



Clinical trial results:

A Phase 3, Open Label Study of Safety and Efficacy with BMS-790052 plus Peg-Interferon Alfa-2a and Ribavirin in Previously Untreated HCV Patients co-infected with Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV).

Summary

EudraCT number	2011-003067-30
Trial protocol	DE ES GB BE IT
Global end of trial date	10 September 2014

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	01 April 2016

Trial information

Trial identification

Sponsor protocol code	AI444-043
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01471574
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee 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	10 September 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of daclatasvir plus peg interferon-alfa 2a and ribavirin in untreated hepatitis C virus in subjects co-infected with HIV.

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 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 75
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 54
Country: Number of subjects enrolled	Argentina: 27
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Brazil: 24
Country: Number of subjects enrolled	Canada: 47
Country: Number of subjects enrolled	Puerto Rico: 22
Country: Number of subjects enrolled	Russian Federation: 60
Country: Number of subjects enrolled	United States: 143
Worldwide total number of subjects	549
EEA total number of subjects	207

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)	533
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 84 sites in 13 countries.

Pre-assignment

Screening details:

Of 549 subjects enrolled, 301 were randomised to receive treatment. Of the 248 subjects who were not randomised, 204 no longer met study criteria, and 44 discontinued due to other reasons.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg

Arm description:

Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 30 mg tablet was administered orally once daily.

Investigational medicinal product name	PegIFNalfa--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalfa--2a solution of 180 µg was administered subcutaneously once weekly.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥75 kg) with meals.

Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Arm description:

Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalfa-2a solution for injection, 180 µg,

subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 60 mg tablet was administered orally once daily.

Investigational medicinal product name	PegIFNalpha--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalpha--2a solution of 180 µg was administered subcutaneously once weekly.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and (for subjects ≥75 kg) with meals.

Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
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Arm description:

Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalpha-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 30 and 60 mg tablets was administered orally once daily.

Investigational medicinal product name	PegIFNalpha--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalpha--2a 180 µg was administered subcutaneously once weekly.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects < 75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥ 75 kg) with meal.

Arm title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Arm description:

Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalpha-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 60 mg tablet was administered orally once daily.

Investigational medicinal product name	PegIFNalpha--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalpha-2a solution of 180 µg was administered subcutaneously once weekly.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥75 kg) with meals.

Number of subjects in period 1^[1]	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Started	132	39	106
Completed	101	29	82
Not completed	31	10	24
Subject no Longer Meets Study Criteria	1	-	-
Consent withdrawn by subject	5	1	1
Not specified	1	-	-
Adverse event	7	3	6
Lost to follow-up	1	2	2

Subject Requested Discontinue Study drug	4	-	1
Lack of efficacy	12	4	14

Number of subjects in period 1 ^[1]	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Started	24
Completed	21
Not completed	3
Subject no Longer Meets Study Criteria	-
Consent withdrawn by subject	-
Not specified	-
Adverse event	1
Lost to follow-up	-
Subject Requested Discontinue Study drug	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 in the baseline period are different from the worldwide number enrolled in the trial, as 204 subjects no longer met study criteria and 44 discontinued due to other reasons.

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg

Arm description:

Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 30 mg tablet was administered orally once daily.

Investigational medicinal product name	PegIFNalfa--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe

Routes of administration	Subcutaneous use
Dosage and administration details:	
PegIFNalpha--2a solution of 180 µg was administered subcutaneously once weekly.	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥75 kg) with meals.	
Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Arm description:	
Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalpha-2a solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.	
Arm type	Experimental
Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Daclatasvir 60 mg tablet was administered orally once daily.	
Investigational medicinal product name	PegIFNalpha--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
PegIFNalpha--2a solution of 180 µg was administered subcutaneously once weekly.	
Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and (for subjects ≥75 kg) with meals.	
Arm title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Arm description:	
Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalpha-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.	
Arm type	Experimental

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

Dosage and administration details:

Daclatasvir 30 and 60 mg tablets was administered orally once daily.

Investigational medicinal product name	PegIFNalfa--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalfa--2a 180 µg was administered subcutaneously once weekly.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects < 75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥ 75 kg) with meal.

Arm title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Arm description:

Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

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

Dosage and administration details:

Daclatasvir 60 mg tablet was administered orally once daily.

Investigational medicinal product name	PegIFNalfa--2a
Investigational medicinal product code	
Other name	Pegasys
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

PegIFNalpha-2a solution of 180 µg was administered subcutaneously once weekly.

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

Dosage and administration details:

Ribavirin 1000 mg total daily dose was administered as 400 mg in morning and 600 mg in evening (for subjects <75 kg) or 1200 mg total daily dose was administered orally as 600 mg in morning and evening (for subjects ≥75 kg) with meals.

Number of subjects in period 2	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Started	101	29	82
Completed	114	32	95
Not completed	7	2	7
Consent withdrawn by subject	3	-	3
Death	-	-	1
Lost to follow-up	4	1	3
Follow-up no longer required	-	1	-
Joined	20	5	20
Rejoined for follow-up	20	5	20

Number of subjects in period 2	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Started	21
Completed	21
Not completed	3
Consent withdrawn by subject	1
Death	-
Lost to follow-up	2
Follow-up no longer required	-
Joined	3
Rejoined for follow-up	3

Baseline characteristics

Reporting groups

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg
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Reporting group description:

Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Reporting group description:

Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
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Reporting group description:

Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Reporting group description:

Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group values	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Number of subjects	132	39	106
Age categorical Units: Subjects			
Adults (18-64 years)	125	39	104
From 65-84 years	7	0	2
Age continuous Units: years			
arithmetic mean	47	47.9	46.5
standard deviation	± 9.72	± 9.03	± 9.42
Gender categorical Units: Subjects			
Female	27	7	27
Male	105	32	79

Reporting group values	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Total	
Number of subjects	24	301	

Age categorical Units: Subjects			
Adults (18-64 years)	24	292	
From 65-84 years	0	9	
Age continuous Units: years			
arithmetic mean	36		
standard deviation	± 9.02	-	
Gender categorical Units: Subjects			
Female	11	72	
Male	13	229	

End points

End points reporting groups

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg
Reporting group description: Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Reporting group description: Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Reporting group description: Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Reporting group description: Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg
Reporting group description: Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Reporting group description: Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Reporting group description: Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.	
Reporting group title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Reporting group description: Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with	

a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalpha-2a and ribavirin for a total duration of 48 weeks.

Subject analysis set title	HAART Therapy: Daclatasvir 30 or 60 or 90 mg
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects with prior exposure to HAART therapy, received daclatasvir tablets, either 30, 60 or 90 mg, orally, once daily; pegIFNα-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for Subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNα-2a and ribavirin for a total duration of 48 weeks.

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

End point title	Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) ^[1]
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End point description:

SVR12 was defined as hepatitis C virus (HCV) values lower than the lower limit of quantitation, target detected or target not detected at follow-up Week 12. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. HAART=highly active antiretroviral therapy. The analysis was performed in all subjects who received at least 1 dose of study therapy.

End point type	Primary
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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 data was planned to be analyzed.

End point values	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	132	39	106	24
Units: Percentage of subjects				
number (confidence interval 95%)	75 (67.6 to 82.4)	71.8 (57.7 to 85.9)	71.7 (63.1 to 80.3)	87.5 (74.3 to 100)

End point values	HAART Therapy: Daclatasvir 30 or 60 or 90 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Percentage of subjects				
number (confidence interval 95%)	73.3 (68.1 to 78.5)			

Statistical analyses

Secondary: Percentage of Subjects Who Achieved Hepatitis C Virus (HCV) RNA Levels Lower Than the Lower Limit of Quantitation (LLOQ), Target Detected (TD) or Target Not Detected (TND)

End point title	Percentage of Subjects Who Achieved Hepatitis C Virus (HCV) RNA Levels Lower Than the Lower Limit of Quantitation (LLOQ), Target Detected (TD) or Target Not Detected (TND) ^[2]
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End point description:

Subjects who achieved HCV RNA levels lower than the LLOQ i.e., 25 IU/ml, TD or TND. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. HAART=highly active antiretroviral therapy. The analysis was performed in all subjects who received at least 1 dose of study therapy.

End point type	Secondary
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End point timeframe:

Week 1, 2, 4, 6, 8, 12 and at both Weeks 4 and 12; end of treatment; and follow-up Weeks 24

Notes:

[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 be assessed for prespecified reporting group: Non-HAART Therapy and HAART Therapy Total.

End point values	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	HAART Therapy: Daclatasvir 30 or 60 or 90 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	24	277		
Units: Percentage of subjects				
number (not applicable)				
Week 1	41.7	39.7		
Week 2	91.7	71.5		
Week 4	95.8	82.7		
Week 6	87.5	84.1		
Week 8	95.8	84.1		
Week 12	91.7	85.2		
Week 4 and 12	91.7	78.7		
End of treatment	95.8	84.8		
Follow-up Week 24	83.3	70.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved Hepatitis C Virus (HCV) RNA Levels Lower Than the Lower Limit of Quantitation (LLOQ), Target Not Detected (TND)

End point title	Percentage of Subjects Who Achieved Hepatitis C Virus (HCV) RNA Levels Lower Than the Lower Limit of Quantitation (LLOQ), Target Not Detected (TND) ^[3]
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End point description:

Subjects who achieved HCV RNA levels lower than the LLOQ, TND. HCV RNA levels were measured by

the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. HAART=highly active antiretroviral therapy. The analysis was performed in all subjects who received at least 1 dose of study therapy.

End point type	Secondary
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End point timeframe:

Week 1, 2, 4, 6, 8, and 12 and at both Weeks 4 and 12; end of treatment; and follow-up Weeks 12 and 24

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 be assessed for prespecified reporting group: Non-HAART Therapy and HAART Therapy Total.

End point values	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	HAART Therapy: Daclatasvir 30 or 60 or 90 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	24	277		
Units: Percentage of subjects				
number (not applicable)				
Week 1	16.7	9		
Week 2	50	33.9		
Week 4	91.7	64.3		
Week 6	87.5	74.4		
Week 8	95.8	78		
Week 12	91.7	81.2		
Week 4 and 12	87.5	61.4		
End of treatment	91.7	81.2		
Follow-up Week 12	87.5	70.8		
Follow-up Week 24	83.3	70.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Received Highly Active Antiretroviral Therapy (HAART), Maintained HIV RNA <40 Copies/mL, and Experienced Confirmed HIV RNA ≥400 Copies/mL

End point title	Percentage of Subjects Who Received Highly Active Antiretroviral Therapy (HAART), Maintained HIV RNA <40 Copies/mL, and Experienced Confirmed HIV RNA ≥400 Copies/mL ^[4]
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End point description:

Subjects who received HAART, maintained HIV RNA <40 copies/mL, and experienced confirmed HIV RNA ≥400 copies/mL were determined. The analysis was performed in all subjects who received at least 1 dose of study therapy.

End point type	Secondary
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End point timeframe:

End of treatment

Notes:

[4] - 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 be assessed for prespecified reporting group: HAART

Therapy: Daclatasvir 30mg, HAART Therapy: Daclatasvir 60 mg and HAART Therapy: Daclatasvir 90 mg.

End point values	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg	HAART Therapy: Daclatasvir 30 or 60 or 90 mg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	132	39	106	277
Units: Percentage of subjects				
number (confidence interval 95%)				
HIV RNA < 40 copies/mL	88.6 (83.2 to 94.1)	89.7 (80.2 to 99.3)	93.4 (88.7 to 98.1)	90.6 (87.2 to 94.1)
HIV RNA >= 400 copies/mL	0 (0 to 0)	2.6 (0 to 7.5)	0 (0 to 0)	0.4 (0 to 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response (SVR12) by rs12979860 Single Nucleotide Polymorphism (SNP) in the IL28B Gene

End point title	Percentage of Subjects With Sustained Virologic Response (SVR12) by rs12979860 Single Nucleotide Polymorphism (SNP) in the IL28B Gene
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End point description:

Percentages calculated as number of responders/number who received treatment. All subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects evaluable at the specified time-point.

End point type	Secondary
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End point timeframe:

Follow-up Week 12

End point values	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	132	39	106	24
Units: Percentage of Subjects				
number (confidence interval 95%)				
CC Genotype (n=36, 14, 39, 89, 6)	94.4 (87 to 100)	92.9 (79.4 to 100)	79.5 (66.8 to 92.2)	100 (100 to 100)
CT Genotype (n=72, 22, 50, 144, 15)	66.7 (55.8 to 77.6)	63.6 (43.5 to 83.7)	70 (57.3 to 82.7)	93.3 (80.7 to 100)
TT Genotype (n=22, 3, 12, 37, 2)	68.2 (48.7 to 87.6)	33.3 (0 to 86.7)	58.3 (30.4 to 86.2)	50 (0 to 100)

Not reported (n=2, 0, 5, 7, 1)	100 (100 to 100)	0 (0 to 0)	60 (17.1 to 100)	0 (0 to 0)
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End point values	HAART Therapy: Daclatasvir 30 or 60 or 90 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Percentage of Subjects				
number (confidence interval 95%)				
CC Genotype (n=36, 14, 39, 89, 6)	87.6 (80.8 to 94.5)			
CT Genotype (n=72, 22, 50, 144, 15)	67.4 (59.7 to 75)			
TT Genotype (n=22, 3, 12, 37, 2)	62.2 (46.5 to 77.8)			
Not reported (n=2, 0, 5, 7, 1)	71.4 (38 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Died and With Serious Adverse Event (SAEs), Grade 3 to 4 Adverse Events (AEs), and AEs Leading to Discontinuation

End point title	Number of Subjects Who Died and With Serious Adverse Event (SAEs), Grade 3 to 4 Adverse Events (AEs), and AEs Leading to Discontinuation
End point description:	
Adverse event was defined as any new unfavorable symptom, sign, or disease or worsening of a pre-existing condition that does not necessarily have a causal relationship with treatment. SAE was defined as a medical event that at any dose resulted in death, persistent or significant disability/incapacity, or drug dependency/abuse; was life-threatening, an important medical event, or a congenital anomaly/birth defect; or required prolonged hospitalization. HAART=highly active antiretroviral therapy. The analysis was performed in all subjects who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe:	
From Day 1 to 7 days post last dose of study treatment (up to Week 48)	

End point values	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	132	39	106	24
Units: Subjects				
Deaths	0	1	1	0

SAEs	12	6	6	0
Grade 3 to 4 AEs	46	12	35	4
AEs Leading to Discontinuation of Study Therapy	7	4	6	1

End point values	HAART Therapy: Daclatasvir 30 or 60 or 90 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	277			
Units: Subjects				
Deaths	2			
SAEs	24			
Grade 3 to 4 AEs	93			
AEs Leading to Discontinuation of Study Therapy	17			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to 7 days post last dose of study treatment (up to Week 48)

Adverse event reporting additional description:

On-treatment period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg
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Reporting group description:

Subjects taking HIV ritonavir-boosted protease inhibitors received daclatasvir tablets, 30 mg, orally once daily; peg-interferon alfa-2a (pegIFNalfa-2a) solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets, orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Reporting group description:

Subjects taking other Highly Active Anti-Retroviral Therapy (HAART), including rilpivirine, received daclatasvir tablets, 60 mg, orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously once weekly; and ribavirin tablets orally twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
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Reporting group description:

Subjects taking non-nucleoside reverse transcriptase inhibitors, except rilpivirine, received 2 daclatasvir tablets (1x30 mg and 1x60 mg), orally once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally twice daily for a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at Weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Reporting group title	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg
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Reporting group description:

Subjects not receiving HAART received daclatasvir tablets, 60 mg, orally, once daily; pegIFNalfa-2a solution for injection, 180 µg, subcutaneously, once weekly; and ribavirin tablets, orally, twice daily with a total dose of 1000 mg for subjects weighing <75 kg and 1200 mg for those weighing ≥75 kg, for up to 24 weeks. Subjects without virologic response at weeks 4 and 12 continued to receive pegIFNalfa-2a and ribavirin for a total duration of 48 weeks.

Serious adverse events	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 132 (9.09%)	6 / 39 (15.38%)	6 / 106 (5.66%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Breast cancer			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
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			
Laryngeal cyst			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Prinzmetal angina			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 132 (1.52%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Diarrhoea			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Gastritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Nausea			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Pancreatitis acute			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Vomiting			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendicitis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 39 (2.56%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Meningitis			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
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 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 39 (2.56%)	0 / 106 (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
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis septic			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperkalaemia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (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
Hypokalaemia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 39 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Laryngeal cyst			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prinzmetal angina			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 24 (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 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pancreatitis acute			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis bacterial			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis septic			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 24 (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	Highly Active Anti-Retroviral Therapy: Daclatasvir, 30 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg	Highly Active Anti-Retroviral Therapy: Daclatasvir, 90 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 132 (92.42%)	38 / 39 (97.44%)	100 / 106 (94.34%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 132 (2.27%)	2 / 39 (5.13%)	4 / 106 (3.77%)
occurrences (all)	3	2	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	45 / 132 (34.09%)	16 / 39 (41.03%)	47 / 106 (44.34%)
occurrences (all)	47	17	50
Asthenia			
subjects affected / exposed	40 / 132 (30.30%)	7 / 39 (17.95%)	19 / 106 (17.92%)
occurrences (all)	41	7	20
Pyrexia			
subjects affected / exposed	28 / 132 (21.21%)	6 / 39 (15.38%)	19 / 106 (17.92%)
occurrences (all)	41	7	25
Influenza like illness			
subjects affected / exposed	28 / 132 (21.21%)	14 / 39 (35.90%)	6 / 106 (5.66%)
occurrences (all)	33	14	7
Chills			
subjects affected / exposed	5 / 132 (3.79%)	4 / 39 (10.26%)	6 / 106 (5.66%)
occurrences (all)	5	4	7
Pain			
subjects affected / exposed	6 / 132 (4.55%)	3 / 39 (7.69%)	4 / 106 (3.77%)
occurrences (all)	6	3	4
Chest pain			
subjects affected / exposed	0 / 132 (0.00%)	2 / 39 (5.13%)	2 / 106 (1.89%)
occurrences (all)	0	2	2
Hyperthermia			
subjects affected / exposed	0 / 132 (0.00%)	0 / 39 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0	0 / 39 (0.00%) 0	0 / 106 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	11 / 132 (8.33%) 11	4 / 39 (10.26%) 4	8 / 106 (7.55%) 9
Dyspnoea subjects affected / exposed occurrences (all)	11 / 132 (8.33%) 11	2 / 39 (5.13%) 2	6 / 106 (5.66%) 6
Dyspnoea exertional subjects affected / exposed occurrences (all)	7 / 132 (5.30%) 7	2 / 39 (5.13%) 2	7 / 106 (6.60%) 7
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 132 (0.76%) 1	1 / 39 (2.56%) 1	2 / 106 (1.89%) 2
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	36 / 132 (27.27%) 39	10 / 39 (25.64%) 10	17 / 106 (16.04%) 17
Depression subjects affected / exposed occurrences (all)	20 / 132 (15.15%) 23	5 / 39 (12.82%) 5	17 / 106 (16.04%) 17
Irritability subjects affected / exposed occurrences (all)	16 / 132 (12.12%) 16	3 / 39 (7.69%) 3	14 / 106 (13.21%) 15
Mood swings subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 4	5 / 39 (12.82%) 5	2 / 106 (1.89%) 2
Anxiety subjects affected / exposed occurrences (all)	5 / 132 (3.79%) 5	3 / 39 (7.69%) 3	2 / 106 (1.89%) 2
Sleep disorder subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 4	1 / 39 (2.56%) 1	2 / 106 (1.89%) 2
Depressed mood			

subjects affected / exposed occurrences (all)	3 / 132 (2.27%) 3	2 / 39 (5.13%) 2	1 / 106 (0.94%) 1
Abnormal dreams subjects affected / exposed occurrences (all)	1 / 132 (0.76%) 1	2 / 39 (5.13%) 2	0 / 106 (0.00%) 0
Investigations Weight decreased subjects affected / exposed occurrences (all)	14 / 132 (10.61%) 14	3 / 39 (7.69%) 3	8 / 106 (7.55%) 8
Nervous system disorders Headache subjects affected / exposed occurrences (all)	29 / 132 (21.97%) 32	13 / 39 (33.33%) 15	28 / 106 (26.42%) 36
Dizziness subjects affected / exposed occurrences (all)	11 / 132 (8.33%) 11	3 / 39 (7.69%) 3	7 / 106 (6.60%) 7
Dysgeusia subjects affected / exposed occurrences (all)	9 / 132 (6.82%) 9	4 / 39 (10.26%) 4	7 / 106 (6.60%) 7
Sciatica subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0	2 / 39 (5.13%) 2	0 / 106 (0.00%) 0
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	42 / 132 (31.82%) 74	7 / 39 (17.95%) 7	35 / 106 (33.02%) 59
Anaemia subjects affected / exposed occurrences (all)	32 / 132 (24.24%) 35	10 / 39 (25.64%) 12	34 / 106 (32.08%) 39
Thrombocytopenia subjects affected / exposed occurrences (all)	9 / 132 (6.82%) 14	1 / 39 (2.56%) 1	8 / 106 (7.55%) 8
Leukopenia subjects affected / exposed occurrences (all)	8 / 132 (6.06%) 13	3 / 39 (7.69%) 3	3 / 106 (2.83%) 3
Lymphopenia			

subjects affected / exposed occurrences (all)	2 / 132 (1.52%) 2	2 / 39 (5.13%) 2	1 / 106 (0.94%) 2
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 132 (2.27%)	2 / 39 (5.13%)	2 / 106 (1.89%)
occurrences (all)	3	2	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	24 / 132 (18.18%)	10 / 39 (25.64%)	21 / 106 (19.81%)
occurrences (all)	27	11	22
Diarrhoea			
subjects affected / exposed	19 / 132 (14.39%)	6 / 39 (15.38%)	18 / 106 (16.98%)
occurrences (all)	22	7	19
Vomiting			
subjects affected / exposed	12 / 132 (9.09%)	5 / 39 (12.82%)	9 / 106 (8.49%)
occurrences (all)	13	6	9
Dry mouth			
subjects affected / exposed	11 / 132 (8.33%)	1 / 39 (2.56%)	9 / 106 (8.49%)
occurrences (all)	11	1	9
Constipation			
subjects affected / exposed	6 / 132 (4.55%)	4 / 39 (10.26%)	4 / 106 (3.77%)
occurrences (all)	6	4	4
Abdominal pain upper			
subjects affected / exposed	8 / 132 (6.06%)	0 / 39 (0.00%)	4 / 106 (3.77%)
occurrences (all)	8	0	4
Dyspepsia			
subjects affected / exposed	4 / 132 (3.03%)	2 / 39 (5.13%)	3 / 106 (2.83%)
occurrences (all)	4	2	3
Abdominal pain			
subjects affected / exposed	2 / 132 (1.52%)	3 / 39 (7.69%)	3 / 106 (2.83%)
occurrences (all)	2	3	3
Cheilitis			
subjects affected / exposed	2 / 132 (1.52%)	3 / 39 (7.69%)	2 / 106 (1.89%)
occurrences (all)	2	3	2
Hepatobiliary disorders			

Hyperbilirubinaemia subjects affected / exposed occurrences (all)	8 / 132 (6.06%) 10	0 / 39 (0.00%) 0	0 / 106 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	20 / 132 (15.15%) 20	3 / 39 (7.69%) 3	14 / 106 (13.21%) 14
Pruritus subjects affected / exposed occurrences (all)	18 / 132 (13.64%) 21	3 / 39 (7.69%) 3	14 / 106 (13.21%) 15
Rash subjects affected / exposed occurrences (all)	20 / 132 (15.15%) 21	4 / 39 (10.26%) 4	10 / 106 (9.43%) 10
Alopecia subjects affected / exposed occurrences (all)	19 / 132 (14.39%) 19	4 / 39 (10.26%) 4	8 / 106 (7.55%) 8
Skin lesion subjects affected / exposed occurrences (all)	1 / 132 (0.76%) 1	2 / 39 (5.13%) 3	2 / 106 (1.89%) 2
Musculoskeletal and connective tissue disorders			
Myalgia subjects affected / exposed occurrences (all)	26 / 132 (19.70%) 28	5 / 39 (12.82%) 6	14 / 106 (13.21%) 16
Arthralgia subjects affected / exposed occurrences (all)	18 / 132 (13.64%) 19	2 / 39 (5.13%) 2	6 / 106 (5.66%) 6
Back pain subjects affected / exposed occurrences (all)	6 / 132 (4.55%) 6	2 / 39 (5.13%) 2	3 / 106 (2.83%) 3
Bone pain subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0	0 / 39 (0.00%) 0	2 / 106 (1.89%) 2
Infections and infestations			
Oral candidiasis subjects affected / exposed occurrences (all)	8 / 132 (6.06%) 9	0 / 39 (0.00%) 0	3 / 106 (2.83%) 3

Bronchitis subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 4	4 / 39 (10.26%) 4	1 / 106 (0.94%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 132 (3.03%) 4	2 / 39 (5.13%) 2	2 / 106 (1.89%) 3
Pharyngitis subjects affected / exposed occurrences (all)	3 / 132 (2.27%) 3	2 / 39 (5.13%) 2	1 / 106 (0.94%) 1
Respiratory tract infection subjects affected / exposed occurrences (all)	2 / 132 (1.52%) 2	1 / 39 (2.56%) 1	0 / 106 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0	2 / 39 (5.13%) 2	0 / 106 (0.00%) 0
Genital herpes subjects affected / exposed occurrences (all)	1 / 132 (0.76%) 1	2 / 39 (5.13%) 3	0 / 106 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	32 / 132 (24.24%) 32	9 / 39 (23.08%) 9	27 / 106 (25.47%) 28

Non-serious adverse events	Non- Highly Active Anti-Retroviral Therapy: Daclatasvir, 60 mg		
Total subjects affected by non-serious adverse events subjects affected / exposed	23 / 24 (95.83%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Asthenia	6 / 24 (25.00%) 6		

subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	12		
Pyrexia			
subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	18		
Influenza like illness			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hyperthermia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Mood swings			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Depressed mood			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Abnormal dreams			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Investigations			
Weight decreased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	8		
Dizziness			

subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all)	4 / 24 (16.67%) 7 4 / 24 (16.67%) 5 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0		
Eye disorders Dry eye subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting	4 / 24 (16.67%) 4 2 / 24 (8.33%) 2		

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Cheilitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	6 / 24 (25.00%)		
occurrences (all)	6		
Rash			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	6		
Alopecia			

subjects affected / exposed occurrences (all) Skin lesion subjects affected / exposed occurrences (all)	5 / 24 (20.83%) 5 0 / 24 (0.00%) 0		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all)	5 / 24 (20.83%) 5 3 / 24 (12.50%) 3 0 / 24 (0.00%) 0 2 / 24 (8.33%) 4		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Respiratory tract infection subjects affected / exposed occurrences (all) Cellulitis	0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 2 / 24 (8.33%) 2		

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Genital herpes			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2012	1. Clarified the exclusion criteria for those subjects who required changes in their HIV treatment to comply with the protocol requirements 2. Addition of rilpivirine to allowable HAART regimen
25 November 2013	The primary endpoint was updated for using the next value carried backwards imputation technique to provide a robust and clinically meaningful analysis of SVR12 for subjects within this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported