Clinical trial results:
Safety and Efficacy of 120 mg and 240 mg BI 201335 once daily in combination with pegylated interferon alpha 2a and ribavirin for treatment of chronic Hepatitis C (HCV) genotype 1 infection in HIV/HCV-co-infected patients. A multinational, randomised, parallel group, open-label trial

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2010-021734-59
Trial protocol	GB ES DE IT
Global end of trial date	19 June 2014

Results information

Result version number	v2 (current)
This version publication date	23 July 2016
First version publication date	26 July 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT - Results

Trial information

Trial identification

Sponsor protocol code	1220.19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01399619
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, 55216 Ingelheim am Rhein, Germany,
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure , Boehringer Ingelheim, +1 800 243 0127 , clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure , Boehringer Ingelheim, +1 800 243 0127 , clintriage.rdg@boehringer-ingelheim.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2013
Global end of trial reached?	Yes
Global end of trial date	19 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial is to evaluate the safety and efficacy of an open-label treatment with BI 201335 240 mg once daily given for 12 or 24 weeks (wk) or BI 201335 120 mg once daily for 24 wk, each in combination with pegylated interferon-alpha2a and ribavirin given for 24 or 48 wk in hepatitis C virus (HCV)/human immunodeficiency virus (HIV) coinfected patients, who are HCV-treatment naive or HCV-treatment relapsers and HIV treatment-naive- or, who are being treated with Highly active antiretroviral therapy (HAART) containing an acceptable combination of the following antiretrovirals: raltegravir, darunavir/ritonavir, efavirenz, atazanavir/ ritonavir (limited to 20 patients), maraviroc, tenofovir, abacavir, emtricitabine, and lamivudine. Results of this trial will be compared with historical efficacy and safety data of randomized trials of 48 wk of treatment with pegylated interferon-alpha2a and ribavirin for HCV genotype 1 (GT-1) infection in HIV/HCV co-infected patients.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy:

All treatment groups included a background therapy of pegylated interferon alpha 2a and ribavirin (pegIFN and RBV)

Evidence for comparator: -

Actual start date of recruitment	04 October 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 119
Country: Number of subjects enrolled	United Kingdom: 72
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Brazil: 28

Country: Number of subjects enrolled	United States: 119
Country: Number of subjects enrolled	Switzerland: 17
Worldwide total number of subjects	453
EEA total number of subjects	289

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)	441
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subject) met all strictly implemented inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Faldaprevir 120 mg-24 Wk

Arm description:

Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Arm type	Experimental
Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	BI 201335
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

one soft gelatine capsule of BI 201335 (Faldaprevir) once a day 120 mg

Investigational medicinal product name	pegIFN
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose: 180 µg once weekly,
Mode of Admin.: Subcutaneous (SC) injection.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.
Mode of Admin.: Oral.

Arm title	Faldaprevir 240 mg-12Wk

Arm description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Arm type	Experimental
Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	BI 201335
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

patient to receive two capsules of BI 201335 once a day (total daily dose 240 mg).

Investigational medicinal product name	pegIFN
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose: 180 µg once weekly;
Mode of Admin.: Subcutaneous (SC) injection.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.
Mode of Admin.: Oral.

Arm title	Faldaprevir 240 mg-24Wk

Arm description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Arm type	Experimental
Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	BI 201335
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

patient to receive two capsules of BI 201335 once a day for 24 weeks (total daily dose 240 mg).

Investigational medicinal product name	pegIFN
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose: 180 µg once weekly,
Mode of Admin.: Subcutaneous (SC) injection.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.
Mode of Admin.: Oral.

Arm title	Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR)

Arm description:

Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.

Arm type	Experimental
Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	BI 201335
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

dose: 240 mg.
mode of admin.: Oral use.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.
Mode of Admin.: Oral.

Investigational medicinal product name	pegIFN
Investigational medicinal product code	
Other name	Pegasys®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose: 180 µg once weekly,
Mode of Admin.: Subcutaneous (SC) injection.

Number of subjects in period 1[1]	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk
Started	123	84	86
Completed	98	84	74
Not completed	25	0	12
Consent withdrawn by subject	6	-	3
not treated	-	-	-

Adverse event, non-fatal	10	-	4
Lack of efficacy	9	-	5
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR)
Started	17
Completed	0
Not completed	17
Consent withdrawn by subject	4
not treated	2
Adverse event, non-fatal	10
Lack of efficacy	-
Protocol deviation	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	Faldaprevir 120 mg-24 Wk
Reporting group description:	
Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.	
Reporting group title	Faldaprevir 240 mg-12Wk
Reporting group description:	
Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.	
Reporting group title	Faldaprevir 240 mg-24Wk
Reporting group description:	
Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.	
Reporting group title	Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR)
Reporting group description:	
Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.	

Reporting group values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk
Number of subjects	123	84	86
Age categorical			
Units: Subjects			
Age continuous			
Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy.			
Units: years			
arithmetic mean	47.6	46.1	46
standard deviation	± 7.63	± 8.64	± 7.97
Gender categorical			
based on FAS population.			
Units: Subjects			
Female	20	18	18
Male	103	66	68

Reporting group values	Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR)	Total	
Number of subjects	17	310	
Age categorical			
Units: Subjects			

Age continuous			
Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy.			
Units: years			
arithmetic mean	51.8		
standard deviation	± 9.09	-	
Gender categorical			
based on FAS population.			
Units: Subjects			
Female	4	60	
Male	13	250	

Subject analysis sets

Subject analysis set title	Faldaprevir 240 mg - Total (T)
Subject analysis set type	Full analysis

Subject analysis set description:

Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12.

Subject analysis set title	Faldaprevir - Total
Subject analysis set type	Full analysis

Subject analysis set description:

Total subjects who were treated with faldaprevir.

Reporting group values	Faldaprevir 240 mg - Total (T)	Faldaprevir - Total	
Number of subjects	185	308	
Age categorical			
Units: Subjects			

Age continuous			
Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy.			
Units: years			
arithmetic mean	46.5	46.9	
standard deviation	± 8.36	± 8.08	
Gender categorical			
based on FAS population.			
Units: Subjects			
Female	40	60	
Male	145	248	

End points

End points reporting groups

Reporting group title	Faldaprevir 120 mg-24 Wk

Reporting group description:

Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg-12Wk

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg-24Wk

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR)

Reporting group description:

Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.

Subject analysis set title	Faldaprevir 240 mg - Total (T)
Subject analysis set type	Full analysis

Subject analysis set description:

Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12.

Subject analysis set title	Faldaprevir - Total
Subject analysis set type	Full analysis

Subject analysis set description:

Total subjects who were treated with faldaprevir.

Primary: Sustained Virological Response (SVR12)

End point title	Sustained Virological Response (SVR12)[1][2]

End point description:

Percentage of participants with sustained Virological Response (SVR12): Plasma Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Level <25 IU/mL, Undetected 12 Weeks After the Planned End of Treatment.

The 95% confidence interval (CI) based on the normal approximation to the binomial distribution was calculated for SVR12 rates

End point type	Primary

End point timeframe:

60 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

[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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[3]	84[4]	86[5]	185[6]
Units: percentage of participants with SVR12				
number (confidence interval 95%)	70.7 (62.7 to 78.8)	78.6 (69.8 to 87.3)	76.7 (67.8 to 85.7)	72.4 (66 to 78.9)

Notes:

[3] - FAS

[4] - FAS

[5] - FAS

[6] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[7]			
Units: percentage of participants with SVR12				
number (confidence interval 95%)	71.8 (66.7 to 76.8)			

Notes:

[7] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Virological Response 24 Weeks Post Treatment (SVR24)

End point title	Virological Response 24 Weeks Post Treatment (SVR24)[8]

End point description:

Percentage of participants with virological response 24 weeks post treatment (SVR24): Plasma HCV RNA Level<25IU/mL undetected 24 Weeks After the Planned End of Treatment.

End point type	Secondary

End point timeframe:

72 weeks

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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[9]	84[10]	86[11]	185[12]
Units: percentage of participants				
number (confidence interval 95%)	69.9 (61.8 to 78)	78.6 (69.8 to 87.3)	74.4 (65.2 to 83.6)	71.4 (64.8 to 77.9)

Notes:

[9] - FAS

[10] - FAS

[11] - FAS

[12] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[13]			
Units: percentage of participants				
number (confidence interval 95%)	70.8 (65.7 to 75.9)			

Notes:

[13] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Early Treatment Success (ETS)

End point title	Early Treatment Success (ETS)[14]

End point description:

Early Treatment Success (ETS): Plasma HCV RNA Level<25 IU/mL (Detected or Undetected) at Week 4 and HCV RNA< 25 IU/mL, Undetected at Week 8

End point type	Secondary

End point timeframe:

Week 4, Week 8 and Week 60.

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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[15]	84[16]	86[17]	185[18]
Units: participant(s)				
number (not applicable)				
number of subjects with ETS =yes	95	70	73	150
number of subjects with SVR12 among ETS=yes group	83	62	63	127

Notes:

[15] - FAS

[16] - FAS

[17] - FAS

[18] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[19]			
Units: participant(s)				
number (not applicable)				
number of subjects with ETS =yes	245			

number of subjects with SVR12 among ETS=yes group	210			

Notes:

[19] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: The number of participants with Alanine Aminotransferase (ALT) Normalisation at post treatment

End point title	The number of participants with Alanine Aminotransferase (ALT) Normalisation at post treatment[20]

End point description:

The number of participants with Alanine Aminotransferase (ALT) Normalisation: ALT in Normal Range at Post Treatment (SVR12 Visit) based on SVR12=yes or SVR12=no.
BL=baseline.

End point type	Secondary

End point timeframe:

60 weeks

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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[21]	84[22]	86[23]	185[24]
Units: participant(s)				
SVR12=yes	87	66	66	134
SVR12=yes, BL normal to SVR12 normal	28	17	26	45
SVR12=yes, BL elevated to SVR12 normal	52	46	35	81
SVR12=yes, no ALT data available at SVR12 visit	4	0	1	1
SVR12=no	36	18	20	51
SVR12=no, BL normal to SVR12 normal	8	1	3	6
SVR12=no, BL elevated to SVR12 normal	1	6	3	9
SVR12=no, no ALT data available at SVR12 visit	16	4	6	20

Notes:

[21] - FAS

[22] - FAS

[23] - FAS

[24] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[25]			

Units: participant(s)				
SVR12=yes	221			
SVR12=yes, BL normal to SVR12 normal	73			
SVR12=yes, BL elevated to SVR12 normal	133			
SVR12=yes, no ALT data available at SVR12 visit	5			
SVR12=no	87			
SVR12=no, BL normal to SVR12 normal	14			
SVR12=no, BL elevated to SVR12 normal	10			
SVR12=no, no ALT data available at SVR12 visit	36			

Notes:

[25] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: The number of participants with Alanine Aminotransferase (ALT) Normalisation at end of treatment

End point title	The number of participants with Alanine Aminotransferase (ALT) Normalisation at end of treatment[26]

End point description:

Alanine Aminotransferase (ALT) normalisation at End of Treatment (EoT) based on SVR12=yes or SVR12=no.
BL = baseline.

End point type	Secondary

End point timeframe:

48 weeks

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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[27]	84[28]	86[29]	185[30]
Units: participant(s)				
SVR12=yes	87	66	66	134
SVR12=yes, BL normal to EoT normal	29	16	26	43
SVR12=yes, BL elevated to EoT normal	45	34	32	66
SVR12=yes, no BL or EoT data	0	0	0	1
SVR12=no	36	18	20	51
SVR12=no, BL normal to EoT normal	18	5	5	18
SVR12=no, BL elevated to EoT normal	12	8	9	21
SVR12=no, no BL or EoT data	2	0	0	0

Notes:

[27] - FAS

[28] - FAS
[29] - FAS
[30] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[31]			
Units: participant(s)				
SVR12=yes	221			
SVR12=yes, BL normal to EoT normal	72			
SVR12=yes, BL elevated to EoT normal	111			
SVR12=yes, no BL or EoT data	1			
SVR12=no	87			
SVR12=no, BL normal to EoT normal	36			
SVR12=no, BL elevated to EoT normal	33			
SVR12=no, no BL or EoT data	2			

Notes:
[31] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: The number of participants with Aspartate Aminotransferase (AST) Normalisation at end of treatment

End point title	The number of participants with Aspartate Aminotransferase (AST) Normalisation at end of treatment[32]

End point description:

Aspartate Aminotransferase (AST) normalisation at End of Treatment (EoT) based on SVR12=yes or SVR12 =no.
BL = baseline.

End point type	Secondary

End point timeframe:

48 weeks

Notes:

[32] - 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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[33]	84[34]	86[35]	185[36]
Units: participant(s)				
SVR12=yes	87	66	66	134
SVR12=yes, BL normal to EoT normal	41	25	28	54
SVR12=yes, BL elevated to EoT normal	32	25	27	52
SVR12=yes, no BL or EoT data	0	0	0	1
SVR12=no	36	18	20	51
SVR12=no, BL normal to EoT normal	14	6	7	19
SVR12=no, BL elevated to EoT normal	12	6	8	19

SVR12=no, no BL or EoT data	2	0	0	0

Notes:

[33] - FAS

[34] - FAS

[35] - FAS

[36] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[37]			
Units: participant(s)				
SVR12=yes	221			
SVR12=yes, BL normal to EoT normal	95			
SVR12=yes, BL elevated to EoT normal	84			
SVR12=yes, no BL or EoT data	1			
SVR12=no	87			
SVR12=no, BL normal to EoT normal	33			
SVR12=no, BL elevated to EoT normal	31			
SVR12=no, no BL or EoT data	2			

Notes:

[37] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: The number of participants with Aspartate Aminotransferase (AST) Normalisation at post treatment

End point title	The number of participants with Aspartate Aminotransferase (AST) Normalisation at post treatment[38]

End point description:

AST in normal range at Post Treatment (SVR12 Visit) based on SVR12=yes or SVR12=no.
BL = baseline.

End point type	Secondary

End point timeframe:

60 weeks

Notes:

[38] - 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: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

End point values	Faldaprevir 120 mg-24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk	Faldaprevir 240 mg - Total (T)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	123[39]	84[40]	86[41]	185[42]
Units: participant(s)				
SVR12=yes	87	66	66	134
SVR12=yes, BL normal to SVR12 normal	41	27	28	57
SVR12=yes, BL elevated to SVR12 normal	36	36	33	69

SVR12=yes, no AST data available at SVR12 visit	4	0	1	1
SVR12=no	36	18	20	51
SVR12=no, BL normal to SVR12 normal	6	4	6	13
SVR12=no, BL elevated to SVR12 normal	2	3	0	3
SVR12=no, no AST data available at SVR12 visit	16	4	6	20

Notes:

[39] - FAS

[40] - FAS

[41] - FAS

[42] - FAS

End point values	Faldaprevir - Total			
Subject group type	Subject analysis set			
Number of subjects analysed	308[43]			
Units: participant(s)				
SVR12=yes	221			
SVR12=yes, BL normal to SVR12 normal	98			
SVR12=yes, BL elevated to SVR12 normal	105			
SVR12=yes, no AST data available at SVR12 visit	5			
SVR12=no	87			
SVR12=no, BL normal to SVR12 normal	19			
SVR12=no, BL elevated to SVR12 normal	5			
SVR12=no, no AST data available at SVR12 visit	36			

Notes:

[43] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from the start date of trial medication up to 52 weeks (AEs occurred from the start date of trial medication up to four weeks after all treatment discontinuation).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Faldaprevir 120 mg -24 Wk

Reporting group description:

Faldaprevir 120 mg QD combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg-12Wk

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg-24Wk

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

Reporting group title	Faldaprevir 240 mg - T

Reporting group description:

Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12.

Serious adverse events	Faldaprevir 120 mg -24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 123 (13.82%)	5 / 84 (5.95%)	5 / 86 (5.81%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			

subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 123 (2.44%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Substance use			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 123 (0.81%)	1 / 84 (1.19%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			

subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Nausea			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash erythematous			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	2 / 123 (1.63%)	0 / 84 (0.00%)	0 / 86 (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

Toxic skin eruption			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Diverticulitis			
subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Escherichia urinary tract infection			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Gastroenteritis viral			

subjects affected / exposed	0 / 123 (0.00%)	1 / 84 (1.19%)	0 / 86 (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
Infected cyst			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Leishmaniasis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Pneumonia			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (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
Urosepsis			

subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 123 (0.81%)	0 / 84 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 123 (0.00%)	0 / 84 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Faldaprevir 240 mg - T		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 185 (8.11%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Sarcoidosis				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Substance use				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accidental overdose				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				

subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 185 (1.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 185 (1.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Enterovesical fistula			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Vomiting				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Drug reaction with eosinophilia and systemic symptoms				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Rash				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash erythematous				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrolithiasis				

subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected cyst			
subjects affected / exposed	0 / 185 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leishmaniasis			

subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neurosyphilis				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	1 / 185 (0.54%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 185 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 185 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Faldaprevir 120 mg -24 Wk	Faldaprevir 240 mg-12Wk	Faldaprevir 240 mg-24Wk
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 123 (94.31%)	80 / 84 (95.24%)	84 / 86 (97.67%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	31 / 123 (25.20%)	21 / 84 (25.00%)	17 / 86 (19.77%)
occurrences (all)	34	23	17
Chills			
subjects affected / exposed	5 / 123 (4.07%)	2 / 84 (2.38%)	7 / 86 (8.14%)
occurrences (all)	6	2	8
Fatigue			
subjects affected / exposed	39 / 123 (31.71%)	29 / 84 (34.52%)	30 / 86 (34.88%)
occurrences (all)	40	31	32
Influenza like illness			
subjects affected / exposed	14 / 123 (11.38%)	17 / 84 (20.24%)	12 / 86 (13.95%)
occurrences (all)	14	18	14
Injection site reaction			
subjects affected / exposed	3 / 123 (2.44%)	2 / 84 (2.38%)	6 / 86 (6.98%)
occurrences (all)	3	2	6
Pyrexia			
subjects affected / exposed	29 / 123 (23.58%)	11 / 84 (13.10%)	10 / 86 (11.63%)
occurrences (all)	37	12	12
Irritability			

subjects affected / exposed	19 / 123 (15.45%)	8 / 84 (9.52%)	5 / 86 (5.81%)
occurrences (all)	19	8	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 123 (10.57%)	8 / 84 (9.52%)	10 / 86 (11.63%)
occurrences (all)	13	8	11
Dyspnoea			
subjects affected / exposed	12 / 123 (9.76%)	8 / 84 (9.52%)	3 / 86 (3.49%)
occurrences (all)	12	8	3
Oropharyngeal pain			
subjects affected / exposed	3 / 123 (2.44%)	6 / 84 (7.14%)	2 / 86 (2.33%)
occurrences (all)	3	7	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 123 (7.32%)	5 / 84 (5.95%)	2 / 86 (2.33%)
occurrences (all)	9	5	2
Depressed mood			
subjects affected / exposed	6 / 123 (4.88%)	4 / 84 (4.76%)	7 / 86 (8.14%)
occurrences (all)	6	4	7
Depression			
subjects affected / exposed	11 / 123 (8.94%)	9 / 84 (10.71%)	13 / 86 (15.12%)
occurrences (all)	11	10	13
Insomnia			
subjects affected / exposed	29 / 123 (23.58%)	11 / 84 (13.10%)	14 / 86 (16.28%)
occurrences (all)	29	11	14
Sleep disorder			
subjects affected / exposed	4 / 123 (3.25%)	3 / 84 (3.57%)	5 / 86 (5.81%)
occurrences (all)	4	3	5
Investigations			
Weight decreased			
subjects affected / exposed	16 / 123 (13.01%)	10 / 84 (11.90%)	13 / 86 (15.12%)
occurrences (all)	16	10	13
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 123 (7.32%)	10 / 84 (11.90%)	6 / 86 (6.98%)
occurrences (all)	9	10	6

Headache			
subjects affected / exposed	29 / 123 (23.58%)	21 / 84 (25.00%)	22 / 86 (25.58%)
occurrences (all)	31	22	24
Lethargy			
subjects affected / exposed	1 / 123 (0.81%)	3 / 84 (3.57%)	5 / 86 (5.81%)
occurrences (all)	1	3	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 123 (21.95%)	13 / 84 (15.48%)	15 / 86 (17.44%)
occurrences (all)	27	14	15
Neutropenia			
subjects affected / exposed	27 / 123 (21.95%)	6 / 84 (7.14%)	15 / 86 (17.44%)
occurrences (all)	32	6	16
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 123 (2.44%)	5 / 84 (5.95%)	0 / 86 (0.00%)
occurrences (all)	3	5	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 123 (5.69%)	11 / 84 (13.10%)	4 / 86 (4.65%)
occurrences (all)	7	11	4
Abdominal pain upper			
subjects affected / exposed	7 / 123 (5.69%)	7 / 84 (8.33%)	3 / 86 (3.49%)
occurrences (all)	7	8	3
Cheilitis			
subjects affected / exposed	8 / 123 (6.50%)	4 / 84 (4.76%)	3 / 86 (3.49%)
occurrences (all)	8	4	4
Diarrhoea			
subjects affected / exposed	32 / 123 (26.02%)	24 / 84 (28.57%)	23 / 86 (26.74%)
occurrences (all)	34	31	27
Dry mouth			
subjects affected / exposed	6 / 123 (4.88%)	5 / 84 (5.95%)	2 / 86 (2.33%)
occurrences (all)	6	5	2
Dyspepsia			
subjects affected / exposed	6 / 123 (4.88%)	4 / 84 (4.76%)	7 / 86 (8.14%)
occurrences (all)	7	4	8
Nausea			

subjects affected / exposed	34 / 123 (27.64%)	38 / 84 (45.24%)	36 / 86 (41.86%)
occurrences (all)	36	44	39
Vomiting			
subjects affected / exposed	12 / 123 (9.76%)	14 / 84 (16.67%)	23 / 86 (26.74%)
occurrences (all)	16	19	28
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	7 / 123 (5.69%)	8 / 84 (9.52%)	10 / 86 (11.63%)
occurrences (all)	8	8	10
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 123 (5.69%)	4 / 84 (4.76%)	6 / 86 (6.98%)
occurrences (all)	7	4	6
Dry skin			
subjects affected / exposed	17 / 123 (13.82%)	9 / 84 (10.71%)	18 / 86 (20.93%)
occurrences (all)	17	9	19
Erythema			
subjects affected / exposed	8 / 123 (6.50%)	5 / 84 (5.95%)	5 / 86 (5.81%)
occurrences (all)	9	5	6
Night sweats			
subjects affected / exposed	7 / 123 (5.69%)	6 / 84 (7.14%)	3 / 86 (3.49%)
occurrences (all)	7	6	3
Pruritus			
subjects affected / exposed	19 / 123 (15.45%)	16 / 84 (19.05%)	17 / 86 (19.77%)
occurrences (all)	21	16	17
Rash			
subjects affected / exposed	22 / 123 (17.89%)	16 / 84 (19.05%)	13 / 86 (15.12%)
occurrences (all)	24	17	14
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 123 (8.94%)	6 / 84 (7.14%)	6 / 86 (6.98%)
occurrences (all)	13	6	6
Muscle spasms			
subjects affected / exposed	3 / 123 (2.44%)	3 / 84 (3.57%)	6 / 86 (6.98%)
occurrences (all)	3	3	6
Myalgia			

subjects affected / exposed	17 / 123 (13.82%)	9 / 84 (10.71%)	15 / 86 (17.44%)
occurrences (all)	20	12	16
Infections and infestations			
Oral herpes			
subjects affected / exposed	8 / 123 (6.50%)	0 / 84 (0.00%)	2 / 86 (2.33%)
occurrences (all)	9	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	29 / 123 (23.58%)	14 / 84 (16.67%)	18 / 86 (20.93%)
occurrences (all)	29	14	19

Non-serious adverse events	Faldaprevir 240 mg - T		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 185 (96.22%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	39 / 185 (21.08%)		
occurrences (all)	41		
Chills			
subjects affected / exposed	11 / 185 (5.95%)		
occurrences (all)	12		
Fatigue			
subjects affected / exposed	65 / 185 (35.14%)		
occurrences (all)	69		
Influenza like illness			
subjects affected / exposed	31 / 185 (16.76%)		
occurrences (all)	34		
Injection site reaction			
subjects affected / exposed	8 / 185 (4.32%)		
occurrences (all)	8		
Pyrexia			
subjects affected / exposed	24 / 185 (12.97%)		
occurrences (all)	27		
Irritability			
subjects affected / exposed	13 / 185 (7.03%)		
occurrences (all)	13		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 185 (9.73%)		
occurrences (all)	19		
Dyspnoea			
subjects affected / exposed	12 / 185 (6.49%)		
occurrences (all)	12		
Oropharyngeal pain			
subjects affected / exposed	9 / 185 (4.86%)		
occurrences (all)	10		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 185 (4.32%)		
occurrences (all)	8		
Depressed mood			
subjects affected / exposed	12 / 185 (6.49%)		
occurrences (all)	12		
Depression			
subjects affected / exposed	24 / 185 (12.97%)		
occurrences (all)	25		
Insomnia			
subjects affected / exposed	28 / 185 (15.14%)		
occurrences (all)	28		
Sleep disorder			
subjects affected / exposed	8 / 185 (4.32%)		
occurrences (all)	8		
Investigations			
Weight decreased			
subjects affected / exposed	25 / 185 (13.51%)		
occurrences (all)	25		
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 185 (10.81%)		
occurrences (all)	21		
Headache			

subjects affected / exposed	47 / 185 (25.41%)		
occurrences (all)	50		
Lethargy			
subjects affected / exposed	8 / 185 (4.32%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 185 (16.22%)		
occurrences (all)	31		
Neutropenia			
subjects affected / exposed	22 / 185 (11.89%)		
occurrences (all)	23		
Eye disorders			
Dry eye			
subjects affected / exposed	6 / 185 (3.24%)		
occurrences (all)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	17 / 185 (9.19%)		
occurrences (all)	17		
Abdominal pain upper			
subjects affected / exposed	10 / 185 (5.41%)		
occurrences (all)	11		
Cheilitis			
subjects affected / exposed	7 / 185 (3.78%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	51 / 185 (27.57%)		
occurrences (all)	62		
Dry mouth			
subjects affected / exposed	7 / 185 (3.78%)		
occurrences (all)	7		
Dyspepsia			
subjects affected / exposed	11 / 185 (5.95%)		
occurrences (all)	12		
Nausea			

subjects affected / exposed	81 / 185 (43.78%)		
occurrences (all)	91		
Vomiting			
subjects affected / exposed	43 / 185 (23.24%)		
occurrences (all)	54		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	19 / 185 (10.27%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 185 (5.41%)		
occurrences (all)	10		
Dry skin			
subjects affected / exposed	27 / 185 (14.59%)		
occurrences (all)	28		
Erythema			
subjects affected / exposed	10 / 185 (5.41%)		
occurrences (all)	11		
Night sweats			
subjects affected / exposed	9 / 185 (4.86%)		
occurrences (all)	9		
Pruritus			
subjects affected / exposed	34 / 185 (18.38%)		
occurrences (all)	34		
Rash			
subjects affected / exposed	31 / 185 (16.76%)		
occurrences (all)	33		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 185 (7.03%)		
occurrences (all)	13		
Muscle spasms			
subjects affected / exposed	9 / 185 (4.86%)		
occurrences (all)	9		
Myalgia			

subjects affected / exposed occurrences (all)	27 / 185 (14.59%) 31		
Infections and infestations Oral herpes subjects affected / exposed occurrences (all)	 2 / 185 (1.08%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 36 / 185 (19.46%) 37		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2011	main amendments: 1. Description and rationale of the new trial design (inclusion of the FDV 120 mg group). 2. Explanation of loading dose. 3. Added information about the results of drug interaction trials with ARVs.
11 October 2011	Main amendments: 1. Clarification of ATZ/RTV intensive PK sampling: medication administration; parameters to be determined; sampling timepoints; assay for ARV concentration determination; and sample handling.
01 May 2012	Main amendments: 1. Clarification and guidance on when and how to conduct the progression of liver disease assessment. 2. Change of the primary efficacy endpoint from SVR24 to SVR12 based on regulatory presentations and retrospective analysis of phase II data indicating a 98% positive predictive value (PPV) of SVR12 predicting SVR24. 3. Clarification of inclusion criteria: definition of stable HAART. 4. Clarification of exclusion criteria: allowed enrolment of patients with Child-Turcotte-Pugh classification (CTP) score above threshold due to comedication effect, but not liver decompensation, consistent with update of RBV label; which patients with chronic obstructive pulmonary disease (COPD) should be excluded; limited exception for the white blood cell (WBC) and absolute neutrophil count (ANC) thresholds. 5. Clarification of the stopping rule implementation. 6. Clarification of the criteria for virologic failure. 7. Clarification in wording for AEs and SAEs to comply with BI SOP. 8. Clarification of use of the eCRF skin form page to capture rashes and photosensitivity reactions (protocol-defined AEs of special interest). 9. Clarification of procedures to be done when a patient prematurely discontinued. 10. Clarification of analyses for the SVR12 timepoint; primary and secondary analyses; and safety analyses for HIV disease characteristics.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported