Clinical trial results:
A Phase 3 Evaluation of a Daclatasvir/Asunaprevir/BMS-791325 Fixed Dose Combination in Subjects with Genotype 1 Chronic Hepatitis C and Compensated Cirrhosis

Summary

EudraCT number	2013-002458-66
Trial protocol	FR
Global end of trial date	26 November 2014

Results information

Result version number	v1
This version publication date	23 April 2016
First version publication date	23 April 2016

Trial information

Trial identification

Sponsor protocol code	AI443-113

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01973049
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Bristol-Myers Squibb International Corporation, Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol Myers Squibb Study Director, Bristol Myers Squibb, clinical.trials@bms.com
Scientific contact	Bristol Myers Squibb Study Director, Bristol Myers Squibb, clinical.trials@bms.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	26 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the proportion of treatment-naive cirrhotic subjects in at least 1 of daclatasvir 3 direct acting antiviral (DCV 3DAA) daclatasvir/asunaprevir/beclabuvir administered as a fixed-dose combination with or without ribavirin (RIBAVIRIN) group with sustained virologic response at follow-up week 12 (SVR12), defined as hepatitis C virus (HCV) RNA below lower limit of quantitation (LLOQ) target detected or target not detected at follow-up week 12, was significantly greater than a historical threshold of 69 percent.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 34
Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	United States: 196
Country: Number of subjects enrolled	France: 35
Worldwide total number of subjects	300
EEA total number of subjects	35

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	251
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 48 sites in the United States, Canada, France and Australia.

Pre-assignment

Screening details:

A total of 300 subjects were enrolled and 202 were randomised and treated. Reason for not being randomised: adverse event (1), subject withdrew consent (2), poor/non-compliance (1), subject no longer meets study criteria (92) and administrative reason by sponsor (2).

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

This study was blinded for RBV/placebo assignment for sites, subjects and the Sponsor but open-label for DCV 3DAA therapy (daclatasvir/asunaprevir/BMS-791325).

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment-naive: DCV 3DAA

Arm description:

Subjects (treatment naïve) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	BMS-790052
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daclatasvir 30 mg tablet was administered orally twice daily (1 tablet in morning and 1 tablet in evening) with food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Asunaprevir
Investigational medicinal product code	BMS-650032
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Asunaprevir 200 mg was administered orally twice daily (1 tablet in morning and 1 tablet in evening) with food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Beclabuvir
Investigational medicinal product code	BMS-791325
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Beclabuvir 75 mg was administered orally twice daily (1 tablet in morning and 1 tablet in evening) with

food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Placebo matched to ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ribavirin was administered orally, twice daily in a body weight stratified dose range of 1000–1200 mg per day [total dose of 1000-mg per day for subjects weighing <75 kg (2 tablets in morning and 3 tablets in evening) and a total dose of 1200 mg per day for subjects weighing >=75 kg (3 tablets in morning and 3 tablets in evening)] by treatment naive subjects.

Arm title	Treatment-naive: DCV 3DAA + RBV

Arm description:

Subjects (treatment naive) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with ribavirin 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	BMS-790052
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daclatasvir 30 mg was administered orally twice daily with food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Asunaprevir
Investigational medicinal product code	BMS-650032
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Asunaprevir 200 mg was administered orally twice daily with food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Beclabuvir
Investigational medicinal product code	BMS-791325
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Beclabuvir 75 mg was administered orally twice daily with food for 12 weeks by treatment naive subjects.

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

Dosage and administration details:

Ribavirin 200 mg tablet was administered orally, twice daily in a body weight stratified dose range of 1000–1200 mg per day [total dose of 1000-mg per day for subjects weighing <75 kg (2 tablets in morning and 3 tablets in evening) and a total dose of 1200 mg per day for subjects weighing >=75 kg (3 tablets in morning and 3 tablets in evening)] by treatment naive subjects.

Arm title	Treatment-experienced: DCV 3DAA

Arm description:

Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24

Arm type	Experimental
Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	BMS-790052
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daclatasvir 30 mg was administered orally twice daily with food for 12 weeks by treatment experienced subjects.

Investigational medicinal product name	Asunaprevir
Investigational medicinal product code	BMS-650032
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Asunaprevir 200 mg was administered orally twice daily with food for 12 weeks by treatment experienced subjects.

Investigational medicinal product name	Beclabuvir
Investigational medicinal product code	BMS-791325
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Beclabuvir 75 mg was administered orally twice daily with food for 12 weeks by treatment experienced subjects.

Investigational medicinal product name	Placebo matched to ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to ribavirin was administered orally, twice daily in a body weight stratified dose range of 1000–1200 mg per day [total dose of 1000-mg per day for subjects weighing <75 kg (2 tablets in morning and 3 tablets in evening) and a total dose of 1200 mg per day for subjects weighing >=75 kg (3 tablets in morning and 3 tablets in evening)].

Arm title	Treatment-experienced: DCV 3DAA +RBV

Arm description:

Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with RIBAVIRIN 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	BMS-790052
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daclatasvir 30 mg tablet was administered orally twice daily with food for 12 weeks by treatment naive subjects.

Investigational medicinal product name	Asunaprevir
Investigational medicinal product code	BMS-650032
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Asunaprevir 200 mg was administered orally twice daily with food for 12 weeks by treatment experienced subjects.

Investigational medicinal product name	Beclabuvir
Investigational medicinal product code	BMS-791325
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Beclabuvir 75 mg was administered orally twice daily with food for 12 weeks by treatment experienced subjects.

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

Dosage and administration details:

Ribavirin 200 mg tablet was administered orally, twice daily in a body weight stratified dose range of 1000–1200 mg per day [total dose of 1000-mg per day for subjects weighing <75 kg (2 tablets in morning and 3 tablets in evening) and a total dose of 1200 mg per day for subjects weighing >=75 kg (3 tablets in morning and 3 tablets in evening)].

Number of subjects in period 1[1]	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA
Started	57	55	45
Completed	57	55	44
Not completed	0	0	1
Adverse event, non-fatal	-	-	-
Lack of efficacy	-	-	1

Number of subjects in period 1[1]	Treatment-experienced: DCV 3DAA +RBV
Started	45
Completed	43
Not completed	2
Adverse event, non-fatal	1
Lack of efficacy	1

Notes:

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

Justification: The number of subjects reported to be in the baseline period are not the same as out of 300 subjects enrolled only 202 were randomized and treated.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment-naive: DCV 3DAA
Reporting group description:	
Subjects (treatment naïve) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.	
Reporting group title	Treatment-naive: DCV 3DAA + RBV
Reporting group description:	
Subjects (treatment naive) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with ribavirin 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.	
Reporting group title	Treatment-experienced: DCV 3DAA
Reporting group description:	
Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24	
Reporting group title	Treatment-experienced: DCV 3DAA +RBV
Reporting group description:	
Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with RIBAVIRIN 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.	

Reporting group values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA
Number of subjects	57	55	45
Age categorical Units: Subjects			
<65 years	43	46	42
>=65 years	14	9	3
Age continuous Units: years			
arithmetic mean	58.1	58.7	57.1
standard deviation	± 9.03	± 6.55	± 8.35
Gender categorical Units: Subjects			
Female	18	20	13
Male	39	35	32

Reporting group values	Treatment-experienced: DCV 3DAA +RBV	Total	
Number of subjects	45	202	

Age categorical Units: Subjects			
<65 years	34	165	
>=65 years	11	37	
Age continuous Units: years			
arithmetic mean	60		
standard deviation	± 6.24	-	
Gender categorical Units: Subjects			
Female	18	69	
Male	27	133	

End points

End points reporting groups

Reporting group title	Treatment-naive: DCV 3DAA

Reporting group description:

Subjects (treatment naïve) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Reporting group title	Treatment-naive: DCV 3DAA + RBV

Reporting group description:

Subjects (treatment naive) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with ribavirin 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Reporting group title	Treatment-experienced: DCV 3DAA

Reporting group description:

Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24

Reporting group title	Treatment-experienced: DCV 3DAA +RBV

Reporting group description:

Subjects (treatment experienced) received a fixed dose combination of daclatasvir 30 mg tablet, asunaprevir 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with RIBAVIRIN 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Primary: Percentage of Subjects in Treatment-naive Cohort With Sustained Virologic Response at Follow-up Week 12 (SVR12)

End point title	Percentage of Subjects in Treatment-naive Cohort With Sustained Virologic Response at Follow-up Week 12 (SVR12)[1][2]

End point description:

SVR12 was defined as hepatitis C virus (HCV) RNA levels <lower limit of quantitation (LLOQ), target detected or target not detected at follow-up week 12. The LLOQ was 25 international unit per milliliter. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. The analysis was performed on all treated subjects using as-randomized treatment arm, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects. Missing values were imputed using Next Value Carried Backwards (NVCB) approach, i.e., missing HCV RNA in the follow-up Week 12 window was imputed using the next and closest available HCV RNA measurement after the follow-up Week 12 HCV RNA window.

End point type	Primary

End point timeframe:

Follow-up week 12

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: Only descriptive summary statistics was planned for this outcome measure.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	55		
Units: Percentage of subject				
number (confidence interval 97.5%)	93 (85.4 to 100)	100 (92.3 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects in Treatment-Experienced Cohort With Sustained Virologic Response at Follow-up Week 12 (SVR12)

End point title	Percentage of Subjects in Treatment-Experienced Cohort With Sustained Virologic Response at Follow-up Week 12 (SVR12)[3]

End point description:

SVR12 was defined as hepatitis C virus (HCV) RNA levels <lower limit of quantitation (LLOQ), target detected or target not detected at follow-up week 12. The LLOQ was 25 international unit per milliliter. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. The analysis was performed on all treated subjects using as-randomized treatment arm, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects. Missing values were imputed using Next Value Carried Backwards (NVCB) approach, i.e., missing HCV RNA in the follow-up Week 12 window was imputed using the next and closest available HCV RNA measurement after the follow-up Week 12 HCV RNA window.

End point type	Secondary

End point timeframe:

Follow-up week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to evaluate for the specified arm only.

End point values	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: Percentage of subjects				
number (confidence interval 97.5%)	86.7 (75.3 to 98)	93.3 (85 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Hepatitis C Virus (HCV) RNA Levels Below Lower Limit of Quantitation (LLOQ) Target Detected (TD) or Target Not Detected (TND)

End point title	Percentage of Subjects With Hepatitis C Virus (HCV) RNA

	Levels Below Lower Limit of Quantitation (LLOQ) Target Detected (TD) or Target Not Detected (TND)

End point description:

Subjects who achieved HCV RNA levels <LLOQ, TD or TND. The LLOQ was 25 international unit per milliliter. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. The analysis was performed in modified intent-to-treat population, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 6, 8, 12; follow-up Week 4, 8, and 24

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Percentage of subjects				
number (not applicable)				
Week 1	22.8	25.5	20	17.8
Week 2	57.9	67.3	55.6	68.9
Week 4	100	98.2	88.9	97.8
Week 6	96.5	98.2	97.8	100
Week 8	98.2	98.2	97.8	95.6
Week 12	100	100	93.3	88.9
Follow-up week 4	94.7	98.2	88.9	91.1
Follow-up week 8	91.2	89.1	84.4	91.1
Follow-up week 24	93	100	86.7	91.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Hepatitis C Virus (HCV) RNA Levels Below Than Lower Limit of Quantitation (LLOQ) Target Not Detected (TND)

End point title	Percentage of Subjects With Hepatitis C Virus (HCV) RNA Levels Below Than Lower Limit of Quantitation (LLOQ) Target Not Detected (TND)

End point description:

Subjects who achieved HCV RNA levels <LLOQ, TND. The LLOQ was 25 international unit per milliliter. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. The analysis was performed in modified intent-to-treat population, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 6, 8, 12; follow-up Week 4, 8, 12 and 24

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Percentage of subjects				
number (not applicable)				
Week 1	1.8	7.3	2.2	2.2
Week 2	24.6	29.1	20	17.8
Week 4	68.4	80	57.8	68.9
Week 6	87.7	94.5	88.9	97.8
Week 8	96.5	94.5	93.3	84.4
Week 12	100	98.2	93.3	88.9
Follow-up week 4	93	98.2	88.9	91.1
Follow-up week 8	91.2	89.1	84.4	91.1
Follow-up week 12	93	98.2	86.7	93.3
Follow-up week 24	93	100	86.7	91.1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with On-Treatment Serious Adverse Events (SAEs) and Discontinuations due to Adverse Events (AEs)

End point title	Number of Subjects with On-Treatment Serious Adverse Events (SAEs) and Discontinuations due to Adverse Events (AEs)

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a subject or clinical investigation subject administered an investigational (medicinal) product. An SAE was defined as any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization. The analysis was performed on all subjects who received at least 1 dose of study therapy.

End point type	Secondary

End point timeframe:

Baseline through the last dose of study therapy plus 7 days

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Subjects				
SAEs	1	5	1	2
Discontinuation due to AEs	0	2	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Anemia on Treatment

End point title	Percentage of Subjects With Anemia on Treatment

End point description:

Anemia was defined as hemoglobin level less than 10 gram per deciliter (g/dL) on treatment for subjects who had hemoglobin level equal to or above 10 g/dL at baseline. The analysis was performed on all subjects who received at least 1 dose of study therapy.

End point type	Secondary

End point timeframe:

Baseline through the last dose of study therapy plus 7 days

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Percentage of subjects				
number (not applicable)	0	9.1	0	20

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Selected Treatment Emergent Grade 3 to 4 Laboratory Test Abnormalities

End point title	Number of Subjects With Selected Treatment Emergent Grade 3 to 4 Laboratory Test Abnormalities

End point description:

Laboratory tests with Division of AIDS Version 1.0 toxicity criteria were performed and assessed. Assessment were done for following: hemoglobin, leukocytes, neutrophils + bands, lymphocytes, platelet count, international normalized Ratio, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, albumin, creatinine and lipase. The analysis was performed on all subjects who received at least 1 dose of study therapy.

End point type	Secondary

End point timeframe:

Baseline through the last dose of study therapy plus 7 days

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Subjects				
Hemoglobin	0	2	0	3
Leukocytes	0	1	0	0
Neutrophils +Bands	1	0	0	1
Lymphocytes	0	0	1	3
Platelets count	1	1	1	1
International Normalized Ratio	0	0	0	0
Alanine aminotransferase	2	0	1	1
Aspartate aminotransferase	1	0	1	1
Total bilirubin	0	2	0	1
Alkaline phosphatase	0	0	0	0
Albumin	0	0	0	0
Creatinine, enzymatic	0	0	0	0
Lipase	4	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) Associated With Hepatitis C Virus (HCV) Genotype Subtype 1a vs 1b

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) Associated With Hepatitis C Virus (HCV) Genotype Subtype 1a vs 1b

End point description:

Subjects categorized into two genotype subtypes that were assessed for SVR12 defined as HCV RNA levels <LLOQ, TD or TND at follow-up week 12. The LLOQ was 25 international unit per milliliter. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. The analysis was performed on treated subjects using as-randomized treatment arm, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects. Here, 'n' signifies number of subjects evaluable at the specified subgroup. Missing values were imputed using NVCB approach.

End point type	Secondary

End point timeframe:

Follow-up week 12

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Percentage of subjects				
number (confidence interval 95%)				

Genotype-1A (n=40, 39, 35, 35)	90 (80.7 to 99.3)	100 (91 to 100)	85.7 (74.1 to 97.3)	91.4 (82.2 to 100)
Genotype-1B (n=17, 15, 10, 10)	100 (80.5 to 100)	100 (78.2 to 100)	90 (55.5 to 99.7)	100 (69.2 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With SVR12 Associated With IL28B rs12979860 Single Nucleotide Polymorphism (SNP) status (CC Genotype or Non-CC Genotype)

End point title	Percentage of Subjects With SVR12 Associated With IL28B rs12979860 Single Nucleotide Polymorphism (SNP) status (CC Genotype or Non-CC Genotype)

End point description:

Subjects categorized into two genotypes based on SNP in the IL28B gene were assessed for SVR12 defined as HCV RNA levels <LLOQ, TD or TND at follow-up week 12. The LLOQ was 25 IU/mL. Here ''99999'' signifies not available as data for the specified time point for this endpoint was not analyzed. The analysis was performed on treated subjects using as-randomized treatment arm, the numerator was based on subjects meeting the response criteria and denominator based on all treated subjects. Here, 'n' signifies number of subjects evaluable for the specified category and '99999' signifies not applicable (NA) as no subject was analysed for that specified category. Missing values were imputed using NVCB approach.

End point type	Secondary

End point timeframe:

Follow-up week 12

End point values	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA	Treatment-experienced: DCV 3DAA +RBV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	45	45
Units: Percentage of subjects				
number (confidence interval 95%)				
CC Genotype (n=13, 18, 15, 09)	84.6 (54.6 to 98.1)	100 (81.5 to 100)	86.7 (59.5 to 98.3)	100 (66.4 to 100)
Non-CC Genotype (n=43, 37, 30, 36)	95.3 (84.2 to 99.4)	100 (90.5 to 100)	86.7 (74.5 to 98.8)	91.7 (82.6 to 100)
Not reported (n=1, 0, 0, 0)	100 (2.5 to 100)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through the last dose of study therapy plus 7 days

Adverse event reporting additional description:

On-treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Treatment-naive: DCV 3DAA

Reporting group description:

Subjects (treatment naïve) received a fixed dose combination of daclatasvir (DCV) 30 mg tablet, asunaprevir (ASV) 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Reporting group title	Treatment-naive: DCV 3DAA + RBV

Reporting group description:

Subjects (treatment naive) received a fixed dose combination of daclatasvir (DCV) 30 mg tablet, ASV 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with ribavirin 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Reporting group title	Treatment-experienced: DCV 3DAA

Reporting group description:

Subjects (treatment experienced) received a fixed dose combination of DCV 30 mg tablet, ASV 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with placebo matched to ribavirin tablet orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Reporting group title	Treatment-experienced: DCV 3DAA +RBV

Reporting group description:

Subjects (treatment experienced) received a fixed dose combination of daclatasvir (DCV) 30 mg tablet, ASV 200 mg tablets and beclabuvir 75 mg tablets orally, twice daily up to 12 weeks along with RIBAVIRIN 200 mg orally twice daily in a body weight stratified dose range of 1000–1200 mg per day (total dose of 1000-mg per day for subjects weighing <75 kg and 1200 mg per day for subjects weighing >=75 kg). After 12 weeks of drug therapy, subjects were followed-up for 24 weeks.

Serious adverse events	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 57 (1.75%)	5 / 55 (9.09%)	1 / 45 (2.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 45 (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
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 57 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 45 (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 / 57 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast hyperplasia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	0 / 45 (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			
Drug-induced liver injury			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	0 / 45 (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			
Asthma			
subjects affected / exposed	1 / 57 (1.75%)	0 / 55 (0.00%)	0 / 45 (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
Infections and infestations			

Pneumonia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment-experienced: DCV 3DAA +RBV		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 45 (4.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast hyperplasia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment-naive: DCV 3DAA	Treatment-naive: DCV 3DAA + RBV	Treatment-experienced: DCV 3DAA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 57 (70.18%)	48 / 55 (87.27%)	31 / 45 (68.89%)
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 57 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 57 (15.79%)	9 / 55 (16.36%)	8 / 45 (17.78%)
occurrences (all)	10	9	9
Dizziness			
subjects affected / exposed	0 / 57 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Lethargy			
subjects affected / exposed	0 / 57 (0.00%)	2 / 55 (3.64%)	2 / 45 (4.44%)
occurrences (all)	0	2	2

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 57 (10.53%)	16 / 55 (29.09%)	6 / 45 (13.33%)
occurrences (all)	6	16	6
Asthenia			
subjects affected / exposed	3 / 57 (5.26%)	4 / 55 (7.27%)	0 / 45 (0.00%)
occurrences (all)	3	4	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 57 (0.00%)	6 / 55 (10.91%)	0 / 45 (0.00%)
occurrences (all)	0	6	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 57 (19.30%)	10 / 55 (18.18%)	3 / 45 (6.67%)
occurrences (all)	11	10	3
Diarrhoea			
subjects affected / exposed	7 / 57 (12.28%)	6 / 55 (10.91%)	6 / 45 (13.33%)
occurrences (all)	9	6	7
Abdominal pain upper			
subjects affected / exposed	1 / 57 (1.75%)	1 / 55 (1.82%)	2 / 45 (4.44%)
occurrences (all)	1	1	2
Vomiting			
subjects affected / exposed	4 / 57 (7.02%)	4 / 55 (7.27%)	0 / 45 (0.00%)
occurrences (all)	4	4	0
Dyspepsia			
subjects affected / exposed	2 / 57 (3.51%)	1 / 55 (1.82%)	2 / 45 (4.44%)
occurrences (all)	2	1	3
Abdominal pain			
subjects affected / exposed	1 / 57 (1.75%)	3 / 55 (5.45%)	0 / 45 (0.00%)
occurrences (all)	1	3	0
Flatulence			
subjects affected / exposed	3 / 57 (5.26%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	3	2	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 57 (0.00%)	6 / 55 (10.91%)	1 / 45 (2.22%)
occurrences (all)	0	6	1
Cough			
subjects affected / exposed	1 / 57 (1.75%)	4 / 55 (7.27%)	0 / 45 (0.00%)
occurrences (all)	1	5	0
Dyspnoea exertional			
subjects affected / exposed	1 / 57 (1.75%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 57 (3.51%)	4 / 55 (7.27%)	4 / 45 (8.89%)
occurrences (all)	2	4	4
Rash			
subjects affected / exposed	1 / 57 (1.75%)	6 / 55 (10.91%)	2 / 45 (4.44%)
occurrences (all)	1	7	2
Dry skin			
subjects affected / exposed	1 / 57 (1.75%)	5 / 55 (9.09%)	1 / 45 (2.22%)
occurrences (all)	1	5	1
Alopecia			
subjects affected / exposed	0 / 57 (0.00%)	2 / 55 (3.64%)	2 / 45 (4.44%)
occurrences (all)	0	2	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 57 (5.26%)	8 / 55 (14.55%)	3 / 45 (6.67%)
occurrences (all)	3	8	3
Irritability			
subjects affected / exposed	0 / 57 (0.00%)	3 / 55 (5.45%)	1 / 45 (2.22%)
occurrences (all)	0	3	1
Anxiety			
subjects affected / exposed	1 / 57 (1.75%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Sleep disorder			
subjects affected / exposed	1 / 57 (1.75%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	3 / 45 (6.67%)
occurrences (all)	0	0	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 57 (5.26%)	1 / 55 (1.82%)	4 / 45 (8.89%)
occurrences (all)	4	1	4
Rhinitis			
subjects affected / exposed	1 / 57 (1.75%)	3 / 55 (5.45%)	1 / 45 (2.22%)
occurrences (all)	1	3	1
Oral herpes			
subjects affected / exposed	0 / 57 (0.00%)	3 / 55 (5.45%)	2 / 45 (4.44%)
occurrences (all)	0	3	2
Bronchitis			
subjects affected / exposed	4 / 57 (7.02%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0

Non-serious adverse events	Treatment-experienced: DCV 3DAA +RBV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 45 (93.33%)		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 45 (31.11%)		
occurrences (all)	16		
Dizziness			
subjects affected / exposed	6 / 45 (13.33%)		
occurrences (all)	6		
Lethargy			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	12 / 45 (26.67%) 14		
Asthenia subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 8		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 7		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 7		
Vomiting subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Flatulence subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4		

Cough			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	5		
Dyspnoea exertional			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	11 / 45 (24.44%)		
occurrences (all)	11		
Rash			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	8		
Irritability			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Anxiety			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Sleep disorder			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2013	Permitted the collection and storage of blood samples for use in future exploratory pharmacogenetic research.
21 April 2014	An interim analysis was added after all subjects complete post-treatment Week 4 in order to support pharmacokinetic modeling and simulations for exposure-response analysis.
24 June 2014	Historical threshold of sustained virologic response for treatment of chronic hepatitis C virus infection was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported