Clinical trial results:
A Phase 2B, randomized study to evaluate the safety and efficacy of Pegylated Interferon Lambda (BMS-914143) administered with Ribavirin plus a single direct antiviral agent (BMS-790052 or BMS-650032) versus Pegasys administered with Ribavirin (Part A) and of Pegylated Interferon Lambda (BMS-914143) administered with or without Ribavirin plus 2 direct antiviral agents (BMS 790052 and BMS-650032) (Part B) in chronic hepatitis C genotype-1 treatment naive subjects

Summary

EudraCT number	2010-022568-11
Trial protocol	DE IT ES
Global end of trial date	01 September 2014

Results information

Result version number	v1 (current)
This version publication date	28 April 2016
First version publication date	28 April 2016

Trial information

Trial identification

Sponsor protocol code	AI452-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01309932
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	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	01 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the trial was to evaluate the safety and tolerability (as measured by the frequency of serious adverse events, dose reductions and discontinuations due to adverse events) of Peginterferon Lambda-1a administered with Ribavirin + a single direct antiviral agent (BMS-790052 or BMS-650032) and describe the antiviral activity as determined by the proportion of hepatitis C virus genotype 1 subjects with SVR24.

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	31 March 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 28
Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	New Zealand: 13
Country: Number of subjects enrolled	Puerto Rico: 12
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United States: 61
Worldwide total number of subjects	233
EEA total number of subjects	102

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	222
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Part A: The study was conducted at 40 sites in 9 countries. Sub-study C: The study was conducted at 6 sites in 3 countries.

Pre-assignment

Screening details:

A total of 233 subjects were enrolled. Of which 140 subjects were treated (119 subjects in Global study and 21 subjects in Japan sub-study) in Part A. A total of 24 subjects were treated in Sub-study C.

Period 1

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

Blinding implementation details:

BMS personnel and investigators were blinded, with the exception of a designated member of the staff at each investigational site (who was unblinded only to dispense study medications as well as required dose reductions.

Arms

Are arms mutually exclusive?	Yes
Arm title	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching- placebo, tablets, oral, once daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

Subjects received Asunaprevir 200-mg tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 24 weeks.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

Arm title	Alfa-2a + Ribavirin (Part A-Global Study)

Arm description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Arm type	Active comparator

Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys ®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Alfa-2a 180-µg/mL as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

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:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

Arm title	Lambda + Ribavirin + Asunaprevir (Japan Substudy)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching-placebo, tablets, oral, once daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

Subjects received Asunaprevir 200-mg tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Japan Substudy)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 24 weeks.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

Arm title	Alfa-2a + Ribavirin (Japan Substudy)

Arm description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys ®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Alfa-2a 180-µg/mL as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

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:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Substudy C)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 6 once daily for up to 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Ribasphere
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 12 weeks.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 12 weeks.

Number of subjects in period 1[1]	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)
Started	38	41	40
Completed	29	35	18
Not completed	9	6	22
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	6	2	5
Subject's request to discontinue study treatment	1	1	4
Poor/Non-compliance	1	1	-
Subject no longer meets study criteria	-	-	1
Lack of efficacy	1	2	11

Number of subjects in period 1[1]	Lambda + Ribavirin + Asunaprevir (Japan Substudy)	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)
Started	6	8	7
Completed	3	8	5
Not completed	3	0	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	3	-	1
Subject's request to discontinue study treatment	-	-	-
Poor/Non-compliance	-	-	-
Subject no longer meets study criteria	-	-	-
Lack of efficacy	-	-	1

Number of subjects in period 1[1]	Lambda + Ribavirin + Daclatasvir (Substudy C)
Started	24
Completed	24
Not completed	0
Consent withdrawn by subject	-

Adverse event, non-fatal	-
Subject's request to discontinue study treatment	-
Poor/Non-compliance	-
Subject no longer meets study criteria	-
Lack of efficacy	-

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 out of 233 subjects only 164 subjects received treatment during the study.

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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching -placebo, tablets, oral, once daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

Subjects received Asunaprevir 200-mg tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 24 weeks.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

Arm title	Alfa-2a + Ribavirin (Part A-Global Study)

Arm description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Arm type	Active comparator

Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys ®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Alfa-2a 180-µg/mL as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

Arm title	Lambda + Ribavirin + Asunaprevir (Japan Substudy)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching-placebo, tablets, oral, once daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

Subjects received Asunaprevir 200-mg tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Japan Substudy)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 24 weeks.

Arm title	Alfa-2a + Ribavirin (Japan Substudy)

Arm description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys ®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Alfa-2a 180-µg/mL as subcutaneous injection once weekly for up to 24 or 48 weeks depending upon the response.

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

Dosage and administration details:

Subjects received asunaprevir matching-placebo tablets, orally, twice daily for up to 24 weeks.

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

Dosage and administration details:

2 daclatasvir matching-placebo tablets were administered, orally, once daily, for up to 24 weeks.

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:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 48 weeks.

Arm title	Lambda + Ribavirin + Daclatasvir (Substudy C)

Arm description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 6 once daily for up to 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated Interferon Lambda
Investigational medicinal product code	BMS-914143
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received Pegylated Interferon Lambda 180-µg/ml as subcutaneous injection once weekly for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Ribasphere
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Subjects received Ribavirin 200-mg tablets, orally, twice daily to make the final dose of 1000 mg or 1200 mg per day (depending upon the body weight) for up to 12 weeks.

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:

2 daclatasvir 30-mg tablets were administered orally, once daily for up to 12 weeks.

Number of subjects in period 2	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)
Started	29	35	18
Completed	36	39	34
Not completed	2	2	6
Consent withdrawn by subject	1	-	5
Subject's request to discontinue study treatment	-	-	-
Poor/Non-compliance	-	1	-
Lost to follow-up	-	-	-
Administrative reason by sponsor	1	-	-
Lack of efficacy	-	1	1
Joined	9	6	22
Subjects rejoined in follow-up period	9	6	22

Number of subjects in period 2	Lambda + Ribavirin + Asunaprevir (Japan Substudy)	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)
Started	3	8	5
Completed	6	8	6
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Subject's request to discontinue study treatment	-	-	1
Poor/Non-compliance	-	-	-
Lost to follow-up	-	-	-
Administrative reason by sponsor	-	-	-
Lack of efficacy	-	-	-
Joined	3	0	2
Subjects rejoined in follow-up period	3	-	2

Number of subjects in period 2	Lambda + Ribavirin + Daclatasvir (Substudy C)
Started	24
Completed	23
Not completed	1
Consent withdrawn by subject	-
Subject's request to discontinue study treatment	-
Poor/Non-compliance	-
Lost to follow-up	1
Administrative reason by sponsor	-
Lack of efficacy	-
Joined	0
Subjects rejoined in follow-up period	-

Baseline characteristics

Reporting groups	
Reporting group title	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching- placebo, tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.	
Reporting group title	Alfa-2a + Ribavirin (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching-placebo, tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Japan Substudy)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.	
Reporting group title	Alfa-2a + Ribavirin (Japan Substudy)
Reporting group description:	
Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Substudy C)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 6 once daily for up to 12 weeks.	

Reporting group values	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)
Number of subjects	38	41	40
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean	47.9	45.6	46.7

standard deviation	± 10.7	± 9.96	± 10.71

Gender categorical Units: Subjects			
Female	12	21	14
Male	26	20	26

Reporting group values	Lambda + Ribavirin + Asunaprevir (Japan Substudy)	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)
Number of subjects	6	8	7
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	52.7	58.5	56.6
standard deviation	± 12.23	± 7.5	± 5.26
Gender categorical Units: Subjects			
Female	4	6	4
Male	2	2	3

Reporting group values	Lambda + Ribavirin + Daclatasvir (Substudy C)	Total	
Number of subjects	24	164	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	54.5		
standard deviation	± 9.979	-	
Gender categorical Units: Subjects			
Female	13	74	
Male	11	90	

End points

End points reporting groups

Reporting group title	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching- placebo, tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.	
Reporting group title	Alfa-2a + Ribavirin (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching-placebo, tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Japan Substudy)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.	
Reporting group title	Alfa-2a + Ribavirin (Japan Substudy)
Reporting group description:	
Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Substudy C)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 6 once daily for up to 12 weeks.	
Reporting group title	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching -placebo, tablets, oral, once daily for up to 24 weeks.	
Reporting group title	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)
Reporting group description:	
Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.	
Reporting group title	Alfa-2a + Ribavirin (Part A-Global Study)

Reporting group description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Reporting group title	Lambda + Ribavirin + Asunaprevir (Japan Substudy)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching-placebo, tablets, oral, once daily for up to 24 weeks.

Reporting group title	Lambda + Ribavirin + Daclatasvir (Japan Substudy)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching-placebo, tablets, oral, twice daily for up to 24 weeks.

Reporting group title	Alfa-2a + Ribavirin (Japan Substudy)

Reporting group description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching-placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching-placebo: tablets, oral, once daily for up to 24 weeks.

Reporting group title	Lambda + Ribavirin + Daclatasvir (Substudy C)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 6 once daily for up to 12 weeks.

Primary: Number of Subjects With Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation of Study Drug, and Grade 3 or 4 AEs

End point title	Number of Subjects With Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation of Study Drug, and Grade 3 or 4 AEs[1][2]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling. Analysis population included all the randomised subjects who received at least 1 dose of the study drug.

End point type	Primary

End point timeframe:

Baseline up to end of treatment (Week 16, 24 or 48)

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 were 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Subjects				
SAEs	3	2	0	1
AEs leading to discontinuation of study drug	6	2	5	3
Grade 3 or 4 AEs	11	7	8	5

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Subjects				
SAEs	0	0		
AEs leading to discontinuation of study drug	0	1		
Grade 3 or 4 AEs	1	5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Hepatitis C Virus (HCV) Genotype 1 Subjects With 24-Week Sustained Virologic Response (SVR24)

End point title	Percentage of Hepatitis C Virus (HCV) Genotype 1 Subjects With 24-Week Sustained Virologic Response (SVR24)[3][4]

End point description:

HCV RNA was measured by the Roche COBAS TaqMan HCV Test v2.0 from the central laboratory. The lower and upper limits of quantitation (LLOQ and ULOQ) of the assay were 25 IU/mL and 3.91 x 10^8 IU/mL. SVR24 was defined as undetectable HCV RNA at end of treatment (maximum of 48 weeks) and undetectable HCV RNA at follow-up Week 24. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria, that is, undetectable HCV RNA at end of treatment and undetectable HCV RNA at follow-up Week 24. The denominator was based on all treated subjects.

End point type	Primary

End point timeframe:

Baseline up to follow-up Week 24

Notes:

[3] - 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 were planned for this outcome measure.

[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 evaluate for the specified arm only.

End point values	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (confidence interval 80%)	68.4 (56.9 to 78.4)	63.4 (52.2 to 73.6)	35 (24.9 to 46.3)	83.3 (49 to 98.3)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (confidence interval 80%)	100 (75 to 100)	28.6 (7.9 to 59.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Substudy C: Percentage of Subjects With 12-Week Sustained Virologic Response (SVR12)

End point title	Substudy C: Percentage of Subjects With 12-Week Sustained Virologic Response (SVR12)[5][6]

End point description:

SVR12 was defined as undetectable Hepatitis C Virus (HCV) RNA at end of treatment and undetectable HCV RNA at follow-up Week 12. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria, that is, undetectable HCV RNA at end of treatment and undetectable HCV RNA at follow-up Week 12. The denominator was based on all treated subjects.

End point type	Primary

End point timeframe:

Baseline to follow-up Week 12

Notes:

[5] - 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 were planned for this outcome measure.

[6] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Subjects				
number (confidence interval 80%)	79.2 (64.8 to 89.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With Protocol Defined Response (PDR)

End point title	Part A: Percentage of Subjects With Protocol Defined Response (PDR)[7]

End point description:

PDR was defined as Hepatitis C Virus (HCV) RNA < LLOQ at Week 4 and undetectable HCV RNA at Week 12. The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Week 4 and Week 12

Notes:

[7] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (confidence interval 80%)	84.2 (73.9 to 91.5)	90.2 (81.4 to 95.7)	12.5 (6.2 to 22)	83.3 (49 to 98.3)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (confidence interval 80%)	87.5 (59.4 to 98.7)	14.3 (1.5 to 45.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Serum Hepatitis C Virus (HCV) RNA Levels Over Time

End point title	Part A: Serum Hepatitis C Virus (HCV) RNA Levels Over Time[8]

End point description:

HCV RNA values outside ULOQ (LLOQ) were assigned a value of 1 more (or 1 less) than the limit. Then HCV RNA was transformed on the log10 scale. The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Here, 'n' signifies the number of subjects with observed HCV RNA values at the specified time point for each arm, respectively. Here, 99999 signifies data not applicable.

End point type	Secondary

End point timeframe:

Days 1, 3, Weeks 1, 2, 4, 6, 8, 12, 16, 20, and end of treatment (Week 16, 24 or 48 depending on treatment assignment)

Notes:

[8] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Day 1 (n=38, 41, 40, 6, 8, 7)	6.34 (± 0.682)	6.33 (± 0.607)	6.31 (± 0.678)	6.54 (± 0.443)
Day 3 (n=35, 30, 31, 6, 8, 7)	2.56 (± 0.616)	2.61 (± 0.618)	5.5 (± 1.045)	2.33 (± 0.346)
Week 1 (n=36, 40, 37, 6, 8, 7)	1.95 (± 0.726)	1.9 (± 0.664)	5.41 (± 1.127)	1.52 (± 0.259)
Week 2 (n=37, 40, 40, 6, 8, 7)	1.48 (± 0.406)	1.48 (± 0.223)	4.87 (± 1.486)	1.38 (± 0)
Week 4 (n=37, 41, 38, 6, 7, 7)	1.47 (± 0.526)	1.38 (± 0)	3.99 (± 1.822)	1.38 (± 0)
Week 6 (n=36, 39, 39, 5, 8, 7)	1.47 (± 0.514)	1.4 (± 0.129)	3.55 (± 1.893)	1.38 (± 0)
Week 8 (n=35, 39, 36, 5, 8, 7)	1.48 (± 0.575)	1.38 (± 0)	3.08 (± 1.838)	1.38 (± 0)
Week 12 (n=35, 39, 37, 5, 8, 6)	1.46 (± 0.474)	1.39 (± 0.048)	2.76 (± 1.761)	1.38 (± 0)
Week 16 (n=26, 32, 28, 3, 8, 6)	1.38 (± 0)	1.54 (± 0.758)	2.35 (± 1.622)	1.38 (± 0)
Week 20 (n=28, 31, 26, 3, 8, 6)	1.4 (± 0.108)	1.59 (± 0.854)	1.57 (± 0.637)	1.38 (± 0)
Week 24 (n=31, 37, 24, 3, 8, 6)	1.54 (± 0.704)	1.68 (± 1.085)	1.7 (± 1.128)	1.38 (± 0)
Week 48 (n=1, 0, 17, 0, 0, 5)	1 (± 99999)	99999 (± 99999)	1.56 (± 0.754)	99999 (± 99999)

End point values	Lambda + Ribavirin +	Alfa-2a + Ribavirin		

	Daclatasvir (Japan Substudy)	(Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Day 1 (n=38, 41, 40, 6, 8, 7)	6.24 (± 0.981)	6.54 (± 0.398)		
Day 3 (n=35, 30, 31, 6, 8, 7)	2.17 (± 0.572)	5.64 (± 0.917)		
Week 1 (n=36, 40, 37, 6, 8, 7)	1.47 (± 0.176)	5.23 (± 1.198)		
Week 2 (n=37, 40, 40, 6, 8, 7)	1.38 (± 0)	4.52 (± 1.704)		
Week 4 (n=37, 41, 38, 6, 7, 7)	1.38 (± 0)	3.36 (± 1.723)		
Week 6 (n=36, 39, 39, 5, 8, 7)	1.38 (± 0)	2.65 (± 1.416)		
Week 8 (n=35, 39, 36, 5, 8, 7)	1.38 (± 0)	2.2 (± 1.12)		
Week 12 (n=35, 39, 37, 5, 8, 6)	1.38 (± 0)	1.8 (± 0.786)		
Week 16 (n=26, 32, 28, 3, 8, 6)	1.38 (± 0)	1.67 (± 0.72)		
Week 20 (n=28, 31, 26, 3, 8, 6)	1.38 (± 0)	1.7 (± 0.777)		
Week 24 (n=31, 37, 24, 3, 8, 6)	1.38 (± 0)	1.75 (± 0.907)		
Week 48 (n=1, 0, 17, 0, 0, 5)	99999 (± 99999)	1.38 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With Undetectable Hepatitis C Virus (HCV) RNA Over Time

End point title	Part A: Percentage of Subjects With Undetectable Hepatitis C Virus (HCV) RNA Over Time[9]

End point description:

The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to--Treat algorithm. The numerator was based on subjects meeting the response criteria, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Days 1, 3, Weeks 1, 2, 4, 6, 8, 12, 16, 20, and end of treatment (24 or 48 depending on treatment assignment)

Notes:

[9] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (confidence interval 80%)				
Day 1	0 (0 to 5.9)	0 (0 to 5.5)	0 (0 to 5.6)	0 (0 to 31.9)

Week 1	0 (0 to 5.9)	0 (0 to 5.5)	2.5 (0.3 to 9.4)	0 (0 to 31.9)
Week 2	31.6 (21.6 to 43.1)	24.4 (15.7 to 35.1)	2.5 (0.3 to 9.4)	50 (20.1 to 79.9)
Week 4	81.6 (71 to 89.4)	70.7 (59.8 to 80.1)	5 (1.3 to 12.8)	83.3 (49 to 98.3)
Week 6	86.8 (77 to 93.5)	90.2 (81.4 to 95.7)	12.5 (6.2 to 22)	83.3 (49 to 98.3)
Week 8	86.8 (77 to 93.5)	90.2 (81.4 to 95.7)	22.5 (14.1 to 33.2)	83.3 (49 to 98.3)
Week 12	84.2 (73.9 to 91.5)	90.2 (81.4 to 95.7)	37.5 (27.1 to 48.9)	83.3 (49 to 98.3)
Week 16	63.2 (51.5 to 73.7)	70.7 (59.8 to 80.1)	32.5 (22.7 to 43.8)	50 (20.1 to 79.9)
Week 20	65.8 (54.2 to 76.1)	65.9 (54.7 to 75.8)	45 (34.1 to 56.3)	50 (20.1 to 79.9)
Week 24	68.4 (56.9 to 78.4)	80.5 (70.2 to 88.3)	50 (38.8 to 61.2)	50 (20.1 to 79.9)
Week 48	0 (0 to 5.9)	0 (0 to 5.5)	40 (29.4 to 51.4)	0 (0 to 31.9)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (confidence interval 80%)				
Day 1	0 (0 to 25)	0 (0 to 28)		
Week 1	12.5 (1.3 to 40.6)	0 (0 to 28)		
Week 2	62.5 (34.5 to 85.3)	0 (0 to 28)		
Week 4	87.5 (59.4 to 98.7)	14.3 (1.5 to 45.3)		
Week 6	100 (75 to 100)	14.3 (1.5 to 45.3)		
Week 8	87.5 (59.4 to 98.7)	42.9 (17 to 72.1)		
Week 12	100 (75 to 100)	42.9 (17 to 72.1)		
Week 16	100 (75 to 100)	42.9 (17 to 72.1)		
Week 20	100 (75 to 100)	42.9 (17 to 72.1)		
Week 24	100 (75 to 100)	71.4 (40.4 to 92.1)		
Week 48	0 (0 to 25)	71.4 (40.4 to 92.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With 12 -Week Sustained Virologic Response (SVR12)

End point title	Part A: Percentage of Subjects With 12 -Week Sustained Virologic Response (SVR12)[10]

End point description:

SVR12 was defined as undetectable Hepatitis C Virus (HCV) RNA at end of treatment and undetectable HCV RNA at follow--up Week 12. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria, that is, undetectable HCV RNA at end of treatment and undetectable HCV RNA at follow--up Week 12. The denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline to follow-up Week 12

Notes:

[10] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (confidence interval 80%)	65.8 (54.2 to 76.1)	68.3 (57.2 to 77.9)	37.5 (27.1 to 48.9)	83.3 (49 to 98.3)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (confidence interval 80%)	100 (75 to 100)	28.6 (7.9 to 59.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Time to Viral Clearance

End point title	Part A: Time to Viral Clearance[11]

End point description:

Time to viral clearance was measured by time to confirmed undetectable HCV RNA from the first dose of study therapy to the first of 2 consecutive undetectable HCV RNA measurements using all available data on treatment. For subjects who never achieved confirmed undetectable HCV RNA while on treatment, time was set to the maximum planned duration of study (72 weeks). The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[11] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Number of subjects with events				
Weeks 0-4	10	8	1	4
Weeks 4-8	33	37	5	6
Weeks 8-12	34	37	9	6
Weeks 12-16	34	37	14	6
Weeks 16-20	34	37	17	6
Weeks 20-24	34	37	20	6
Weeks 24-28	34	37	21	6
Weeks 28-32	34	37	21	6
Weeks 32-36	34	37	21	6
Weeks 36-72	34	37	22	6

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Number of subjects with events				
Weeks 0-4	5	0		
Weeks 4-8	8	1		
Weeks 8-12	8	2		
Weeks 12-16	8	3		
Weeks 16-20	8	4		
Weeks 20-24	8	4		
Weeks 24-28	8	5		
Weeks 28-32	8	5		
Weeks 32-36	8	5		
Weeks 36-72	8	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With Viral Breakthrough

End point title	Part A: Percentage of Subjects With Viral Breakthrough[12]

End point description:

Viral breakthrough was defined as confirmed >1 log10 increase in HCV RNA over nadir or confirmed HCV RNA >= LLOQ after confirmed undetectable HCV RNA while on treatment. The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects with viral breakthrough, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[12] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (not applicable)	5.3	4.9	7.5	0

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects With Relapse

End point title	Part A: Percentage of Subjects With Relapse[13]

End point description:

Relapse was defined as undetectable HCV RNA at EOT followed by HCV RNA >=LLOQ in any follow-up visit. The analysis was performed in all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Relapse rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects with relapse, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline up to Follow-up Week 24

Notes:

[13] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	41	40	6
Units: Percentage of subjects				
number (not applicable)	13.2	17.1	10	16.7

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: Percentage of subjects				
number (not applicable)	0	42.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Maximum Observed Plasma Concentration (Cmax)

End point title	Part A: Maximum Observed Plasma Concentration (Cmax)[14]

End point description:

Cmax was defined as the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve. The analysis was performed in subjects who received at least 1 dose of study drug with any plasma concentration data. The Cmax was derived by using non compartmental method. Here, "Number of subjects analysed" signifies number of subjects evaluated for this outcome measure. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms, and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline to 0-12 h for Asunaprevir, 0-24 h for Daclatasvir, and 0-168 h for pegIFNλ and pegIFNα-2a at Week 4

Notes:

[14] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	2.51 (± 103.46)	3.19 (± 26.15)	99999 (± 99999)	2.12 (± 37.35)
Daclatasvir (n=0, 4, 0, 0, 4, 0)	99999 (± 99999)	1414 (± 24.54)	99999 (± 99999)	99999 (± 99999)
Asunaprevir (n=6, 0, 0, 2, 0, 0)	337.46 (± 127.18)	99999 (± 99999)	99999 (± 99999)	660.06 (± 48.15)
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	99999 (± 99999)	15.21 (± 48.27)	99999 (± 99999)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	1.85 (± 33.83)	99999 (± 99999)		
Daclatasvir (n=0, 4, 0, 0, 4, 0)	1512 (± 16.02)	99999 (± 99999)		
Asunaprevir (n=6, 0, 0, 2, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	18.9 (± 3.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Observed Plasma Concentration (Tmax)

End point title	Time of Maximum Observed Plasma Concentration (Tmax)[15]

End point description:

Time to reach the maximum plasma concentration was directly determined from concentration time data. The analysis was performed in subjects who received at least 1 dose of study drug with any plasma concentration data. The Tmax was derived by using non compartmental method. Here, "Number of subjects analysed" signifies number of subjects evaluated for this outcome measure. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms, and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline to 0-12 h for Asunaprevir, 0-24 h for Daclatasvir, and 0-168 h for pegIFNλ and pegIFNα-2a at Week 4

Notes:

[15] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	2
Units: hour				
median (full range (min-max))				
Lambda (n=6, 4, 0, 2, 4, 0)	23.79 (12 to 71.6)	10.58 (8 to 48)	99999 (-99999 to 99999)	21.46 (20.2 to 22.8)
Daclatasvir (n=0, 4, 0, 0, 4, 0)	99999 (-99999 to 99999)	1 (1 to 2)	99999 (-99999 to 99999)	99999 (-99999 to 99999)
Asunaprevir (n=6, 0, 0, 2, 0, 0)	3.99 (1 to 8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	2.04 (2 to 2.1)
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	35.44 (11.9 to 72.6)	99999 (-99999 to 99999)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: hour				
median (full range (min-max))				
Lambda (n=6, 4, 0, 2, 4, 0)	22.98 (22 to 24)	99999 (-99999 to 99999)		
Daclatasvir (n=0, 4, 0, 0, 4, 0)	2.94 (1 to 4)	99999 (-99999 to 99999)		
Asunaprevir (n=6, 0, 0, 2, 0, 0)	99999 (-99999 to 99999)	99999 (-99999 to 99999)		
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (-99999 to 99999)	47.97 (45.7 to 94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Observed Plasma Concentration (Cmin)

End point title	Minimal Observed Plasma Concentration (Cmin)[16]

End point description:

Cmin was observed directly from 12-hour and 24-hour post-dose concentration depending upon the dosing schedule (once daily or twice daily). The analysis was performed in subjects who received at least 1 dose of study drug with any plasma concentration data. The Cmin was derived by using non compartmental method. Here, "Number of subjects analysed" signifies number of subjects evaluated for this outcome measure. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms, and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline to 0-12 h for Asunaprevir, 0-24 h for Daclatasvir, and 0-168 h for pegIFNλ and pegIFNα-2a at Week 4

Notes:

[16] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	0.42 (± 41.85)	0.72 (± 36.92)	99999 (± 99999)	0.72 (± 47.08)
Daclatasvir (n=0, 4, 0, 0, 4, 0)	99999 (± 99999)	283.13 (± 53.2)	99999 (± 99999)	99999 (± 99999)
Asunaprevir (n=6, 0, 0, 2, 0, 0)	98.4 (± 140.55)	99999 (± 99999)	99999 (± 99999)	52.96 (± 57.15)
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	99999 (± 99999)	4.17 (± 81.36)	99999 (± 99999)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	0.3 (± 63.77)	99999 (± 99999)		
Daclatasvir (n=0, 4, 0, 0, 4, 0)	352.94 (± 29.43)	99999 (± 99999)		

Asunaprevir (n=6, 0, 0, 2, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	13.66 (± 4.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval, From time 0 to 24 Hours Post-dose [AUC(TAU)]

End point title	Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval, From time 0 to 24 Hours Post-dose [AUC(TAU)][17]

End point description:

AUC (TAU)=Area under concentration time profile from time 0 to tau, where tau was the dosing interval of 12 or 24 hours depending upon the dosing schedule (once daily or twice daily). The analysis was performed in subjects who received at least 1 dose of study drug with any plasma concentration data. The AUC(TAU) was derived by using non compartmental method. Here, "Number of subjects analysed" signifies number of subjects evaluated for this outcome measure. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms, and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline to 0-12 h for Asunaprevir, 0-24 h for Daclatasvir, and 0-168 h for pegIFNλ and pegIFNα-2a at Week 4

Notes:

[17] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	2
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	214.04 (± 75.57)	291.97 (± 23.9)	99999 (± 99999)	243.49 (± 37.06)
Daclatasvir (n=0, 4, 0, 0, 4, 0)	99999 (± 99999)	20592.61 (± 57.98)	99999 (± 99999)	99999 (± 99999)
Asunaprevir (n=6, 0, 0, 2, 0, 0)	1739.97 (± 159.4)	99999 (± 99999)	99999 (± 99999)	2007.03 (± 15.72)
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	99999 (± 99999)	1923.13 (± 41.76)	99999 (± 99999)

End point values	Lambda + Ribavirin + Daclatasvir (Japan	Alfa-2a + Ribavirin (Japan Substudy)		

	Substudy)			
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	3		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=6, 4, 0, 2, 4, 0)	187.8 (± 22.48)	99999 (± 99999)		
Daclatasvir (n=0, 4, 0, 0, 4, 0)	21783.59 (± 18.65)	99999 (± 99999)		
Asunaprevir (n=6, 0, 0, 2, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Alfa-2a (n=0, 0, 4, 0, 0, 3)	99999 (± 99999)	2748.88 (± 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Trough Plasma Concentration (Ctrough)

End point title	Observed Trough Plasma Concentration (Ctrough)[18]

End point description:

Geometric mean of a subject's trough concentrations through Week 24, was summarised by treatment regimen. The analysis was performed in subjects who received at least 1 dose of study drug with any plasma concentration data. The Ctrough was derived by using non compartmental method. Here, "Number of subjects analysed" signifies number of subjects evaluated for this outcome measure. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms, and '99999' represents not estimable data for specified categories in respective arms.

End point type	Secondary

End point timeframe:

Baseline to 0-12 h for Asunaprevir, 0-24 h for Daclatasvir, and 0-168 h for pegIFNλ and pegIFNα-2a at Week 4

Notes:

[18] - 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	Lambda + Ribavirin + Asunaprevir (Part A-Global Study)	Lambda + Ribavirin + Daclatasvir (Part A-Global Study)	Alfa-2a + Ribavirin (Part A-Global Study)	Lambda + Ribavirin + Asunaprevir (Japan Substudy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	41	37	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=37, 41, 0, 6, 8, 0)	0.187 (± 69.2)	0.285 (± 96.52)	99999 (± 99999)	0.735 (± 31.79)
Daclatasvir (n=0, 41, 0, 0, 8, 0)	99999 (± 99999)	198.1 (± 112.1)	99999 (± 99999)	99999 (± 99999)
Asunaprevir (n=37, 0, 0, 6, 0, 0)	81.716 (± 118.51)	99999 (± 99999)	99999 (± 99999)	99.808 (± 148)
Alfa-2a (n=0, 0, 37, 0, 0, 7)	99999 (± 99999)	99999 (± 99999)	7.208 (± 49.84)	99999 (± 99999)

End point values	Lambda + Ribavirin + Daclatasvir (Japan Substudy)	Alfa-2a + Ribavirin (Japan Substudy)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Lambda (n=37, 41, 0, 6, 8, 0)	0.332 (± 37.92)	99999 (± 99999)		
Daclatasvir (n=0, 41, 0, 0, 8, 0)	272.316 (± 41.7)	99999 (± 99999)		
Asunaprevir (n=37, 0, 0, 6, 0, 0)	99999 (± 99999)	99999 (± 99999)		
Alfa-2a (n=0, 0, 37, 0, 0, 7)	99999 (± 99999)	9.911 (± 54.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Percentage of Hepatitis C Virus (HCV) Subjects With Sustained Virologic Response (SVR24)

End point title	Substudy C: Percentage of Hepatitis C Virus (HCV) Subjects With Sustained Virologic Response (SVR24)[19]

End point description:

HCV RNA was measured by the Roche COBAS TaqMan HCV Test v2.0 from the central laboratory. The lower and upper limits of quantitation (LLOQ and ULOQ) of the assay were 25 IU/mL and 3.91 x 108 IU/mL. SVR24 was defined as undetectable HCV RNA at end of treatment (maximum of 48 weeks) and undetectable HCV RNA at follow-up Week 24. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria, that is, undetectable HCV RNA at end of treatment and undetectable HCV RNA at follow-up Week 24. The denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline up to follow-up Week 24

Notes:

[19] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Subjects				
number (confidence interval 80%)	79.2 (64.8 to 89.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With Extended Rapid Virologic Response (eRVR)

End point title	Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With Extended Rapid Virologic Response (eRVR)[20]

End point description:

eRVR was defined as undetectable Hepatitis C virus RNA at Week 4 and Week 12 of treatment. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects meeting the response criteria, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Weeks 4 and 12

Notes:

[20] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of subjects				
number (confidence interval 80%)	79.2 (64.8 to 89.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With Treatment-Emergent Cytopenic Abnormalities on Treatment (Maximum of 12 Weeks)

End point title	Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With Treatment-Emergent Cytopenic Abnormalities on

	Treatment (Maximum of 12 Weeks)[21]

End point description:

Cytopenic abnormalities were defined as anemia as defined by haemoglobin <10 g/dL, and/or neutropenia as defined by absolute neutrophil count <750 mm^3, and/or thrombocytopenia as defined by platelets < 50,000 mm^3. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects with abnormalities, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

On-treatment up to Week 12

Notes:

[21] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of subjects				
number (confidence interval 80%)	4.2 (0.4 to 15.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With On-Treatment (Maximum of 12 Weeks) Interferon-Associated Symptoms

End point title	Substudy C: Percentage of Non-Cirrhotic Genotype-1b Subjects With On-Treatment (Maximum of 12 Weeks) Interferon-Associated Symptoms[22]

End point description:

Interferon-associated symptoms were evaluated as flu-like symptoms defined by pyrexia or chills or pain and musculoskeletal symptoms as defined by arthralgia or myalgia or back pain. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects with symptoms, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline up to Week 12

Notes:

[22] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of subjects				
number (confidence interval 80%)				
Flu-like symptoms	8.3 (2.2 to 20.7)			
Musculoskeletal symptoms	12.5 (4.7 to 25.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Number of Subjects With Adverse events (AEs), Deaths and Serious Adverse Events (SAEs)

End point title	Substudy C: Number of Subjects With Adverse events (AEs), Deaths and Serious Adverse Events (SAEs)[23]

End point description:

AE = any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE = a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalisation. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[23] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of Subjects				
AEs	20			
SAEs	0			
Deaths	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Number of Subjects With Drug Related Adverse Events (AEs), Dose Reductions And Discontinuations Due to AE

End point title	Substudy C: Number of Subjects With Drug Related Adverse Events (AEs), Dose Reductions And Discontinuations Due to AE[24]

End point description:

AE = any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. Treatment-related = having certain, probable, possible, or unknown relationship to study drug. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[24] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of Subjects				
Grade 2 to 4 Drug related AEs	6			
Dose reduction	1			
Discontinuation due to AEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Percentage of Non-Cirrhotic Hepatitis C Virus (HCV) Genotype-1b Subjects With Psychiatric Symptoms (Depression or Irritability or Insomnia) Through The End of Treatment (Maximum of 12 Weeks)

End point title	Substudy C: Percentage of Non-Cirrhotic Hepatitis C Virus (HCV) Genotype-1b Subjects With Psychiatric Symptoms (Depression or Irritability or Insomnia) Through The End of Treatment (Maximum of 12 Weeks)[25]

End point description:

Interferon-associated symptoms were evaluated for psychiatric, neurologic, constitutional symptoms defined as depression or irritability or insomnia, headache or dizziness and fatigue or asthenia, respectively. Analysis population included all treated subjects, ie, randomised subjects who received at least 1 dose of the study drug. Response rates were assessed using modified Intent-to-Treat algorithm. The numerator was based on subjects with symptoms, and the denominator was based on all treated subjects.

End point type	Secondary

End point timeframe:

Baseline up to Week 12

Notes:

[25] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of subjects				
number (confidence interval 80%)				
Psychiatric symptoms	16.7 (7.5 to 30.6)			
Neurologic symptoms	8.3 (2.2 to 20.7)			
Constitutional symptoms	41.7 (27.7 to 56.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Substudy C: Number of Subjects With Treatment Emergent Grade 3-4 Laboratory Abnormalities

End point title	Substudy C: Number of Subjects With Treatment Emergent Grade 3-4 Laboratory Abnormalities[26]

End point description:

Laboratory abnormalities were determined and graded using the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, version 1.0. International Normalized Ratio (INR): >2.0*Upper limit of normal (ULN); Hemoglobin: <9.0 g/dL; Alanine aminotransferase (ALT) : >5*ULN; Aspartate aminotransferase (AST): >5*ULN; Bilirubin (Total): >2.5*ULN. The analysis was performed on all subjects who received at least 1 dose of study therapy.

End point type	Secondary

End point timeframe:

Baseline up to end of treatment

Notes:

[26] - 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	Lambda + Ribavirin + Daclatasvir (Substudy C)			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of Subjects				
Hemoglobin (n=24)	1			
Alanine aminotransferase (ALT) (n=24)	1			
Aspartate aminotransferase (AST) (n=24)	1			

Bilirubin, Total (n=24)	1			
Bilirubin, Direct (n=11)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to end of treatment

Adverse event reporting additional description:

On-treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Lambda + Ribavirin+ Asunaprevir (Global study +Japan substudy)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response); Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks ; Asunaprevir: tablets, oral, 200 mg, twice daily for up to 24 weeks; Placebo: Daclatasvir matching placebo, tablets, oral, once daily for up to 24 weeks. The arm consists of subjects from global study and Japan substudy.

Reporting group title	Lambda + Ribavirin+ Daclatasvir (Global study +Japan substudy)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for up to 24 or 48 weeks (depending upon response);Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 24 weeks; Placebo: Asunaprevir matching placebo, tablets, oral, twice daily for up to 24 weeks. The arm consists of subjects from global study and Japan substudy.

Reporting group title	Alfa-2a +Ribavirin (Global study + Japan substudy)

Reporting group description:

Pegylated Interferon Alfa-2a: solution, subcutaneous, 180 µg/mL, once weekly for up to 48 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for up to 48 weeks; Asunaprevir matching placebo: tablets, oral, twice daily for up to 24 weeks; Daclatasvir matching -placebo: tablets, oral, once daily for up to 24 weeks. The arm consists of subjects from global study and japan substudy.

Reporting group title	Lambda +Ribavirin +Daclatasvir (Substudy C)

Reporting group description:

Pegylated Interferon Lambda: solution, subcutaneous, 180 µg/mL, once weekly for 12 weeks; Ribavirin: tablets, oral, 1000 or 1200 mg based on weight, twice daily for 12 weeks; Daclatasvir: tablets, oral, 60 mg, once daily for up to 12 weeks.

Serious adverse events	Lambda + Ribavirin+ Asunaprevir (Global study +Japan substudy)	Lambda + Ribavirin+ Daclatasvir (Global study +Japan substudy)	Alfa-2a +Ribavirin (Global study + Japan substudy)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 44 (9.09%)	2 / 49 (4.08%)	0 / 47 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	3 / 44 (6.82%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 49 (0.00%)	0 / 47 (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
Blood bilirubin increased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 49 (0.00%)	0 / 47 (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
Transaminases abnormal			
subjects affected / exposed	0 / 44 (0.00%)	1 / 49 (2.04%)	0 / 47 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer in situ			
subjects affected / exposed	0 / 44 (0.00%)	1 / 49 (2.04%)	0 / 47 (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
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 44 (2.27%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	1 / 44 (2.27%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Lambda +Ribavirin +Daclatasvir (Substudy C)		
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			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transaminases abnormal			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer in situ			
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			
Hyperbilirubinaemia			
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			
Enterocolitis infectious			
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	Lambda + Ribavirin+ Asunaprevir (Global study +Japan substudy)	Lambda + Ribavirin+ Daclatasvir (Global study +Japan substudy)	Alfa-2a +Ribavirin (Global study + Japan substudy)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 44 (88.64%)	47 / 49 (95.92%)	47 / 47 (100.00%)
General disorders and administration site conditions			
Dry mouth			
subjects affected / exposed	1 / 44 (2.27%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Fatigue			
subjects affected / exposed	12 / 44 (27.27%)	15 / 49 (30.61%)	19 / 47 (40.43%)
occurrences (all)	12	16	19
Asthenia			
subjects affected / exposed	7 / 44 (15.91%)	9 / 49 (18.37%)	7 / 47 (14.89%)
occurrences (all)	7	10	9
Injection site erythema			
subjects affected / exposed	0 / 44 (0.00%)	2 / 49 (4.08%)	6 / 47 (12.77%)
occurrences (all)	0	2	7
Chills			
subjects affected / exposed	0 / 44 (0.00%)	2 / 49 (4.08%)	7 / 47 (14.89%)
occurrences (all)	0	2	7
Malaise			
subjects affected / exposed	4 / 44 (9.09%)	1 / 49 (2.04%)	7 / 47 (14.89%)
occurrences (all)	4	1	7
Pyrexia			
subjects affected / exposed	2 / 44 (4.55%)	3 / 49 (6.12%)	10 / 47 (21.28%)
occurrences (all)	5	5	12
Feeling Hot			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3

Influenza like illness			
subjects affected / exposed	4 / 44 (9.09%)	0 / 49 (0.00%)	8 / 47 (17.02%)
occurrences (all)	4	0	8
Injection site rash			
subjects affected / exposed	0 / 44 (0.00%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	0	1	3
Injection site reaction			
subjects affected / exposed	1 / 44 (2.27%)	2 / 49 (4.08%)	3 / 47 (6.38%)
occurrences (all)	1	2	3
Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 44 (9.09%)	1 / 49 (2.04%)	8 / 47 (17.02%)
occurrences (all)	4	1	8
Cough			
subjects affected / exposed	3 / 44 (6.82%)	7 / 49 (14.29%)	10 / 47 (21.28%)
occurrences (all)	3	7	10
Oropharyngeal pain			
subjects affected / exposed	3 / 44 (6.82%)	0 / 49 (0.00%)	6 / 47 (12.77%)
occurrences (all)	3	0	7
Dyspnoea exertional			
subjects affected / exposed	0 / 44 (0.00%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	0	1	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 44 (20.45%)	13 / 49 (26.53%)	13 / 47 (27.66%)
occurrences (all)	9	14	13
Irritability			
subjects affected / exposed	7 / 44 (15.91%)	10 / 49 (20.41%)	10 / 47 (21.28%)
occurrences (all)	7	10	10
Sleep disorder			
subjects affected / exposed	1 / 44 (2.27%)	3 / 49 (6.12%)	5 / 47 (10.64%)
occurrences (all)	1	3	5
Depressed mood			

subjects affected / exposed	1 / 44 (2.27%)	3 / 49 (6.12%)	5 / 47 (10.64%)
occurrences (all)	1	3	5
Depression			
subjects affected / exposed	2 / 44 (4.55%)	5 / 49 (10.20%)	3 / 47 (6.38%)
occurrences (all)	2	5	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 44 (13.64%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences (all)	6	1	0
Blood bilirubin increased			
subjects affected / exposed	3 / 44 (6.82%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	4	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 44 (15.91%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences (all)	7	1	0
Weight decreased			
subjects affected / exposed	0 / 44 (0.00%)	3 / 49 (6.12%)	6 / 47 (12.77%)
occurrences (all)	0	3	6
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 44 (4.55%)	4 / 49 (8.16%)	6 / 47 (12.77%)
occurrences (all)	2	4	7
Dizziness			
subjects affected / exposed	6 / 44 (13.64%)	1 / 49 (2.04%)	6 / 47 (12.77%)
occurrences (all)	6	1	6
Headache			
subjects affected / exposed	7 / 44 (15.91%)	15 / 49 (30.61%)	24 / 47 (51.06%)
occurrences (all)	12	20	24
Hyperaesthesia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Lethargy			
subjects affected / exposed	1 / 44 (2.27%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Syncope			

subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 44 (4.55%)	5 / 49 (10.20%)	3 / 47 (6.38%)
occurrences (all)	2	5	3
Neutropenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	11 / 47 (23.40%)
occurrences (all)	0	0	12
Eye disorders			
Dry eye			
subjects affected / exposed	4 / 44 (9.09%)	2 / 49 (4.08%)	4 / 47 (8.51%)
occurrences (all)	4	3	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 44 (18.18%)	7 / 49 (14.29%)	12 / 47 (25.53%)
occurrences (all)	10	7	14
Abdominal pain upper			
subjects affected / exposed	5 / 44 (11.36%)	6 / 49 (12.24%)	2 / 47 (4.26%)
occurrences (all)	5	6	2
Nausea			
subjects affected / exposed	12 / 44 (27.27%)	14 / 49 (28.57%)	9 / 47 (19.15%)
occurrences (all)	14	15	9
Toothache			
subjects affected / exposed	0 / 44 (0.00%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	0	1	4
Vomiting			
subjects affected / exposed	5 / 44 (11.36%)	4 / 49 (8.16%)	5 / 47 (10.64%)
occurrences (all)	6	6	9
Abdominal Discomfort			
subjects affected / exposed	4 / 44 (9.09%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences (all)	4	1	0
Cheilitis			
subjects affected / exposed	0 / 44 (0.00%)	3 / 49 (6.12%)	3 / 47 (6.38%)
occurrences (all)	0	3	3
Abdominal pain			

subjects affected / exposed	1 / 44 (2.27%)	2 / 49 (4.08%)	4 / 47 (8.51%)
occurrences (all)	1	2	5
Constipation			
subjects affected / exposed	2 / 44 (4.55%)	2 / 49 (4.08%)	5 / 47 (10.64%)
occurrences (all)	2	2	5
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 44 (2.27%)	4 / 49 (8.16%)	2 / 47 (4.26%)
occurrences (all)	1	4	2
Dyspepsia			
subjects affected / exposed	4 / 44 (9.09%)	1 / 49 (2.04%)	4 / 47 (8.51%)
occurrences (all)	4	1	4
Mouth ulceration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	4 / 47 (8.51%)
occurrences (all)	0	0	9
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	6 / 44 (13.64%)	3 / 49 (6.12%)	0 / 47 (0.00%)
occurrences (all)	10	3	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	8 / 44 (18.18%)	17 / 49 (34.69%)	16 / 47 (34.04%)
occurrences (all)	10	19	19
Dry skin			
subjects affected / exposed	3 / 44 (6.82%)	8 / 49 (16.33%)	10 / 47 (21.28%)
occurrences (all)	3	8	10
Hyperhidrosis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	2	1	4
Rash			
subjects affected / exposed	4 / 44 (9.09%)	8 / 49 (16.33%)	9 / 47 (19.15%)
occurrences (all)	5	8	9
Alopecia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 49 (4.08%)	9 / 47 (19.15%)
occurrences (all)	2	2	9
Eczema			

subjects affected / exposed	1 / 44 (2.27%)	3 / 49 (6.12%)	3 / 47 (6.38%)
occurrences (all)	1	3	3
Erythema			
subjects affected / exposed	4 / 44 (9.09%)	1 / 49 (2.04%)	1 / 47 (2.13%)
occurrences (all)	4	2	1
Rash maculo-papular			
subjects affected / exposed	2 / 44 (4.55%)	1 / 49 (2.04%)	4 / 47 (8.51%)
occurrences (all)	2	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 44 (11.36%)	6 / 49 (12.24%)	14 / 47 (29.79%)
occurrences (all)	5	7	15
Myalgia			
subjects affected / exposed	4 / 44 (9.09%)	9 / 49 (18.37%)	12 / 47 (25.53%)
occurrences (all)	4	11	12
Back pain			
subjects affected / exposed	3 / 44 (6.82%)	4 / 49 (8.16%)	3 / 47 (6.38%)
occurrences (all)	3	4	4
Muscle spasms			
subjects affected / exposed	0 / 44 (0.00%)	3 / 49 (6.12%)	4 / 47 (8.51%)
occurrences (all)	0	4	4
Musculoskeletal pain			
subjects affected / exposed	1 / 44 (2.27%)	2 / 49 (4.08%)	3 / 47 (6.38%)
occurrences (all)	1	2	3
Pain in extremity			
subjects affected / exposed	1 / 44 (2.27%)	2 / 49 (4.08%)	3 / 47 (6.38%)
occurrences (all)	1	2	3
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	0 / 49 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	4
Nasopharyngitis			
subjects affected / exposed	4 / 44 (9.09%)	4 / 49 (8.16%)	2 / 47 (4.26%)
occurrences (all)	4	7	4
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	6 / 44 (13.64%)	7 / 49 (14.29%)	11 / 47 (23.40%)
occurrences (all)	6	7	11

Non-serious adverse events	Lambda +Ribavirin +Daclatasvir (Substudy C)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 24 (75.00%)		
General disorders and administration site conditions			
Dry mouth			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	8 / 24 (33.33%)		
occurrences (all)	8		
Injection site erythema			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	3		
Feeling Hot			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Injection site rash			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Cough			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Irritability			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Depression			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hyperaesthesia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	15		
Abdominal pain upper			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Abdominal Discomfort			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Cheilitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Constipation			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Dry skin			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Hyperhidrosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Erythema			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2010	Permitted the collection and storage of blood samples for use in future exploratory pharmacogenetics research.
14 February 2011	Randomised 21 additional Japanese subjects in Part A only of this study.
17 May 2011	The purpose of this amendment was to require blood samples for Hepatitis C virus (HCV) RNA and HCV resistance testing at treatment Weeks 16 and 20 for study subjects treated with direct antiviral agents (DAAs) for >16 weeks duration; Require a blood sample for pegylated interferon (pegIFN) lambda or pegIFN Alfa-2a at 168 hours post-dosing Week 4 in the Part A and B pharmacokinetic sub-studies; Include criteria for the Definition and reporting of potential drug-induced liver injury; Modify Part A futility criteria to allow subjects randomised to the reference regimen (Pegylated interferon Alfa -2a + ribavirin) who exhibit Week 12 treatment futility criteria to be discontinued from treatment at Week 16 and provided the option to participate in a future open-label roll-over study with a DAA based regimen; Modify the definition for relapse to undetectable Hepatitis C virus (HCV) RNA at end of treatment followed by detectable HCV RNA in any follow-up visit window; Modify the efficacy criteria to proceed from Part A to Part B based on achieving a Part A protocol defined response rate of no less than 50% instead of 65% for each experimental cohort; Modify the requirement for pregnancy testing in women of childbearing potential from weekly to monthly during treatment; Remove the requirement for a second set of local laboratory assessments to be performed at the site's local laboratory after Week 12; Restrict the use of sensitive CYP2D6 substrates such as desipramine, dextromethorphan, and atomoxetine with BMS-650032.
25 July 2011	Allowed systemic antibiotics and antivirals without anti-Hepatitis C virus activity to be used with caution instead of prohibited in Japanese subjects during the study.
12 March 2012	Added interim analyses with unblinded data after all subjects (including Japanese sub-study subjects) in Part A on arms containing Pegylated Interferon Lambda that achieve Part A PDR complete 4 and 12 weeks of follow-up to evaluate early sustained virologic response (SVR). SVR4 and SVR12 have a good correlation with SVR24 success.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported