Clinical trial results:
Phase 3 open label study evaluating the efficacy and safety of pegylated interferon lambda-1a, in combination with ribavirin and daclatasvir, for treatment of chronic HCV infection with treatment naïve genotypes 1, 2, 3 or 4 in subjects co-infected with HIV.

Summary

EudraCT number	2012-003280-22
Trial protocol	GB BE IT DE ES FR
Global end of trial date	27 August 2015

Results information

Result version number	v1 (current)
This version publication date	21 August 2016
First version publication date	21 August 2016

Trial information

Trial identification

Sponsor protocol code	AI452-032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01866930
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	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com
Scientific contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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	27 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate Sustained Virologic Response at post treatment Week 12 (SVR12) following treatment with Lambda/RBV/DCV in chronic HCV GT-1, -2, -3 or -4 subjects co-infected with HIV-1.

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 May 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Spain: 93
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	Argentina: 38
Country: Number of subjects enrolled	Canada: 43
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Russian Federation: 54
Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	453
EEA total number of subjects	258

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	450
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 58 investigational sites in 13 countries.

Pre-assignment

Screening details:

A total of 453 subjects were enrolled in the study. 300 subjects were randomized and received treatment. 153 subjects were not randomized to a treatment group due to Adverse Event (3), withdrawal of consent (13), loss to follow-up (4), administrative reasons per sponsor (5), no longer met study criteria (105), or other reasons (23).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: HCV GT-2 or GT-3

Arm description:

Subjects with HCV (Genotype 2 or 3) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks, for a total treatment duration of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated interferon Lambda-1a
Investigational medicinal product code	
Other name	Lambda, pegIFN-1a, BMS-914143
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered 180µg of Lambda via subcutaneous injection, once weekly, for a planned duration of 24 weeks.

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

Dosage and administration details:

Subjects were administered 200 mg Ribavirin tablets , orally, twice daily, for a planned duration of 24 weeks. Subjects received a total dose of 800 mg/day in two divided doses (two 200 mg tablets in the morning with food and two 200 mg tablets in the evening with food).

Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	
Other name	DCV, BMS-790052
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered 30 mg Daclatasvir tablets, orally, once daily, for a maximum of 12 weeks. The total daily dose was 30, 60 or 90 mg depending on the HIV concomitant regimen.

Arm title	Cohort B: HCV GT-1 or GT-4

Arm description:

Subjects with HCV (Genotype 1 or 4) and HIV co-infection were treated with Lambda/RBV/DCV for 12

weeks followed by Lambda/RBV for either 12 or 36 weeks. Subjects who achieved an extended rapid virologic response (eRVR) during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 12 weeks for a total of 24 weeks. Subjects who did not achieve eRVR during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 36 weeks for a total of 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Pegylated interferon Lambda-1a
Investigational medicinal product code	
Other name	Lambda, pegIFN-1a, BMS-914143
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were administered 180µg of Lambda via subcutaneous injection, once weekly, for a maximum of 48 weeks.

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

Dosage and administration details:

Subjects were administered 200 mg Ribavirin tablets , orally, twice daily, for a maximum duration of 48 weeks. For subjects weighing < 75 kg, the total dose was 1000 mg/day in two divided doses (two 200 mg tablets in the morning with food and three 200 mg tablets in the evening with food). For subjects weighing >= 75 kg, the total dose was 1200 mg/day in two divided doses (three 200 mg tablets in morning with food and three 200 mg tablets in evening with food).

Investigational medicinal product name	Daclatasvir
Investigational medicinal product code	
Other name	DCV, BMS-790052
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered 30 mg Daclatasvir tablets, orally, once daily, for a maximum of 12 weeks. The total daily dose was 30, 60 or 90 mg depending on the HIV concomitant regimen.

Number of subjects in period 1[1]	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4
Started	104	196
Completed	95	161
Not completed	9	35
Consent withdrawn by subject	-	3
Adverse event, non-fatal	4	12
Subject request to discontinue study treatment	2	5
Death	-	2
Lost to follow-up	1	1
Poor/non-compliance	-	2
Subject no longer meets study criteria	-	1
unspecified	1	-
Lack of efficacy	1	9

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: Of the 453 subjects enrolled, 300 were randomized and received treatment.

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	Cohort A: HCV GT-2 or GT-3

Arm description:

Subjects with HCV (Genotype 2 or 3) and HIV co-infection were to be followed up for a planned duration of 24 weeks after 24 weeks of treatment (Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Cohort B: HCV GT-1 or GT-4

Arm description:

Subjects with HCV (Genotype 1 or 4) and HIV co-infection were to be followed up for a planned duration of 24 weeks after 24 or 48 weeks of treatment (Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for either 12 or 36 weeks).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4
Started	95	161
Completed	96	176
Not completed	6	9
Consent withdrawn by subject	3	3
Follow-up no longer required per protocol	1	-
Lost to follow-up	1	1
unspecified	1	5
Joined	7	24
Rejoined for follow-up	7	24

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: HCV GT-2 or GT-3
Reporting group description:	
Subjects with HCV (Genotype 2 or 3) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks, for a total treatment duration of 24 weeks.	
Reporting group title	Cohort B: HCV GT-1 or GT-4
Reporting group description:	
Subjects with HCV (Genotype 1 or 4) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for either 12 or 36 weeks. Subjects who achieved an extended rapid virologic response (eRVR) during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 12 weeks for a total of 24 weeks. Subjects who did not achieve eRVR during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 36 weeks for a total of 48 weeks.	

Reporting group values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4	Total
Number of subjects	104	196	300
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	104	195	299
From 65-84 years	0	1	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	28	40	68
Male	76	156	232
HCV Genotype Units: Subjects			
HCV GT-1	0	149	149
HCV GT-2	20	0	20
HCV GT-3	83	0	83
HCV GT-4	0	41	41
Unknown	1	6	7

End points

End points reporting groups

Reporting group title	Cohort A: HCV GT-2 or GT-3
Reporting group description:	
Subjects with HCV (Genotype 2 or 3) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks, for a total treatment duration of 24 weeks.	
Reporting group title	Cohort B: HCV GT-1 or GT-4
Reporting group description:	
Subjects with HCV (Genotype 1 or 4) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for either 12 or 36 weeks. Subjects who achieved an extended rapid virologic response (eRVR) during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 12 weeks for a total of 24 weeks. Subjects who did not achieve eRVR during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 36 weeks for a total of 48 weeks.	
Reporting group title	Cohort A: HCV GT-2 or GT-3
Reporting group description:	
Subjects with HCV (Genotype 2 or 3) and HIV co-infection were to be followed up for a planned duration of 24 weeks after 24 weeks of treatment (Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks).	
Reporting group title	Cohort B: HCV GT-1 or GT-4
Reporting group description:	
Subjects with HCV (Genotype 1 or 4) and HIV co-infection were to be followed up for a planned duration of 24 weeks after 24 or 48 weeks of treatment (Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for either 12 or 36 weeks).	

Primary: Number of subjects with Sustained Virologic Response at post-treatment week 12 (SVR12)

End point title	Number of subjects with Sustained Virologic Response at post-treatment week 12 (SVR12)[1]
End point description:	
SVR12 was defined as HCV RNA less than lower limit of quantification (< LLOQ) (25 IU/mL; target detected or not detected) at follow-up week 12. The analysis was performed in all treated subjects using modified intent-to-treat algorithm, where the numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure).	
End point type	Primary
End point timeframe:	
Follow-up week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive summary statistics were planned for this outcome measure.

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects	88	149		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rapid virologic response (RVR) and extended rapid virologic response (eRVR)

End point title	Number of subjects with rapid virologic response (RVR) and extended rapid virologic response (eRVR)

End point description:

RVR is defined as HCV RNA < LLOQ target not detected at Week 4 and eRVR defined as HCV RNA < LLOQ target not detected at Weeks 4 and 12. The analysis was performed in all treated subjects using modified intent-to-treat algorithm, where the numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure).

End point type	Secondary

End point timeframe:

Treatment weeks 4 and 12

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects				
RVR	82	149		
eRVR	80	138		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Sustained Virologic Response at post-treatment week 24 (SVR24)

End point title	Number of subjects with Sustained Virologic Response at post-treatment week 24 (SVR24)

End point description:

SVR24 was defined as HCV RNA < LLOQ (25 IU/mL; target detected or not detected) at 24 weeks post treatment. The analysis was performed in all treated subjects using modified intent-to-treat algorithm (numerator is based on subjects meeting the response criteria and the denominator is based on all treated subjects (Non-completer = Failure).

End point type	Secondary

End point timeframe:

Follow-up week 24

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: subjects				

Notes:

[2] - The study was ended prematurely, giving few subjects an opportunity to reach follow-up week 24

[3] - The study was ended prematurely, giving few subjects an opportunity to reach follow-up week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment emergent cytopenic abnormalities

End point title	Number of subjects with treatment emergent cytopenic abnormalities

End point description:

All treated subjects were monitored for treatment emergent cytopenic abnormalities (anemia as defined by hemoglobin (Hb) < 10 g/dL, and/or neutropenia as defined by absolute neutrophil count (ANC) < 750 mm3 and/or thrombocytopenia as defined by platelets < 50,000/mm3) during the treatment period (Weeks 1, 2, 4, 6, 8, 12, 20, and 24, and at Weeks 28, 32, 36, 40, 44, and 48 for subjects requiring those visits).

End point type	Secondary

End point timeframe:

After Day 1 to end of treatment; up to Weeks 24 or 48.

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects	4	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with on-treatment IFN-associated Flu-like or Musculoskeletal symptoms

End point title	Number of subjects with on-treatment IFN-associated Flu-like or Musculoskeletal symptoms

End point description:

All treated subjects were monitored for IFN-associated Flu-like and Musculoskeletal symptoms. Flu-like symptoms were defined as pyrexia, chills, or pain. Musculoskeletal symptoms were defined as arthralgia, myalgia, or back pain. Subjects were monitored throughout the treatment period during the treatment period (After day 1 up to week 24, or After day 1 up to week 48 for subjects requiring those visits).

End point type	Secondary

End point timeframe:

After day 1 until end of treatment; Up to weeks 24 or 48.

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects				
Musculoskeletal symptoms	6	21		
Flu-like symptoms	6	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who died or experienced Severe Adverse Events (SAEs), Dose reductions of Lambda or Discontinuation due to Adverse Events (AEs)

End point title	Number of subjects who died or experienced Severe Adverse Events (SAEs), Dose reductions of Lambda or Discontinuation due to Adverse Events (AEs)

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 missing relationship to study drug. The analysis included all treated subjects up to the end of the treatment period (Day 1 to week 24, or Day 1 to week 48 for subjects requiring those visits).

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects				
Deaths	0	3		
SAEs	6	12		
Lambda Dose Reduction	4	19		
Discontinuation due to AEs	4	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Grade 3/4 Lab Abnormalities

End point title	Number of Subjects with Treatment-emergent Grade 3/4 Lab Abnormalities

End point description:

Grade 3/4 treatment-emergent lab abnormalities that occurred in >=5% of subjects in either cohort are reported. The analysis included all treated subjects up to the end of the treatment period (Day 1 to week 24, or Day 1 to week 48 for subjects requiring those visits). Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4= Potentially Life-threatening or disabling. AST = Aspartate aminotransferase, ALT = Alanine aminotransferase.

End point type	Secondary

End point timeframe:

After day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	196		
Units: subjects				
Total Bilirubin	26	63		
AST	10	13		
ALT	2	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Absolute CD4 T Lymphocyte Count from Baseline to End of Treatment

End point title	Mean Change in Absolute CD4 T Lymphocyte Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for change in Absolute CD4 T Lymphocyte count from Baseline to the end of the treatment period. The mean change in each arm for all evaluable subjects is reported in Cells/µL.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	192		
Units: Cells/µL				
arithmetic mean (standard deviation)	-42.4 (± 99999)	-104.9 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percent Change in Absolute CD4 T Lymphocyte Count from Baseline to End of Treatment

End point title	Mean Percent Change in Absolute CD4 T Lymphocyte Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for percent change in Absolute CD4 T Lymphocyte count from Baseline to the end of the treatment period. The mean percent change in each arm is presented for all evaluable subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	192		
Units: Percent change from baseline				
arithmetic mean (standard deviation)	-4 (± 99999)	-13.4 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Total Lymphocyte Count from Baseline to End of Treatment

End point title	Mean Change in Total Lymphocyte Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for change in Total Lymphocyte Count from Baseline to the end of the treatment period. The mean change in each arm for all evaluable subjects is reported in Cells/µL.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	195		
Units: cells/µL				
arithmetic mean (standard deviation)	-0.38 (± 99999)	-0.5 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percent Change in Total Lymphocyte Count from Baseline to End of Treatment

End point title	Mean Percent Change in Total Lymphocyte Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for percent change in Total Lymphocyte Count from Baseline to the end of the treatment period. The mean percent change in each arm is reported for all evaluable subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	195		
Units: percent change				
arithmetic mean (standard deviation)	-15.33 (± 99999)	-22.95 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in Platelet Count from Baseline to End of Treatment

End point title	Mean change in Platelet Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for change in Platelet Count from Baseline to the end of the treatment period. The mean change in each arm is reported for all evaluable subjects (units of measurement = x10*9 cells/L)

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	195		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)	32.7 (± 99999)	33.3 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percent change in Platelet Count from Baseline to End of Treatment

End point title	Mean percent change in Platelet Count from Baseline to End of Treatment

End point description:

All treated subjects were monitored for percent change in Platelet Count from Baseline to the end of the treatment period. The mean percent change in each arm is reported for all evaluable subjects.

End point type	Secondary

End point timeframe:

Day 1 to end of treatment; up to week 24 or week 48

End point values	Cohort A: HCV GT-2 or GT-3	Cohort B: HCV GT-1 or GT-4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	195		
Units: percent change				
arithmetic mean (standard deviation)	16.9 (± 99999)	20.1 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to end of treatment; up to week 24 or week 48

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Cohort B: HCV GT-1 or GT-4

Reporting group description:

Subjects with HCV (Genotype 1 or 4) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for either 12 or 36 weeks. Subjects who achieved an extended rapid virologic response (eRVR) during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 12 weeks for a total of 24 weeks. Subjects who did not achieve eRVR during the initial 12 weeks of treatment with Lambda/RBV/DCV were then treated with Lambda/RBV for 36 weeks for a total of 48 weeks.

Reporting group title	Cohort A: HCV GT-2 or GT-3

Reporting group description:

Subjects with HCV (Genotype 2 or 3) and HIV co-infection were treated with Lambda/RBV/DCV for 12 weeks followed by Lambda/RBV for 12 weeks, for a total treatment duration of 24 weeks.

Serious adverse events	Cohort B: HCV GT-1 or GT-4	Cohort A: HCV GT-2 or GT-3	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 196 (6.12%)	6 / 104 (5.77%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 196 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multi-Organ failure			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sudden death			
subjects affected / exposed	2 / 196 (1.02%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Gastrointestinal disorders			
Small intestinal haemorrhage			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	2 / 196 (1.02%)	2 / 104 (1.92%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Dysthymic disorder			
subjects affected / exposed	0 / 196 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 196 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary syphilis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 196 (0.00%)	1 / 104 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort B: HCV GT-1 or GT-4	Cohort A: HCV GT-2 or GT-3	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 196 (81.12%)	70 / 104 (67.31%)	
Investigations			
Aspartate aminotransferase increased			

subjects affected / exposed	4 / 196 (2.04%)	8 / 104 (7.69%)	
occurrences (all)	6	10	
Weight decreased			
subjects affected / exposed	11 / 196 (5.61%)	4 / 104 (3.85%)	
occurrences (all)	11	5	
Nervous system disorders			
Headache			
subjects affected / exposed	32 / 196 (16.33%)	10 / 104 (9.62%)	
occurrences (all)	39	13	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 196 (8.16%)	7 / 104 (6.73%)	
occurrences (all)	16	7	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	12 / 196 (6.12%)	0 / 104 (0.00%)	
occurrences (all)	12	0	
Asthenia			
subjects affected / exposed	32 / 196 (16.33%)	22 / 104 (21.15%)	
occurrences (all)	34	24	
Fatigue			
subjects affected / exposed	47 / 196 (23.98%)	9 / 104 (8.65%)	
occurrences (all)	53	9	
Influenza like illness			
subjects affected / exposed	5 / 196 (2.55%)	8 / 104 (7.69%)	
occurrences (all)	6	9	
Pyrexia			
subjects affected / exposed	13 / 196 (6.63%)	3 / 104 (2.88%)	
occurrences (all)	13	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	30 / 196 (15.31%)	7 / 104 (6.73%)	
occurrences (all)	43	7	
Abdominal pain			
subjects affected / exposed	15 / 196 (7.65%)	4 / 104 (3.85%)	
occurrences (all)	15	4	

Dyspepsia			
subjects affected / exposed	12 / 196 (6.12%)	4 / 104 (3.85%)	
occurrences (all)	12	4	
Nausea			
subjects affected / exposed	36 / 196 (18.37%)	10 / 104 (9.62%)	
occurrences (all)	51	11	
Vomiting			
subjects affected / exposed	23 / 196 (11.73%)	4 / 104 (3.85%)	
occurrences (all)	32	4	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	10 / 196 (5.10%)	6 / 104 (5.77%)	
occurrences (all)	11	6	
Hyperbilirubinaemia			
subjects affected / exposed	12 / 196 (6.12%)	4 / 104 (3.85%)	
occurrences (all)	12	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 196 (5.10%)	4 / 104 (3.85%)	
occurrences (all)	10	4	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	33 / 196 (16.84%)	15 / 104 (14.42%)	
occurrences (all)	35	17	
Dry skin			
subjects affected / exposed	27 / 196 (13.78%)	9 / 104 (8.65%)	
occurrences (all)	27	10	
Rash			
subjects affected / exposed	26 / 196 (13.27%)	8 / 104 (7.69%)	
occurrences (all)	28	9	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	14 / 196 (7.14%)	2 / 104 (1.92%)	
occurrences (all)	15	2	
Anxiety			

subjects affected / exposed	15 / 196 (7.65%)	4 / 104 (3.85%)	
occurrences (all)	15	4	
Depression			
subjects affected / exposed	18 / 196 (9.18%)	6 / 104 (5.77%)	
occurrences (all)	18	7	
Insomnia			
subjects affected / exposed	31 / 196 (15.82%)	16 / 104 (15.38%)	
occurrences (all)	31	19	
Irritability			
subjects affected / exposed	23 / 196 (11.73%)	15 / 104 (14.42%)	
occurrences (all)	24	16	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 196 (12.24%)	9 / 104 (8.65%)	
occurrences (all)	27	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2013	-Add additional exclusion criteria specific to cirrhotic subjects, -Add Peripheral Blood Mononuclear Cell (PBMC) collection in a subset of 30 subjects who are receiving HAART at selected US sites at Baseline (Day 1), End of Treatment and Post Treatment Week 24 as an exploratory endpoint, -Add that of the total of 200 subjects with GT-1 or -4, there will be at least 10% (n = 20) subjects with GT-4, -Add GT-4 to the evaluation of SVR12 by genotype subtype, -Modify the futility criteria at Week 24 from HCV RNA detected after previously having HCV RNA not detected to HCV RNA ≥ LLOQ, -Remove HDV serology testing as a screening requirement, -Add the exclusion of subjects with psychotic disorder, such as bipolar disease, or history of hospitalization for suicidal ideation/attempt, -Add that Investigators should advise subjects to avoid excessive ultraviolet exposure since the potential for Lambda to induce photosensitivity has not been assessed, -Add that the assay being used for HIV-1 RNA quantification is the Abbott Real Time assay on the automated m2000 System with a linear range of 40 - 10,000,000 copies/mL, -Add that Quintiles will be the central laboratory used in the study, -Add that Monogram Biosciences/LabCorps will perform HIV-1 genotypic and phenotypic resistance assays.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported