method was used because logistic regression failed due to separation or quasi-separation. No adjustment for multiple comparison.

Secondary: Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment for 12 Weeks With 3 DAAs With Versus Without Ribavirin

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose Following Treatment for 12 Weeks With 3 DAAs With Versus Without Ribavirin

End point description:

This endpoint compares the percentage of participants achieving sustained virologic response 24 weeks post-dose (HCV RNA < LLOQ at post-treatment Week 24) following treatment with 3 DAAs with or without ribavirin (Group E versus Groups F + G + K + L).
Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Post-Treatment Week 24

End point values	Group E	Groups F + G + K + L		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79	124		
Units: Percentage of participants				
number (not applicable)	88.6	95.2		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The percentage of participants with SVR24 after treatment with 3 DAAs with and without ribavirin was compared using a stratum-adjusted Mantel-Haenszel (MH) method with Interleukin 28B genotype (CC or non-CC) and HCV subgenotype (1a or non-1a).

Comparison groups	Group E v Groups F + G + K + L
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.106 [15]
Method	Mantel-Haenszel
Parameter estimate	Difference (Group E - Group F+G+K+L)
Point estimate	-7.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.77
upper limit	1.51

Notes:

[14] - Pre-specified 2-sided significance level of 0.05.

[15] - The Mantel-Haenszel method was used because logistic regression failed due to separation or quasi-separation. No adjustment for multiple comparison.

Secondary: Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose in Treatment-naïve Versus Null-responders

End point title	Percentage of Participants With Sustained Virologic Response 24 Weeks Post-dose in Treatment-naïve Versus Null-responders

End point description:

This endpoint compares the percentage of participants achieving sustained virologic response 24 weeks post-dose (HCV RNA < LLOQ at post-treatment Week 24) following treatment with 3 DAAs and ribavirin in participants who were treatment-naïve versus those who were null-responders to previous HCV therapy (Groups F + G + H + I versus Groups K + L + M + N).
Participants with missing data were counted as non-responders.

End point type	Secondary

End point timeframe:

Post-Treatment Week 24

End point values	Groups F + G + H + I	Groups K + L + M + N		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	88		
Units: percentage of participants				
number (not applicable)	93.7	94.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The percentage of participants with SVR24 after treatment with 3 DAAs and ribavirin in treatment-naïve versus null-responders was compared using logistic regression with treatment group, baseline log10 HCV RNA level, HCV subgenotype (1a or non-1a), geographic region (US or non-US), Interleukin 28B genotype (CC or non-CC), and ABT-450/ritonavir dose as predictors.

Comparison groups	Groups F + G + H + I v Groups K + L + M + N
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.616 [17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	5.34

Notes:

[16] - Pre-specified 2-sided significance level of 0.05.

[17] - No adjustment for multiple comparison.

Adverse events information

Timeframe for reporting adverse events:

Up to 28 weeks

Adverse event reporting additional description:

Treatment groups differing only in ABT-450 dose (100 mg, 150 mg or 200 mg) were combined for safety analyses.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Group A

Reporting group description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 8 weeks.

Reporting group title	Group B

Reporting group description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily for 12 weeks.

Reporting group title	Group C + D

Reporting group description:

Treatment-naïve participants received ABT-450 (100 mg or 200 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Reporting group title	Group E

Reporting group description:

Treatment-naïve participants received ABT-450 150 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ABT-333 400 mg twice daily for 12 weeks.

Reporting group title	Group F + G

Reporting group description:

Treatment-naïve participants received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Reporting group title	Group H + I

Reporting group description:

Treatment-naïve participants received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Reporting group title	Group J

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 200 mg and ritonavir 100 mg once daily, ABT-267 25 mg once daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Reporting group title	Group K + L

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 12 weeks.

Reporting group title	Group M + N

Reporting group description:

Participants who were null-responders to previous HCV treatment received ABT-450 (100 mg or 150 mg) and ritonavir 100 mg once daily, ABT-267 25 mg once daily, ABT-333 400 mg twice daily, and ribavirin dosed by weight, twice daily, for 24 weeks.

Serious adverse events	Group A	Group B	Group C + D
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	2 / 79 (2.53%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	1 / 79 (1.27%)
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			
Animal bite			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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
Facial paresis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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			
Lung disorder			

subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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
Neck pain			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (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 E	Group F + G	Group H + I
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 79 (2.53%)	1 / 79 (1.27%)	1 / 80 (1.25%)
number of deaths (all causes)	1	0	0

number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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			
Animal bite			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	0 / 80 (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
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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
Facial paresis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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			
Lung disorder			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 79 (0.00%)	1 / 79 (1.27%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	1 / 80 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (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
Pneumonia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	0 / 80 (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

Serious adverse events	Group J	Group K + L	Group M + N
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 43 (4.65%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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			
Animal bite			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
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			
Lung disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Neck pain			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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

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

Non-serious adverse events	Group A	Group B	Group C + D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 80 (80.00%)	33 / 41 (80.49%)	66 / 79 (83.54%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 80 (8.75%)	1 / 41 (2.44%)	8 / 79 (10.13%)
occurrences (all)	7	1	8
Chest pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 41 (2.44%)	2 / 79 (2.53%)
occurrences (all)	0	1	2
Chills			
subjects affected / exposed	4 / 80 (5.00%)	1 / 41 (2.44%)	1 / 79 (1.27%)
occurrences (all)	4	1	1
Fatigue			

subjects affected / exposed	29 / 80 (36.25%)	13 / 41 (31.71%)	22 / 79 (27.85%)
occurrences (all)	33	13	25
Irritability			
subjects affected / exposed	1 / 80 (1.25%)	4 / 41 (9.76%)	5 / 79 (6.33%)
occurrences (all)	1	5	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 80 (15.00%)	5 / 41 (12.20%)	11 / 79 (13.92%)
occurrences (all)	12	5	11
Dyspnoea			
subjects affected / exposed	8 / 80 (10.00%)	3 / 41 (7.32%)	4 / 79 (5.06%)
occurrences (all)	8	3	4
Dyspnoea exertional			
subjects affected / exposed	2 / 80 (2.50%)	0 / 41 (0.00%)	3 / 79 (3.80%)
occurrences (all)	2	0	3
Oropharyngeal pain			
subjects affected / exposed	3 / 80 (3.75%)	0 / 41 (0.00%)	4 / 79 (5.06%)
occurrences (all)	3	0	4
Sinus congestion			
subjects affected / exposed	4 / 80 (5.00%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences (all)	4	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 80 (1.25%)	2 / 41 (4.88%)	2 / 79 (2.53%)
occurrences (all)	1	2	2
Anxiety			
subjects affected / exposed	2 / 80 (2.50%)	2 / 41 (4.88%)	0 / 79 (0.00%)
occurrences (all)	3	2	0
Depressed mood			
subjects affected / exposed	1 / 80 (1.25%)	3 / 41 (7.32%)	1 / 79 (1.27%)
occurrences (all)	1	3	1
Depression			
subjects affected / exposed	3 / 80 (3.75%)	3 / 41 (7.32%)	3 / 79 (3.80%)
occurrences (all)	3	3	3
Insomnia			

subjects affected / exposed	10 / 80 (12.50%)	8 / 41 (19.51%)	9 / 79 (11.39%)
occurrences (all)	10	8	9
Sleep disorder			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	2 / 80 (2.50%)	1 / 41 (2.44%)	2 / 79 (2.53%)
occurrences (all)	2	1	2
Dizziness			
subjects affected / exposed	5 / 80 (6.25%)	7 / 41 (17.07%)	2 / 79 (2.53%)
occurrences (all)	5	8	2
Dysgeusia			
subjects affected / exposed	2 / 80 (2.50%)	1 / 41 (2.44%)	3 / 79 (3.80%)
occurrences (all)	2	1	3
Headache			
subjects affected / exposed	28 / 80 (35.00%)	13 / 41 (31.71%)	23 / 79 (29.11%)
occurrences (all)	31	18	30
Lethargy			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Memory impairment			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 80 (6.25%)	1 / 41 (2.44%)	3 / 79 (3.80%)
occurrences (all)	5	1	3
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	1 / 80 (1.25%)	3 / 41 (7.32%)	0 / 79 (0.00%)
occurrences (all)	3	3	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 80 (0.00%)	1 / 41 (2.44%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	1 / 80 (1.25%)	3 / 41 (7.32%)	4 / 79 (5.06%)
occurrences (all)	1	3	4
Abdominal pain upper			
subjects affected / exposed	0 / 80 (0.00%)	2 / 41 (4.88%)	5 / 79 (6.33%)
occurrences (all)	0	2	5
Constipation			
subjects affected / exposed	3 / 80 (3.75%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	4	1	5
Diarrhoea			
subjects affected / exposed	8 / 80 (10.00%)	10 / 41 (24.39%)	8 / 79 (10.13%)
occurrences (all)	8	12	8
Dry mouth			
subjects affected / exposed	4 / 80 (5.00%)	0 / 41 (0.00%)	2 / 79 (2.53%)
occurrences (all)	4	0	3
Dyspepsia			
subjects affected / exposed	7 / 80 (8.75%)	1 / 41 (2.44%)	9 / 79 (11.39%)
occurrences (all)	8	1	9
Flatulence			
subjects affected / exposed	0 / 80 (0.00%)	1 / 41 (2.44%)	4 / 79 (5.06%)
occurrences (all)	0	1	4
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	2 / 79 (2.53%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	12 / 80 (15.00%)	7 / 41 (17.07%)	16 / 79 (20.25%)
occurrences (all)	13	9	16
Vomiting			

subjects affected / exposed	7 / 80 (8.75%)	4 / 41 (9.76%)	4 / 79 (5.06%)
occurrences (all)	8	4	4
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	3 / 80 (3.75%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences (all)	3	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	4 / 80 (5.00%)	3 / 41 (7.32%)	3 / 79 (3.80%)
occurrences (all)	4	4	3
Pruritus			
subjects affected / exposed	12 / 80 (15.00%)	3 / 41 (7.32%)	8 / 79 (10.13%)
occurrences (all)	13	3	10
Pruritus generalised			
subjects affected / exposed	2 / 80 (2.50%)	5 / 41 (12.20%)	0 / 79 (0.00%)
occurrences (all)	2	5	0
Rash			
subjects affected / exposed	10 / 80 (12.50%)	2 / 41 (4.88%)	6 / 79 (7.59%)
occurrences (all)	12	2	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 80 (2.50%)	2 / 41 (4.88%)	6 / 79 (7.59%)
occurrences (all)	2	3	6
Back pain			
subjects affected / exposed	2 / 80 (2.50%)	1 / 41 (2.44%)	3 / 79 (3.80%)
occurrences (all)	2	1	3
Muscle spasms			
subjects affected / exposed	2 / 80 (2.50%)	1 / 41 (2.44%)	2 / 79 (2.53%)
occurrences (all)	2	1	2
Myalgia			
subjects affected / exposed	4 / 80 (5.00%)	3 / 41 (7.32%)	5 / 79 (6.33%)
occurrences (all)	4	3	5
Pain in extremity			

subjects affected / exposed	2 / 80 (2.50%)	1 / 41 (2.44%)	1 / 79 (1.27%)
occurrences (all)	2	1	1
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 80 (5.00%)	3 / 41 (7.32%)	4 / 79 (5.06%)
occurrences (all)	4	3	4
Oral herpes			
subjects affected / exposed	2 / 80 (2.50%)	0 / 41 (0.00%)	2 / 79 (2.53%)
occurrences (all)	3	0	2
Rhinitis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 41 (0.00%)	5 / 79 (6.33%)
occurrences (all)	1	0	6
Sinusitis			
subjects affected / exposed	4 / 80 (5.00%)	0 / 41 (0.00%)	7 / 79 (8.86%)
occurrences (all)	4	0	8
Tooth infection			
subjects affected / exposed	2 / 80 (2.50%)	0 / 41 (0.00%)	0 / 79 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	5 / 80 (6.25%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	5	2	5
Urinary tract infection			
subjects affected / exposed	4 / 80 (5.00%)	3 / 41 (7.32%)	2 / 79 (2.53%)
occurrences (all)	4	3	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 80 (10.00%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	8	1	5

Non-serious adverse events	Group E	Group F + G	Group H + I
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 79 (74.68%)	66 / 79 (83.54%)	74 / 80 (92.50%)
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	5 / 79 (6.33%)	3 / 79 (3.80%)	12 / 80 (15.00%)
occurrences (all)	7	4	17
Chest pain			
subjects affected / exposed	0 / 79 (0.00%)	1 / 79 (1.27%)	4 / 80 (5.00%)
occurrences (all)	0	1	4
Chills			
subjects affected / exposed	1 / 79 (1.27%)	1 / 79 (1.27%)	3 / 80 (3.75%)
occurrences (all)	1	1	3
Fatigue			
subjects affected / exposed	16 / 79 (20.25%)	22 / 79 (27.85%)	30 / 80 (37.50%)
occurrences (all)	17	23	35
Irritability			
subjects affected / exposed	5 / 79 (6.33%)	1 / 79 (1.27%)	10 / 80 (12.50%)
occurrences (all)	5	1	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 79 (2.53%)	8 / 79 (10.13%)	12 / 80 (15.00%)
occurrences (all)	2	8	14
Dyspnoea			
subjects affected / exposed	1 / 79 (1.27%)	5 / 79 (6.33%)	8 / 80 (10.00%)
occurrences (all)	1	5	8
Dyspnoea exertional			
subjects affected / exposed	0 / 79 (0.00%)	4 / 79 (5.06%)	9 / 80 (11.25%)
occurrences (all)	0	4	11
Oropharyngeal pain			
subjects affected / exposed	0 / 79 (0.00%)	1 / 79 (1.27%)	4 / 80 (5.00%)
occurrences (all)	0	1	4
Sinus congestion			
subjects affected / exposed	1 / 79 (1.27%)	1 / 79 (1.27%)	2 / 80 (2.50%)
occurrences (all)	1	1	2
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 79 (1.27%)	1 / 79 (1.27%)	5 / 80 (6.25%)
occurrences (all)	1	1	5
Anxiety			

subjects affected / exposed	3 / 79 (3.80%)	4 / 79 (5.06%)	6 / 80 (7.50%)
occurrences (all)	3	4	6
Depressed mood			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	0 / 80 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 79 (1.27%)	3 / 79 (3.80%)	12 / 80 (15.00%)
occurrences (all)	1	4	13
Insomnia			
subjects affected / exposed	6 / 79 (7.59%)	16 / 79 (20.25%)	20 / 80 (25.00%)
occurrences (all)	6	17	22
Sleep disorder			
subjects affected / exposed	0 / 79 (0.00%)	0 / 79 (0.00%)	2 / 80 (2.50%)
occurrences (all)	0	0	2
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 79 (1.27%)	1 / 79 (1.27%)	0 / 80 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 79 (1.27%)	2 / 79 (2.53%)	9 / 80 (11.25%)
occurrences (all)	1	2	9
Dizziness			
subjects affected / exposed	4 / 79 (5.06%)	3 / 79 (3.80%)	8 / 80 (10.00%)
occurrences (all)	4	3	8
Dysgeusia			
subjects affected / exposed	2 / 79 (2.53%)	3 / 79 (3.80%)	4 / 80 (5.00%)
occurrences (all)	2	3	4
Headache			
subjects affected / exposed	15 / 79 (18.99%)	21 / 79 (26.58%)	28 / 80 (35.00%)
occurrences (all)	15	22	29
Lethargy			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	1 / 80 (1.25%)
occurrences (all)	1	0	1
Memory impairment			

subjects affected / exposed	3 / 79 (3.80%)	0 / 79 (0.00%)	5 / 80 (6.25%)
occurrences (all)	3	0	5
Paraesthesia			
subjects affected / exposed	1 / 79 (1.27%)	1 / 79 (1.27%)	2 / 80 (2.50%)
occurrences (all)	1	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 79 (1.27%)	7 / 79 (8.86%)	6 / 80 (7.50%)
occurrences (all)	1	7	6
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	3 / 80 (3.75%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 79 (3.80%)	3 / 79 (3.80%)	5 / 80 (6.25%)
occurrences (all)	3	3	5
Abdominal pain			
subjects affected / exposed	3 / 79 (3.80%)	3 / 79 (3.80%)	7 / 80 (8.75%)
occurrences (all)	4	4	8
Abdominal pain upper			
subjects affected / exposed	3 / 79 (3.80%)	4 / 79 (5.06%)	4 / 80 (5.00%)
occurrences (all)	3	4	4
Constipation			
subjects affected / exposed	5 / 79 (6.33%)	1 / 79 (1.27%)	9 / 80 (11.25%)
occurrences (all)	5	2	11
Diarrhoea			
subjects affected / exposed	13 / 79 (16.46%)	10 / 79 (12.66%)	11 / 80 (13.75%)
occurrences (all)	15	11	13
Dry mouth			
subjects affected / exposed	2 / 79 (2.53%)	1 / 79 (1.27%)	2 / 80 (2.50%)
occurrences (all)	2	1	2
Dyspepsia			
subjects affected / exposed	2 / 79 (2.53%)	4 / 79 (5.06%)	6 / 80 (7.50%)
occurrences (all)	2	4	6
Flatulence			

subjects affected / exposed	4 / 79 (5.06%)	2 / 79 (2.53%)	1 / 80 (1.25%)
occurrences (all)	4	2	1
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 79 (3.80%)	2 / 79 (2.53%)	2 / 80 (2.50%)
occurrences (all)	3	2	2
Nausea			
subjects affected / exposed	11 / 79 (13.92%)	19 / 79 (24.05%)	20 / 80 (25.00%)
occurrences (all)	12	21	23
Vomiting			
subjects affected / exposed	4 / 79 (5.06%)	4 / 79 (5.06%)	4 / 80 (5.00%)
occurrences (all)	4	5	5
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 79 (0.00%)	3 / 79 (3.80%)	3 / 80 (3.75%)
occurrences (all)	0	3	3
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 79 (2.53%)	0 / 79 (0.00%)	6 / 80 (7.50%)
occurrences (all)	2	0	7
Dry skin			
subjects affected / exposed	1 / 79 (1.27%)	4 / 79 (5.06%)	6 / 80 (7.50%)
occurrences (all)	1	4	7
Pruritus			
subjects affected / exposed	3 / 79 (3.80%)	6 / 79 (7.59%)	11 / 80 (13.75%)
occurrences (all)	3	6	12
Pruritus generalised			
subjects affected / exposed	1 / 79 (1.27%)	4 / 79 (5.06%)	3 / 80 (3.75%)
occurrences (all)	2	4	3
Rash			
subjects affected / exposed	6 / 79 (7.59%)	11 / 79 (13.92%)	15 / 80 (18.75%)
occurrences (all)	6	11	18
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 79 (8.86%)	5 / 79 (6.33%)	8 / 80 (10.00%)
occurrences (all)	8	6	9
Back pain			

subjects affected / exposed	4 / 79 (5.06%)	2 / 79 (2.53%)	5 / 80 (6.25%)
occurrences (all)	4	2	5
Muscle spasms			
subjects affected / exposed	1 / 79 (1.27%)	5 / 79 (6.33%)	2 / 80 (2.50%)
occurrences (all)	1	5	2
Myalgia			
subjects affected / exposed	2 / 79 (2.53%)	3 / 79 (3.80%)	9 / 80 (11.25%)
occurrences (all)	2	3	10
Pain in extremity			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	3 / 80 (3.75%)
occurrences (all)	1	0	3
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 79 (2.53%)	1 / 79 (1.27%)	1 / 80 (1.25%)
occurrences (all)	2	2	1
Nasopharyngitis			
subjects affected / exposed	8 / 79 (10.13%)	7 / 79 (8.86%)	7 / 80 (8.75%)
occurrences (all)	8	7	8
Oral herpes			
subjects affected / exposed	2 / 79 (2.53%)	1 / 79 (1.27%)	3 / 80 (3.75%)
occurrences (all)	2	1	3
Rhinitis			
subjects affected / exposed	2 / 79 (2.53%)	0 / 79 (0.00%)	0 / 80 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	2 / 79 (2.53%)	5 / 79 (6.33%)	3 / 80 (3.75%)
occurrences (all)	2	5	3
Tooth infection			
subjects affected / exposed	1 / 79 (1.27%)	4 / 79 (5.06%)	4 / 80 (5.00%)
occurrences (all)	1	4	4
Upper respiratory tract infection			
subjects affected / exposed	5 / 79 (6.33%)	4 / 79 (5.06%)	5 / 80 (6.25%)
occurrences (all)	5	4	5
Urinary tract infection			
subjects affected / exposed	1 / 79 (1.27%)	0 / 79 (0.00%)	6 / 80 (7.50%)
occurrences (all)	2	0	6

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 79 (3.80%)	3 / 79 (3.80%)	6 / 80 (7.50%)
occurrences (all)	3	3	7

Non-serious adverse events	Group J	Group K + L	Group M + N
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 45 (88.89%)	36 / 45 (80.00%)	34 / 43 (79.07%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 45 (22.22%)	4 / 45 (8.89%)	4 / 43 (9.30%)
occurrences (all)	11	4	4
Chest pain			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	0 / 43 (0.00%)
occurrences (all)	1	3	0
Chills			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences (all)	1	0	2
Fatigue			
subjects affected / exposed	12 / 45 (26.67%)	12 / 45 (26.67%)	9 / 43 (20.93%)
occurrences (all)	13	15	12
Irritability			
subjects affected / exposed	7 / 45 (15.56%)	2 / 45 (4.44%)	3 / 43 (6.98%)
occurrences (all)	7	2	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 45 (15.56%)	3 / 45 (6.67%)	9 / 43 (20.93%)
occurrences (all)	7	3	12
Dyspnoea			
subjects affected / exposed	4 / 45 (8.89%)	3 / 45 (6.67%)	3 / 43 (6.98%)
occurrences (all)	4	3	4
Dyspnoea exertional			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Oropharyngeal pain			

subjects affected / exposed	2 / 45 (4.44%)	4 / 45 (8.89%)	2 / 43 (4.65%)
occurrences (all)	3	4	2
Sinus congestion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 45 (2.22%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Anxiety			
subjects affected / exposed	4 / 45 (8.89%)	1 / 45 (2.22%)	3 / 43 (6.98%)
occurrences (all)	4	1	4
Depressed mood			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Depression			
subjects affected / exposed	2 / 45 (4.44%)	5 / 45 (11.11%)	1 / 43 (2.33%)
occurrences (all)	2	5	1
Insomnia			
subjects affected / exposed	8 / 45 (17.78%)	6 / 45 (13.33%)	7 / 43 (16.28%)
occurrences (all)	8	6	8
Sleep disorder			
subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	2 / 43 (4.65%)
occurrences (all)	0	4	2
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	4 / 43 (9.30%)
occurrences (all)	0	1	4
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 45 (6.67%)	3 / 45 (6.67%)	3 / 43 (6.98%)
occurrences (all)	4	3	4
Dizziness			
subjects affected / exposed	4 / 45 (8.89%)	1 / 45 (2.22%)	4 / 43 (9.30%)
occurrences (all)	4	1	5
Dysgeusia			

subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	4 / 43 (9.30%)
occurrences (all)	0	4	4
Headache			
subjects affected / exposed	15 / 45 (33.33%)	13 / 45 (28.89%)	14 / 43 (32.56%)
occurrences (all)	17	13	20
Lethargy			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	2 / 43 (4.65%)
occurrences (all)	1	4	2
Memory impairment			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences (all)	1	0	2
Paraesthesia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	5 / 43 (11.63%)
occurrences (all)	1	0	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 45 (6.67%)	3 / 45 (6.67%)	2 / 43 (4.65%)
occurrences (all)	3	3	2
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)	6 / 45 (13.33%)	0 / 43 (0.00%)
occurrences (all)	1	7	0
Abdominal pain upper			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	2 / 43 (4.65%)
occurrences (all)	0	1	2
Constipation			
subjects affected / exposed	2 / 45 (4.44%)	1 / 45 (2.22%)	4 / 43 (9.30%)
occurrences (all)	2	2	4
Diarrhoea			

subjects affected / exposed	7 / 45 (15.56%)	8 / 45 (17.78%)	8 / 43 (18.60%)
occurrences (all)	9	10	12
Dry mouth			
subjects affected / exposed	1 / 45 (2.22%)	2 / 45 (4.44%)	2 / 43 (4.65%)
occurrences (all)	1	2	2
Dyspepsia			
subjects affected / exposed	2 / 45 (4.44%)	2 / 45 (4.44%)	2 / 43 (4.65%)
occurrences (all)	3	2	2
Flatulence			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 45 (2.22%)	1 / 45 (2.22%)	4 / 43 (9.30%)
occurrences (all)	1	1	4
Nausea			
subjects affected / exposed	6 / 45 (13.33%)	9 / 45 (20.00%)	8 / 43 (18.60%)
occurrences (all)	6	11	8
Vomiting			
subjects affected / exposed	4 / 45 (8.89%)	4 / 45 (8.89%)	3 / 43 (6.98%)
occurrences (all)	4	4	3
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	1 / 43 (2.33%)
occurrences (all)	1	3	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	4 / 43 (9.30%)
occurrences (all)	0	0	4
Dry skin			
subjects affected / exposed	6 / 45 (13.33%)	4 / 45 (8.89%)	4 / 43 (9.30%)
occurrences (all)	6	4	4
Pruritus			
subjects affected / exposed	6 / 45 (13.33%)	7 / 45 (15.56%)	6 / 43 (13.95%)
occurrences (all)	8	7	6
Pruritus generalised			

subjects affected / exposed	5 / 45 (11.11%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences (all)	6	0	1
Rash			
subjects affected / exposed	2 / 45 (4.44%)	4 / 45 (8.89%)	6 / 43 (13.95%)
occurrences (all)	5	4	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 45 (6.67%)	5 / 45 (11.11%)	7 / 43 (16.28%)
occurrences (all)	3	5	7
Back pain			
subjects affected / exposed	2 / 45 (4.44%)	2 / 45 (4.44%)	4 / 43 (9.30%)
occurrences (all)	3	2	4
Muscle spasms			
subjects affected / exposed	2 / 45 (4.44%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	5 / 45 (11.11%)	4 / 45 (8.89%)	6 / 43 (13.95%)
occurrences (all)	5	4	7
Pain in extremity			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	0 / 43 (0.00%)
occurrences (all)	1	3	0
Nasopharyngitis			
subjects affected / exposed	2 / 45 (4.44%)	4 / 45 (8.89%)	3 / 43 (6.98%)
occurrences (all)	2	4	4
Oral herpes			
subjects affected / exposed	3 / 45 (6.67%)	3 / 45 (6.67%)	2 / 43 (4.65%)
occurrences (all)	5	4	2
Rhinitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Sinusitis			

subjects affected / exposed	1 / 45 (2.22%)	2 / 45 (4.44%)	3 / 43 (6.98%)
occurrences (all)	1	2	3
Tooth infection			
subjects affected / exposed	1 / 45 (2.22%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 45 (6.67%)	4 / 45 (8.89%)	0 / 43 (0.00%)
occurrences (all)	3	4	0
Urinary tract infection			
subjects affected / exposed	2 / 45 (4.44%)	3 / 45 (6.67%)	2 / 43 (4.65%)
occurrences (all)	2	4	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 45 (6.67%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences (all)	3	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2011	The purpose of this amendment was to: • modify the post-treatment pregnancy monitoring to be in compliance with local labeling requirements for RBV; • clarify that the RBV Pregnancy Registry Brochure and RBV Medication Guide were to be distributed where applicable/locally available; • define the primary and secondary endpoints of SVR24 as HCV RNA < LLOQ 24 weeks after the last dose of study drug; • incorporate Administrative Change 1; and • address inconsistencies throughout the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported