Clinical trial results:
An International, Multicenter, Open-Label Study Evaluating Sustained Virological Response and Safety With Boceprevir in Triple Combination Therapy With Peginterferon Alfa-2a (40KD) and Ribavirin in Treatment-Naive Patients With Genotype 1 Chronic Hepatitis C

Summary

EudraCT number	2011-004810-41
Trial protocol	AT HU ES PL DE
Global end of trial date	20 June 2014

Results information

Result version number	v1 (current)
This version publication date	04 May 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	MV28073

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01591460
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This prospective, international, multicenter, open-label, uncontrolled Phase 3b/4 study in treatment-naive participants with chronic hepatitis C (CHC) genotype 1 was designed to evaluate the efficacy and safety of triple combination therapy with peginterferon alfa-2a (PEG-IFN), ribavirin (RBV), and boceprevir when given as a response-guided treatment regimen for 28 to 48 weeks.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) according to the regulations and procedures described in the protocol. Investigators were trained according to applicable Sponsor Standard Operating Procedures (SOPs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Romania: 39
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Austria: 21
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Hungary: 31
Worldwide total number of subjects	165
EEA total number of subjects	165

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)	153
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a Screening phase which began within up to 4 weeks (in exceptional cases up to 8 weeks) prior to the first dose of study medication. Inclusion/exclusion criteria were checked.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Total Population

Arm description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 micrograms (mcg) subcutaneous (SC) once weekly, weight-based RBV 1000 to 1200 milligrams (mg) orally (PO) daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Those with undetectable hepatitis C virus (HCV) ribonucleic acid (RNA) at Weeks 8 and 24 stopped treatment at Week 28. Those with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 continued triple therapy until Week 36 and received dual therapy from Week 36 to 48. Those with a less than (<) 1-log decrease in HCV RNA at Week 4 continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated. Participants with compensated cirrhosis, regardless of response, received triple therapy until Week 48.

Arm type	Experimental
Investigational medicinal product name	Peginterferon alfa-2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received PEG-IFN 180 mcg SC once weekly for up to 48 weeks.

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

Dosage and administration details:

Participants received weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses for up to 48 weeks.

Investigational medicinal product name	Boceprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received boceprevir 800 mg PO every 7 to 9 hours for up to 44 weeks.

Number of subjects in period 1	Total Population
Started	165
Completed	139
Not completed	26
Consent withdrawn by subject	1
Protocol violation	1
Rebound or breakthrough	3
Futility rule (Week 24)	3
Participant refusal	3
Lost to follow-up	1
Treatment discontinued by error	1
Futility rule (Week 12)	7
Adverse event or intercurrent illness	5
Noncompliance	1

Baseline characteristics

Reporting groups

Reporting group title	Total Population

Reporting group description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 micrograms (mcg) subcutaneous (SC) once weekly, weight-based RBV 1000 to 1200 milligrams (mg) orally (PO) daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Those with undetectable hepatitis C virus (HCV) ribonucleic acid (RNA) at Weeks 8 and 24 stopped treatment at Week 28. Those with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 continued triple therapy until Week 36 and received dual therapy from Week 36 to 48. Those with a less than (<) 1-log decrease in HCV RNA at Week 4 continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated. Participants with compensated cirrhosis, regardless of response, received triple therapy until Week 48.

Reporting group values	Total Population	Total	
Number of subjects	165	165	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 45.8 ± 12.53	 -	
Gender categorical Units: Subjects			
Female	83	83	
Male	82	82	

End points

End points reporting groups

Reporting group title	Total Population

Reporting group description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 micrograms (mcg) subcutaneous (SC) once weekly, weight-based RBV 1000 to 1200 milligrams (mg) orally (PO) daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Those with undetectable hepatitis C virus (HCV) ribonucleic acid (RNA) at Weeks 8 and 24 stopped treatment at Week 28. Those with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 continued triple therapy until Week 36 and received dual therapy from Week 36 to 48. Those with a less than (<) 1-log decrease in HCV RNA at Week 4 continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated. Participants with compensated cirrhosis, regardless of response, received triple therapy until Week 48.

Subject analysis set title	Cirrhotics
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Response-guided treatment was determined by assessments of virologic response at Weeks 4, 8, and 24. Participants with compensated cirrhosis (Cirrhotics), regardless of response, received triple therapy until Week 48.

Subject analysis set title	Poor Responders
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Response-guided treatment was determined by assessments of virologic response at Weeks 4, 8, and 24. Those without cirrhosis and with a <1-log decrease in HCV RNA at Week 4 (Poor Responders) continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated.

Subject analysis set title	Late Responders
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Response-guided treatment was determined by assessments of virologic response at Weeks 4, 8, and 24. Those without cirrhosis and with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 (Late Responders) continued triple therapy until Week 36 and received dual therapy from Week 36 to 48.

Subject analysis set title	Early Responders
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Response-guided treatment was determined by assessments of virologic response at Weeks 4, 8, and 24. Those without cirrhosis and with undetectable HCV RNA at Weeks 8 and 24 (Early Responders) stopped treatment at Week 28.

Subject analysis set title	Others
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Response-guided treatment was determined by assessments of virologic

response at Weeks 4, 8, and 24. Those not meeting criteria for the other treatment groups (Cirrhotics, Poor Responders, Late Responders, or Early Responders) were classified separately (as Others) and were not treated per response-guided therapy.

Primary: Percentage of Participants With Sustained Virological Response (SVR) at 12 Weeks After End of Treatment (EOT)

End point title	Percentage of Participants With Sustained Virological Response (SVR) at 12 Weeks After End of Treatment (EOT)[1]

End point description:

SVR at 12 weeks after EOT was defined as an undetectable HCV RNA viral load obtained 12 weeks following completion of treatment. HCV RNA viral load was measured using the Roche COBAS TaqMan 2.0 HCV Test, with a lower limit of detection (LOD) of 10 to 15 international units per milliliter (IU/mL). The percentage of participants with SVR was calculated as [number of participants with undetectable HCV RNA at 12 weeks after EOT divided by the number of participants analyzed] multiplied by 100. All-Treated Population: All enrolled participants who received at least one dose of study medication. Arms were not mutually exclusive.

End point type	Primary

End point timeframe:

At 12 weeks after EOT (up to 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: The study was of an explorative nature; therefore only descriptive and exploratory statistical methods were applied, and no statistical hypothesis testing was carried out.

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	20	24	24
Units: percentage of participants				
number (confidence interval 95%)	81 (74 to 86)	70 (46 to 88)	75 (53 to 90)	88 (68 to 97)

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	19		
Units: percentage of participants				
number (confidence interval 95%)	95 (87 to 99)	32 (13 to 57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SVR at 24 Weeks After EOT

End point title	Percentage of Participants With SVR at 24 Weeks After EOT

End point description:

SVR at 24 weeks after EOT was defined as an undetectable HCV RNA viral load obtained 24 weeks following completion of treatment. HCV RNA viral load was measured using the Roche COBAS TaqMan 2.0 HCV Test, with a lower LOD of 10 to 15 IU/mL. The percentage of participants with SVR was calculated as [number of participants with undetectable HCV RNA at 24 weeks after EOT divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

At 24 weeks after EOT (up to 72 weeks)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	20	24	24
Units: percentage of participants				
number (confidence interval 95%)	80 (73 to 86)	70 (46 to 88)	71 (49 to 87)	88 (68 to 97)

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	19		
Units: percentage of participants				
number (confidence interval 95%)	95 (87 to 99)	32 (13 to 57)		

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA Levels

End point title	HCV RNA Levels

End point description:

HCV RNA levels were obtained routinely during and after treatment. Mean HCV RNA levels were calculated by averaging the HCV RNA levels among all participants analyzed at each collection timepoint and expressed in log10 IU/mL. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

At Baseline; Weeks 2, 4, 6, 8, 12, 16, 24, 28, and 36; EOT; and 12 and 24 weeks after EOT (up to 72 weeks)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165[2]	20[3]	24[4]	24[5]
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=165,20,24,24,78,19)	6.29 (± 0.722)	6.34 (± 0.71)	6.4 (± 0.592)	6.46 (± 0.53)
Week 2 (n=159,18,24,23,76,18)	4.86 (± 1.418)	5.06 (± 1.288)	6.07 (± 0.61)	5.38 (± 0.767)
Week 4 (n=158,20,24,22,75,17)	4.06 (± 1.525)	4.3 (± 1.533)	5.78 (± 0.55)	4.6 (± 0.874)
Week 6 (n=151,18,24,21,73,15)	1.75 (± 0.882)	2.01 (± 1.002)	2.7 (± 0.972)	1.91 (± 0.57)

Week 8 (n=160,20,24,24,77,15)	1.47 (± 0.638)	1.69 (± 0.65)	1.95 (± 0.874)	1.52 (± 0.329)
Week 12 (n=160,20,24,24,77,15)	1.35 (± 0.682)	1.41 (± 0.393)	1.69 (± 1.316)	1.25 (± 0.107)
Week 16 (n=156,19,22,24,78,13)	1.25 (± 0.405)	1.34 (± 0.459)	1.46 (± 0.906)	1.19 (± 0.045)
Week 24 (n=152,17,23,24,78,10)	1.41 (± 1.042)	1.8 (± 1.753)	1.83 (± 1.696)	1.18 (± 0)
Week 28 (n=143,15,19,23,76,10)	1.23 (± 0.48)	1.18 (± 0)	1.45 (± 1.173)	1.18 (± 0)
Week 36 (n=71,16,21,24,3,7)	1.69 (± 1.563)	1.54 (± 1.412)	2 (± 2.069)	1.33 (± 0.745)
EOT (n=162,20,24,23,78,17)	1.52 (± 1.12)	1.58 (± 1.167)	1.87 (± 1.563)	1.38 (± 0.996)
12 weeks after EOT (n=152,19,24,23,74,12)	1.92 (± 1.792)	2.53 (± 2.34)	2.48 (± 2.345)	1.48 (± 1.087)
24 weeks after EOT (n=159,20,23,24,78,14)	2 (± 1.874)	2.66 (± 2.351)	2.39 (± 2.327)	1.77 (± 1.605)

Notes:

[2] - number (n) equals (=) number of participants who provided evaluable data at the respective visit.

[3] - n = number of participants who provided evaluable data at the respective visit.

[4] - n = number of participants who provided evaluable data at the respective visit.

[5] - n = number of participants who provided evaluable data at the respective visit.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78[6]	19[7]		
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=165,20,24,24,78,19)	6.18 (± 0.796)	6.34 (± 0.762)		
Week 2 (n=159,18,24,23,76,18)	4.27 (± 1.441)	4.9 (± 1.597)		
Week 4 (n=158,20,24,22,75,17)	3.25 (± 1.289)	4.24 (± 1.689)		
Week 6 (n=151,18,24,21,73,15)	1.25 (± 0.154)	2.18 (± 1.337)		
Week 8 (n=160,20,24,24,77,15)	1.18 (± 0)	1.84 (± 1.236)		
Week 12 (n=160,20,24,24,77,15)	1.18 (± 0)	1.74 (± 1.292)		
Week 16 (n=156,19,22,24,78,13)	1.18 (± 0)	1.32 (± 0.458)		
Week 24 (n=152,17,23,24,78,10)	1.18 (± 0)	2.21 (± 1.916)		
Week 28 (n=143,15,19,23,76,10)	1.18 (± 0.025)	1.48 (± 0.822)		
Week 36 (n=71,16,21,24,3,7)	2.6 (± 2.466)	1.91 (± 1.93)		
EOT (n=162,20,24,23,78,17)	1.18 (± 0.025)	2.73 (± 1.943)		
12 weeks after EOT (n=152,19,24,23,74,12)	1.4 (± 0.946)	3.83 (± 2.789)		
24 weeks after EOT (n=159,20,23,24,78,14)	1.42 (± 1.053)	4.05 (± 2.592)		

Notes:

[6] - n = number of participants who provided evaluable data at the respective visit.

[7] - n = number of participants who provided evaluable data at the respective visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virological Response

End point title	Percentage of Participants With Virological Response

End point description:

HCV RNA levels were obtained routinely during and after treatment. The percentage of participants with undetectable HCV RNA viral load (ie, virological response) was calculated as [number of participants with undetectable HCV RNA at each timepoint divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:
At Weeks 2, 4, 6, 8, 12, 16, 24, 28, and 36; and EOT (up to 48 weeks)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	20	24	24
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	4 (1 to 8)	0 (0 to 17)	0 (0 to 14)	0 (0 to 14)
Week 4	7 (4 to 12)	0 (0 to 17)	0 (0 to 14)	0 (0 to 14)
Week 6	41 (34 to 49)	35 (15 to 59)	0 (0 to 14)	4 (0 to 21)
Week 8	61 (53 to 68)	45 (23 to 68)	13 (3 to 32)	0 (0 to 14)
Week 12	82 (75 to 87)	65 (41 to 85)	75 (53 to 90)	67 (45 to 84)
Week 16	87 (81 to 91)	70 (46 to 88)	71 (49 to 87)	96 (79 to 100)
Week 24	88 (82 to 92)	80 (56 to 94)	79 (58 to 93)	100 (86 to 100)
Week 28	87 (81 to 91)	80 (56 to 94)	79 (58 to 93)	96 (79 to 100)
Week 36	83 (76 to 88)	75 (51 to 91)	75 (53 to 90)	96 (79 to 100)
EOT	87 (81 to 92)	80 (56 to 94)	79 (58 to 93)	96 (79 to 100)

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	19		
Units: percentage of participants				
number (confidence interval 95%)				
Week 2	6 (2 to 14)	5 (0 to 26)		
Week 4	14 (7 to 24)	5 (0 to 26)		
Week 6	71 (59 to 80)	26 (9 to 51)		
Week 8	100 (95 to 100)	53 (29 to 76)		
Week 12	100 (95 to 100)	53 (29 to 76)		
Week 16	100 (95 to 100)	58 (33 to 80)		
Week 24	100 (95 to 100)	42 (20 to 67)		
Week 28	99 (93 to 100)	42 (20 to 67)		
Week 36	95 (87 to 99)	37 (16 to 62)		
EOT	99 (93 to 100)	47 (24 to 71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least a 1-Log, 2-Log, or 3-Log Reduction in HCV RNA

End point title	Percentage of Participants With at Least a 1-Log, 2-Log, or 3-Log Reduction in HCV RNA

End point description:

HCV RNA levels were obtained routinely during and after treatment. Reductions in HCV RNA viral load by 1-log, 2-log, or 3-log increments were determined relative to Baseline HCV RNA. Each increment represents a reduction greater than or equal to (≥) the specified log value, including results for which HCV RNA was below the limit of quantification (25 IU/mL). The percentage of participants with each log reduction in HCV RNA was calculated as [number of participants with log reduction divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 6, 8, 12, 16, 24, and 28

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	20	24	24
Units: percentage of participants				
number (confidence interval 95%)				
3-log, Week 2	12 (7 to 17)	5 (0 to 25)	0 (0 to 14)	0 (0 to 14)
3-log, Week 4	29 (22 to 37)	20 (6 to 44)	0 (0 to 14)	8 (1 to 27)
3-log, Week 6	88 (82 to 92)	85 (62 to 97)	75 (53 to 90)	92 (73 to 99)
3-log, Week 8	93 (88 to 97)	95 (75 to 100)	83 (63 to 95)	100 (86 to 100)
3-log, Week 12	95 (91 to 98)	100 (83 to 100)	88 (68 to 97)	100 (86 to 100)
3-log, Week 16	94 (89 to 97)	95 (75 to 100)	88 (68 to 97)	100 (86 to 100)
3-log, Week 24	90 (84 to 94)	80 (56 to 94)	83 (63 to 95)	100 (86 to 100)
3-log, Week 28	88 (83 to 93)	80 (56 to 94)	79 (58 to 93)	96 (79 to 100)
2-log, Week 2	27 (20 to 34)	20 (6 to 44)	0 (0 to 14)	8 (1 to 27)
2-log, Week 4	51 (43 to 59)	50 (27 to 73)	0 (0 to 14)	33 (16 to 55)
2-log, Week 6	95 (90 to 97)	95 (75 to 100)	96 (79 to 100)	96 (79 to 100)
2-log, Week 8	97 (93 to 99)	100 (83 to 100)	100 (86 to 100)	100 (86 to 100)
2-log, Week 12	95 (91 to 98)	100 (83 to 100)	88 (68 to 97)	100 (86 to 100)
2-log, Week 16	94 (89 to 97)	95 (75 to 100)	88 (68 to 97)	100 (86 to 100)
2-log, Week 24	90 (84 to 94)	80 (56 to 94)	83 (63 to 95)	100 (86 to 100)
2-log, Week 28	88 (83 to 93)	80 (56 to 94)	79 (58 to 93)	96 (79 to 100)
1-log, Week 2	55 (47 to 62)	60 (36 to 81)	0 (0 to 14)	54 (33 to 74)
1-log, Week 4	81 (74 to 86)	75 (51 to 91)	0 (0 to 14)	100 (86 to 100)
1-log, Week 6	98 (94 to 99)	95 (75 to 100)	100 (86 to 100)	100 (86 to 100)
1-log, Week 8	98 (95 to 100)	100 (83 to 100)	100 (86 to 100)	100 (86 to 100)
1-log, Week 12	96 (92 to 99)	100 (83 to 100)	96 (79 to 100)	100 (86 to 100)

1-log, Week 16	94 (89 to 97)	95 (75 to 100)	88 (68 to 97)	100 (86 to 100)
1-log, Week 24	91 (85 to 95)	80 (56 to 94)	88 (68 to 97)	100 (86 to 100)
1-log, Week 28	88 (83 to 93)	80 (56 to 94)	79 (58 to 93)	96 (79 to 100)

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	19		
Units: percentage of participants				
number (confidence interval 95%)				
3-log, Week 2	19 (11 to 30)	16 (3 to 40)		
3-log, Week 4	47 (36 to 59)	26 (9 to 51)		
3-log, Week 6	97 (91 to 100)	63 (38 to 84)		
3-log, Week 8	100 (95 to 100)	68 (43 to 87)		
3-log, Week 12	100 (95 to 100)	74 (49 to 91)		
3-log, Week 16	100 (95 to 100)	68 (43 to 87)		
3-log, Week 24	100 (95 to 100)	53 (29 to 76)		
3-log, Week 28	100 (95 to 100)	53 (29 to 76)		
2-log, Week 2	42 (31 to 54)	26 (9 to 51)		
2-log, Week 4	76 (65 to 85)	37 (16 to 62)		
2-log, Week 6	99 (93 to 100)	74 (49 to 91)		
2-log, Week 8	100 (95 to 100)	74 (49 to 91)		
2-log, Week 12	100 (95 to 100)	74 (49 to 91)		
2-log, Week 16	100 (95 to 100)	68 (43 to 87)		
2-log, Week 24	100 (95 to 100)	53 (29 to 76)		
2-log, Week 28	100 (95 to 100)	53 (29 to 76)		
1-log, Week 2	73 (62 to 82)	42 (20 to 67)		
1-log, Week 4	100 (95 to 100)	84 (60 to 97)		
1-log, Week 6	100 (95 to 100)	84 (60 to 97)		
1-log, Week 8	100 (95 to 100)	84 (60 to 97)		
1-log, Week 12	100 (95 to 100)	74 (49 to 91)		
1-log, Week 16	100 (95 to 100)	68 (43 to 87)		
1-log, Week 24	100 (95 to 100)	58 (33 to 80)		
1-log, Week 28	100 (95 to 100)	53 (29 to 76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virological Relapse Following EOT Response

End point title	Percentage of Participants With Virological Relapse Following EOT Response

End point description:

Virological relapse was defined as a detectable post-treatment HCV RNA viral load following a previously undetectable EOT level (ie, virological response). The percentage of participants with virological relapse was calculated as [number of participants meeting the above criteria divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

Up to 72 weeks (at 12 and 24 weeks after EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143[8]	16[9]	19[10]	23[11]
Units: percentage of participants				
number (confidence interval 95%)	7 (3 to 12)	13 (2 to 38)	5 (0 to 26)	9 (1 to 28)

Notes:

[8] - Only participants with a previous EOT virological response were included in the analysis.

[9] - Only participants with a previous EOT virological response were included in the analysis.

[10] - Only participants with a previous EOT virological response were included in the analysis.

[11] - Only participants with a previous EOT virological response were included in the analysis.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77[12]	8[13]		
Units: percentage of participants				
number (confidence interval 95%)	4 (1 to 11)	25 (3 to 65)		

Notes:

[12] - Only participants with a previous EOT virological response were included in the analysis.

[13] - Only participants with a previous EOT virological response were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virological Breakthrough Following On-Treatment Response

End point title	Percentage of Participants With Virological Breakthrough Following On-Treatment Response

End point description:

Virological breakthrough was defined as an HCV RNA viral load greater than (>) 1000 IU/mL following a previously undetectable level at any time during treatment (ie, virological response). Participants who ultimately achieved an EOT response were not considered for virological breakthrough. The percentage of participants with virological breakthrough was calculated as [number of participants meeting the above criteria divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

Up to 48 weeks (at Baseline; Weeks 2, 4, 6, 8, 12, 16, 24, 28, and 36; and EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	151[14]	17[15]	19[16]	24[17]
Units: percentage of participants				
number (confidence interval 95%)	3 (1 to 7)	0 (0 to 20)	0 (0 to 18)	4 (0 to 21)

Notes:

[14] - Only participants with a previous on-treatment virological response were included in the analysis.

[15] - Only participants with a previous on-treatment virological response were included in the analysis.

[16] - Only participants with a previous on-treatment virological response were included in the analysis.

[17] - Only participants with a previous on-treatment virological response were included in the analysis.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78[18]	13[19]		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 5)	23 (5 to 54)		

Notes:

[18] - Only participants with a previous on-treatment virological response were included in the analysis.

[19] - Only participants with a previous on-treatment virological response were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virological Rebound Following On-Treatment Decline in HCV RNA

End point title	Percentage of Participants With Virological Rebound Following On-Treatment Decline in HCV RNA

End point description:

Virological rebound was defined as an HCV RNA viral load >1000 IU/mL and a ≥1-log increase from nadir following a decline in HCV RNA from Baseline at any time during treatment (ie, on-treatment decline). Participants who ultimately achieved an EOT response were not considered for virological rebound. The percentage of participants with virological rebound was calculated as [number of participants meeting the above criteria divided by the number of participants analyzed] multiplied by 100.

End point type	Secondary

End point timeframe:

Up to 48 weeks (at Baseline; Weeks 2, 4, 6, 8, 12, 16, 24, 28, and 36; and EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	164[20]	20[21]	24[22]	24[23]
Units: percentage of participants				
number (confidence interval 95%)	6 (3 to 11)	5 (0 to 25)	17 (5 to 37)	4 (0 to 21)

Notes:

[20] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

[21] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

[22] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

[23] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78[24]	18[25]		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 5)	22 (6 to 48)		

Notes:

[24] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

[25] - Only participants with a previous on-treatment decline in HCV RNA were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment Discontinued Based Upon Elevated (Week 12) or Detectable (Week 24) HCV RNA

End point title	Percentage of Participants With Treatment Discontinued Based Upon Elevated (Week 12) or Detectable (Week 24) HCV RNA

End point description:

Treatment was to be discontinued for participants who met prespecified criteria, termed the futility rule, after 12 or 24 weeks of treatment. Participants were discontinued from treatment for one of the following reasons: HCV RNA viral load ≥100 IU/mL (Week 12) or a detectable HCV RNA viral load (Week 24). HCV RNA viral load was measured using the Roche COBAS TaqMan 2.0 HCV Test, with a lower LOD of 10 to 15 IU/mL. The percentage of participants with treatment discontinued for each reason was calculated as [number of participants meeting one of the above criteria divided by the number of participants analyzed] multiplied by 100. All-Treated Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

At 12 and 24 weeks

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	20	24	24
Units: percentage of participants				
number (not applicable)				
Week 12	4	10	13	0
Week 24	3	5	8	0

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78	19		
Units: percentage of participants				
number (not applicable)				
Week 12	0	11		
Week 24	0	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment With PEG-IFN, RBV, and Boceprevir

End point title	Duration of Treatment With PEG-IFN, RBV, and Boceprevir

End point description:

The duration of treatment with each study drug was determined as the time from treatment start until the last dose of PEG-IFN, RBV, or boceprevir. Median duration of treatment was determined using the actual duration of treatment among individual participants and expressed in weeks. Safety Population: All participants who received at least one dose of study medication and had at least one post-baseline safety assessment. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

Up to 48 weeks (from Baseline until EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165[26]	20[27]	24[28]	24[29]
Units: weeks				
median (full range (min-max))				
PEG-IFN (n=165,20,24,24,78,19)	28 (1 to 49)	48 (14 to 48)	48 (13 to 49)	48 (32 to 48)
RBV (n=165,20,24,24,78,19)	28 (1 to 49)	48 (13 to 48)	48 (14 to 49)	48 (30 to 49)
Boceprevir (n=164,20,24,24,78,18)	24 (1 to 45)	44 (8 to 44)	44 (10 to 45)	32 (2 to 33)

Notes:

[26] - n = number of participants who received the respective study medication.

[27] - n = number of participants who received the respective study medication.

[28] - n = number of participants who received the respective study medication.

[29] - n = number of participants who received the respective study medication.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78[30]	19[31]		
Units: weeks				
median (full range (min-max))				
PEG-IFN (n=165,20,24,24,78,19)	28 (24 to 32)	26 (1 to 48)		
RBV (n=165,20,24,24,78,19)	28 (10 to 33)	27 (1 to 48)		
Boceprevir (n=164,20,24,24,78,18)	24 (6 to 25)	10 (1 to 44)		

Notes:

[30] - n = number of participants who received the respective study medication.

[31] - n = number of participants who received the respective study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Dose Modification of PEG-IFN, RBV, or Boceprevir By Reason

End point title	Percentage of Participants With a Dose Modification of PEG-IFN, RBV, or Boceprevir By Reason

End point description:

Dose modifications for each study drug included any dose reduction, treatment interruption, or premature withdrawal. Adverse event (AE)-related reasons were documented, as well as reasons related to insufficient efficacy ('Poor efficacy') or other safety-related reasons ('Safety/other'). The percentage of participants with a dose modification documented for each reason was calculated as [number of participants with dose modification divided by the number of participants analyzed] multiplied by 100. Safety Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

Up to 48 weeks (from Baseline until EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165[32]	20[33]	24[34]	24[35]
Units: percentage of participants				
number (not applicable)				
PEG-IFN, Any reason (n=165,20,24,24,78,19)	52	60	54	46
PEG-IFN, Anemia (n=165,20,24,24,78,19)	1	0	0	0
PEG-IFN, Asthenia (n=165,20,24,24,78,19)	1	0	4	4
PEG-IFN, Nausea/vomiting (n=165,20,24,24,78,19)	0.6	0	0	0

PEG-IFN, Neutropenia (n=165,20,24,24,78,19)	36	30	38	33
PEG-IFN, Rash (n=165,20,24,24,78,19)	0.6	5	0	0
PEG-IFN, Thrombocytopenia (n=165,20,24,24,78,19)	5	35	4	0
PEG-IFN, Safety/other (n=165,20,24,24,78,19)	4	10	4	13
PEG-IFN, Poor efficacy (n=165,20,24,24,78,19)	8	15	21	4
PEG-IFN, Not specified (n=165,20,24,24,78,19)	12	0	8	13
RBV, Any reason (n=165,20,24,24,78,19)	64	65	67	46
RBV, Anemia (n=165,20,24,24,78,19)	46	50	46	38
RBV, Asthenia (n=165,20,24,24,78,19)	0.6	0	0	0
RBV, Nausea/vomiting (n=165,20,24,24,78,19)	1	0	0	0
RBV, Neutropenia (n=165,20,24,24,78,19)	3	0	0	4
RBV, Rash (n=165,20,24,24,78,19)	1	5	0	0
RBV, Safety/other (n=165,20,24,24,78,19)	8	15	8	13
RBV, Poor efficacy (n=165,20,24,24,78,19)	8	15	21	4
RBV, Not specified (n=165,20,24,24,78,19)	11	0	8	8
Boceprevir, Any reason (n=164,20,24,24,78,18)	28	45	29	21
Boceprevir, Anemia (n=164,20,24,24,78,18)	2	10	0	4
Boceprevir, Asthenia (n=164,20,24,24,78,18)	0.6	0	0	0
Boceprevir, Nausea/vomiting (n=164,20,24,24,78,18)	1	0	0	0
Boceprevir, Neutropenia (n=164,20,24,24,78,18)	4	0	0	4
Boceprevir, Rash (n=164,20,24,24,78,18)	1	5	0	0
Boceprevir, Safety/other (n=164,20,24,24,78,18)	4	10	0	4
Boceprevir, Poor efficacy (n=164,20,24,24,78,18)	7	15	21	0
Boceprevir, Not specified (n=164,20,24,24,78,18)	12	10	8	8

Notes:

[32] - n = number of participants who received the respective study medication.

[33] - n = number of participants who received the respective study medication.

[34] - n = number of participants who received the respective study medication.

[35] - n = number of participants who received the respective study medication.

End point values	Early Responders	Others		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	78[36]	19[37]		
Units: percentage of participants				
number (not applicable)				
PEG-IFN, Any reason (n=165,20,24,24,78,19)	42	84		

PEG-IFN, Anemia (n=165,20,24,24,78,19)	1	5		
PEG-IFN, Asthenia (n=165,20,24,24,78,19)	0	0		
PEG-IFN, Nausea/vomiting (n=165,20,24,24,78,19)	1	0		
PEG-IFN, Neutropenia (n=165,20,24,24,78,19)	36	47		
PEG-IFN, Rash (n=165,20,24,24,78,19)	0	0		
PEG-IFN, Thrombocytopenia (n=165,20,24,24,78,19)	1	0		
PEG-IFN, Safety/other (n=165,20,24,24,78,19)	0	0		
PEG-IFN, Poor efficacy (n=165,20,24,24,78,19)	0	21		
PEG-IFN, Not specified (n=165,20,24,24,78,19)	8	42		
RBV, Any reason (n=165,20,24,24,78,19)	62	89		
RBV, Anemia (n=165,20,24,24,78,19)	53	26		
RBV, Asthenia (n=165,20,24,24,78,19)	1	0		
RBV, Nausea/vomiting (n=165,20,24,24,78,19)	0	11		
RBV, Neutropenia (n=165,20,24,24,78,19)	0	21		
RBV, Rash (n=165,20,24,24,78,19)	0	5		
RBV, Safety/other (n=165,20,24,24,78,19)	3	16		
RBV, Poor efficacy (n=165,20,24,24,78,19)	0	21		
RBV, Not specified (n=165,20,24,24,78,19)	8	42		
Boceprevir, Any reason (n=164,20,24,24,78,18)	12	89		
Boceprevir, Anemia (n=164,20,24,24,78,18)	0	0		
Boceprevir, Asthenia (n=164,20,24,24,78,18)	1	0		
Boceprevir, Nausea/vomiting (n=164,20,24,24,78,18)	0	11		
Boceprevir, Neutropenia (n=164,20,24,24,78,18)	0	28		
Boceprevir, Rash (n=164,20,24,24,78,18)	0	6		
Boceprevir, Safety/other (n=164,20,24,24,78,18)	0	17		
Boceprevir, Poor efficacy (n=164,20,24,24,78,18)	0	17		
Boceprevir, Not specified (n=164,20,24,24,78,18)	10	28		

Notes:

[36] - n = number of participants who received the respective study medication.

[37] - n = number of participants who received the respective study medication.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Receiving Target Administrations of PEG-IFN, RBV, and Boceprevir

End point title	Percentage of Participants Receiving Target Administrations of PEG-IFN, RBV, and Boceprevir

End point description:

The frequency of missed treatments was examined using the number of administrations received as a percentage of target administrations for each study drug. The maximum number of possible administrations was considered in terms of once-weekly injections with PEG-IFN and in terms of treatment days with RBV and boceprevir. The percentage of target administrations each participant received was separated into ranges of <60%, 60 to <80%, 80 to <95%, and ≥95% for each study drug. The percentage of participants who received each range of target administrations was calculated as [number of participants in each range divided by the number of participants analyzed] multiplied by 100. Safety Population. Arms were not mutually exclusive.

End point type	Secondary

End point timeframe:

Up to 48 weeks (from Baseline until EOT)

End point values	Total Population	Cirrhotics	Poor Responders	Late Responders
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	146[38]	20[39]	24[40]	24[41]
Units: percentage of participants				
number (not applicable)				
PEG-IFN, <60%	8	25	25	0
PEG-IFN, 60 to <80%	0.7	0	0	4
PEG-IFN, 80 to <95%	5	5	0	17
PEG-IFN, 95% or more	86	70	75	79
RBV, <60%	9	25	25	4
RBV, 60 to <80%	0.7	0	0	4
RBV, 80 to <95%	5	10	0	8
RBV, 95% or more	86	65	75	83
Boceprevir, <60%	10	30	25	8
Boceprevir, 60 to <80%	0.7	5	0	0
Boceprevir, 80 to <95%	3	5	0	4
Boceprevir, 95% or more	86	60	75	88

Notes:

[38] - Only participants providing evaluable data were included in the analysis.

[39] - Only participants providing evaluable data were included in the analysis.

[40] - Only participants providing evaluable data were included in the analysis.

[41] - Only participants providing evaluable data were included in the analysis.

End point values	Early Responders			
Subject group type	Subject analysis set			
Number of subjects analysed	78[42]			
Units: percentage of participants				
number (not applicable)				
PEG-IFN, <60%	0			
PEG-IFN, 60 to <80%	0			
PEG-IFN, 80 to <95%	4			
PEG-IFN, 95% or more	96			
RBV, <60%	1			
RBV, 60 to <80%	0			
RBV, 80 to <95%	4			

RBV, 95% or more	95			
Boceprevir, <60%	1			
Boceprevir, 60 to <80%	0			
Boceprevir, 80 to <95%	3			
Boceprevir, 95% or more	96			

Notes:

[42] - Only participants providing evaluable data were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With a Safety-Related Dose Modification

End point title	Number of Participants With a Safety-Related Dose Modification

End point description:

Dose modifications for each study drug included any dose reduction, treatment interruption, or premature withdrawal. The percentage of participants with a safety-related dose modification (eg, modification due to adverse event or laboratory abnormality) of any study drug was calculated as [number of participants with dose modification divided by the number of participants analyzed] multiplied by 100. Safety Population.

End point type	Secondary

End point timeframe:

Up to 48 weeks (from Baseline until EOT)

End point values	Total Population			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: participants	113			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Safety-Related Dose Modification

End point title	Time to Safety-Related Dose Modification

End point description:

Dose modifications for each study drug included any dose reduction, treatment interruption, or premature withdrawal. Median time to safety-related dose modification (eg, modification due to adverse event or laboratory abnormality) of any study drug was estimated using Kaplan-Meier and expressed in weeks. Safety Population.

End point type	Secondary

End point timeframe:

Up to 48 weeks (from Baseline until EOT)

End point values	Total Population			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: weeks				
median (confidence interval 95%)	12.1 (10.3 to 16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Using Concomitant Hematopoietic Stimulants During Treatment and Follow-Up

End point title	Percentage of Participants Using Concomitant Hematopoietic Stimulants During Treatment and Follow-Up

End point description:

Use of concomitant hematopoietic stimulants (such as epoetin) during the 48-week treatment period and/or within 24 weeks of follow-up was documented. The percentage of participants using concomitant hematopoietic stimulants was calculated as [number of participants reporting concomitant use divided by the number of participants analyzed] multiplied by 100. Safety Population.

End point type	Secondary

End point timeframe:

Up to 72 weeks (from Baseline until 24 weeks after EOT)

End point values	Total Population			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of participants				
number (not applicable)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Concomitant Disease Prior to or During the Study

End point title	Percentage of Participants With a Concomitant Disease Prior to or During the Study

End point description:

The prevalence of concomitant disease at any time from Screening through the end of follow-up was documented. The percentage of participants with a concomitant disease was calculated as [number of participants reporting or diagnosed with concomitant disease divided by the number of participants analyzed] multiplied by 100. Diseases documented for ≥5% of participants included hypertension, diabetes mellitus, hypothyroidism, and vitamin D deficiency as reported here. Safety Population.

End point type	Secondary

End point timeframe:

Up to 76 weeks (from Screening until 24 weeks after EOT)

End point values	Total Population			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of participants				
number (not applicable)				
Any disease	53			
Hypertension	18			
Diabetes mellitus	8			
Hypothyroidism	6			
Vitamin D deficiency	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Using Concomitant Medications During Treatment and Follow-Up

End point title	Percentage of Participants Using Concomitant Medications During Treatment and Follow-Up

End point description:

Use of concomitant prescription or nonprescription medications during the 48-week treatment period and/or within 24 weeks of follow-up was documented. The percentage of participants using concomitant medications was calculated as [number of participants reporting concomitant use divided by the number of participants analyzed] multiplied by 100. Medication classes reported by >10% of participants included analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), antihistamines, corticosteroids, proton pump inhibitors, vitamins and minerals, and beta-adrenoceptor blocking agents as reported here. Safety Population.

End point type	Secondary

End point timeframe:

Up to 72 weeks (from Baseline until 24 weeks after EOT)

End point values	Total Population			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of participants				
number (not applicable)				
Any medication	79			
Analgesics	29			
NSAIDs	22			
Antihistamines	19			
Corticosteroids	19			

Proton pump inhibitors	17			
Vitamins and minerals	12			
Beta-adrenoceptor blocking agents	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 72 weeks (from Baseline until 24 weeks after EOT)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Cirrhotics (Safety)

Reporting group description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Those with undetectable HCV RNA at Weeks 8 and 24 stopped treatment at Week 28. Those with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 continued triple therapy until Week 36 and received dual therapy from Week 36 to 48. Those with a <1-log decrease in HCV RNA at Week 4 continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated. Participants with compensated cirrhosis, regardless of response, received triple therapy until Week 48. Participants with liver cirrhosis were grouped separately in the safety analysis.

Reporting group title	Noncirrhotics (Safety)

Reporting group description:

Treatment-naive participants with CHC received treatment with PEG-IFN 180 mcg SC once weekly, weight-based RBV 1000 to 1200 mg PO daily in 2 divided doses, and boceprevir 800 mg PO every 7 to 9 hours. Participants received dual therapy with PEG-IFN and RBV from Week 0 to 4, and triple therapy was initiated at Week 4. Those with undetectable HCV RNA at Weeks 8 and 24 stopped treatment at Week 28. Those with detectable HCV RNA at Week 8 but undetectable HCV RNA at Week 24 continued triple therapy until Week 36 and received dual therapy from Week 36 to 48. Those with a <1-log decrease in HCV RNA at Week 4 continued triple therapy until Week 48, with optional dual therapy from Week 32 to 48 if triple therapy was not tolerated. Participants with compensated cirrhosis, regardless of response, received triple therapy until Week 48. Participants without liver cirrhosis, including those with transition to cirrhosis, were grouped separately in the safety analysis.

Serious adverse events	Cirrhotics (Safety)	Noncirrhotics (Safety)	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 21 (33.33%)	8 / 144 (5.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic neoplasm			
subjects affected / exposed	1 / 21 (4.76%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			

subjects affected / exposed	1 / 21 (4.76%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
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	2 / 21 (9.52%)	2 / 144 (1.39%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 144 (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			
Fatigue			

subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	2 / 21 (9.52%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Epididymitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cirrhotics (Safety)	Noncirrhotics (Safety)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	135 / 144 (93.75%)	

Investigations			
Weight decreased			
subjects affected / exposed	2 / 21 (9.52%)	8 / 144 (5.56%)	
occurrences (all)	2	8	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 21 (9.52%)	4 / 144 (2.78%)	
occurrences (all)	2	4	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	6 / 21 (28.57%)	45 / 144 (31.25%)	
occurrences (all)	6	46	
Headache			
subjects affected / exposed	2 / 21 (9.52%)	32 / 144 (22.22%)	
occurrences (all)	2	46	
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)	13 / 144 (9.03%)	
occurrences (all)	1	13	
Somnolence			
subjects affected / exposed	2 / 21 (9.52%)	4 / 144 (2.78%)	
occurrences (all)	2	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 21 (33.33%)	40 / 144 (27.78%)	
occurrences (all)	7	47	
Influenza like illness			
subjects affected / exposed	6 / 21 (28.57%)	34 / 144 (23.61%)	
occurrences (all)	6	37	
Fatigue			
subjects affected / exposed	4 / 21 (19.05%)	31 / 144 (21.53%)	
occurrences (all)	4	36	
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	26 / 144 (18.06%)	
occurrences (all)	0	38	
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	5 / 21 (23.81%)	47 / 144 (32.64%)	
occurrences (all)	5	65	
Anaemia			
subjects affected / exposed	7 / 21 (33.33%)	57 / 144 (39.58%)	
occurrences (all)	7	59	
Thrombocytopenia			
subjects affected / exposed	6 / 21 (28.57%)	13 / 144 (9.03%)	
occurrences (all)	6	14	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 21 (14.29%)	23 / 144 (15.97%)	
occurrences (all)	3	24	
Diarrhoea			
subjects affected / exposed	4 / 21 (19.05%)	15 / 144 (10.42%)	
occurrences (all)	4	16	
Dyspepsia			
subjects affected / exposed	3 / 21 (14.29%)	11 / 144 (7.64%)	
occurrences (all)	3	11	
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)	8 / 144 (5.56%)	
occurrences (all)	1	10	
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	9 / 144 (6.25%)	
occurrences (all)	0	10	
Gastritis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 144 (1.39%)	
occurrences (all)	2	2	
Stomatitis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 144 (1.39%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 21 (14.29%)	31 / 144 (21.53%)	
occurrences (all)	3	34	
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	4 / 21 (19.05%)	30 / 144 (20.83%)	
occurrences (all)	4	31	
Rash			
subjects affected / exposed	3 / 21 (14.29%)	19 / 144 (13.19%)	
occurrences (all)	4	22	
Alopecia			
subjects affected / exposed	1 / 21 (4.76%)	19 / 144 (13.19%)	
occurrences (all)	1	19	
Dry skin			
subjects affected / exposed	0 / 21 (0.00%)	8 / 144 (5.56%)	
occurrences (all)	0	8	
Erythema			
subjects affected / exposed	2 / 21 (9.52%)	5 / 144 (3.47%)	
occurrences (all)	2	5	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 21 (14.29%)	17 / 144 (11.81%)	
occurrences (all)	3	20	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 21 (4.76%)	13 / 144 (9.03%)	
occurrences (all)	1	23	
Arthralgia			
subjects affected / exposed	1 / 21 (4.76%)	13 / 144 (9.03%)	
occurrences (all)	1	14	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 21 (4.76%)	13 / 144 (9.03%)	
occurrences (all)	1	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported