



Clinical trial results:

A phase III randomised, partially double-blind and placebo controlled study of BI 207127 in combination with faldaprevir and ribavirin for chronic genotype 1 hepatitis C infection in an extended population of treatment naïve patients that includes those ineligible to receive peginterferon. This trial was prematurely discontinued due to discontinuation of the deleobuvir (DBV) drug development program.

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-003535-27
Trial protocol	BE DE PT GB ES GR IT
Global end of trial date	15 January 2015

Results information

Result version number	v1 (current)
This version publication date	05 May 2016
First version publication date	05 May 2016

Trial information

Trial identification

Sponsor protocol code	1241.36
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01728324
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	173 Binger Strasse, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, 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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2014
Global end of trial reached?	Yes
Global end of trial date	15 January 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The aim of the study was to confirm efficacy and safety of treatment with 600 mg of BID (twice daily) deleobuvir (DBV) in combination with 120 mg (milligram) QD (once a day) faldaprevir (FDV) and ribavirin (RBV) for 16 or 24 weeks in chronically infected hepatitis C virus (HCV) GT1b treatment-naïve patients, including patients with compensated cirrhosis.

The primary objective was to determine if a minimum historical target SVR12 rate of 71% for pegylated interferon-alfa (PegIFN)-eligible patients and 50% for PegIFN-ineligible patients could be achieved by the combination treatments of DBV, FDV and RBV in GT1b patients, including patients with compensated cirrhosis. The comparison with historical control was framed as a statistical superiority test.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 53
Country: Number of subjects enrolled	Belgium: 61
Country: Number of subjects enrolled	Canada: 64
Country: Number of subjects enrolled	France: 55
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Greece: 29
Country: Number of subjects enrolled	Italy: 132
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Portugal: 24
Country: Number of subjects enrolled	Spain: 73
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	United States: 167

Worldwide total number of subjects	755
EEA total number of subjects	465

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)	650
From 65 to 84 years	105
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 subjects) 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	Termination of DBV
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

Groups 1 (24-wk NC) and Group 2 (16-wk NC) were double-blinded to treatment duration and Group 3 (24-wk CR) was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	24-wk non-cirrhotic (NC) treatment group 1

Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 24 weeks.

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

Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 24 weeks.

Investigational medicinal product name	faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily in non-cirrhotic patients for 24 weeks.

Arm title	16-wk non-cirrhotic (NC) treatment group 2
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Arm description:

Matching placebo to DBV, matching placebo to FDV and matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to DBV for 8 weeks followed by 600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 16 weeks.

Investigational medicinal product name	faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to FDV for 8 weeks followed by 120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily for 16 weeks.

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

Dosage and administration details:

Matching placebo to RBV for 8 weeks followed by 500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 16 weeks.

Arm title	24-wk cirrhotic (CR) treatment group 3
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Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in cirrhotic patients for 24 weeks.

Investigational medicinal product name	faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily in cirrhotic patients for 24 weeks.

Investigational medicinal product name	ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
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Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in cirrhotic patients for 24 weeks.

Number of subjects in period 1^[1]	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Started	211	213	72
Completed	173	177	58
Not completed	38	36	14
Consent withdrawn by subject	9	6	2
Adverse Event (Placebo Period)	-	1	-
Adverse event, non-fatal	14	13	4
Lack of efficacy	14	12	8
Other than stated above	1	3	-
Protocol Violation (Placebo Period)	-	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 the patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

Period 2

Period 2 title	Termination of FDV
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Groups 1 (24-wk NC) and Group 2 (16-wk NC) were double-blinded to treatment duration and Group 3 (24-wk CR) was open-label.

Arms

Are arms mutually exclusive?	No
Arm title	24-wk non-cirrhotic (NC) treatment group 1

Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 24 weeks.

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

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily mg in non-cirrhotic patients for 24 weeks.

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

Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 24 weeks.

Arm title	16-wk non-cirrhotic (NC) treatment group 2
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Arm description:

Matching placebo to DBV, matching placebo to FDV and Matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to DBV for 8 weeks followed by 600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 16 weeks.

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

Dosage and administration details:

Matching placebo to RBV for 8 weeks followed by 500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 16 weeks.

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

Dosage and administration details:

Matching placebo to FDV for 8 weeks followed by 120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily for 16 weeks.

Arm title	24-wk cirrhotic (CR) treatment group 3
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Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.

Arm type	Experimental
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Investigational medicinal product name	faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily mg in cirrhotic patients for 24 weeks.

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

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in cirrhotic patients for 24 weeks.

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

Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in cirrhotic patients for 24 weeks.

Number of subjects in period 2	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Started	211	213	72
Completed	173	177	58
Not completed	38	36	14
Consent withdrawn by subject	9	6	2
Adverse Event (Placebo Period)	-	1	-
Adverse event, non-fatal	14	13	4
Lack of efficacy	14	12	8
Other than stated above	1	3	-
Protocol Violation (Placebo Period)	-	1	-

Period 3

Period 3 title	Termination of RBV
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Groups 1 (24-wk NC) and Group 2 (16-wk NC) were double-blinded to treatment duration and Group 3 (24-wk CR) was open-label.

Arms

Are arms mutually exclusive?	No
Arm title	24-wk non-cirrhotic (NC) treatment group 1

Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 24 weeks.

Investigational medicinal product name	ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Oral use

Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 24 weeks.

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

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily mg in non-cirrhotic patients for 24 weeks.

Arm title	16-wk non-cirrhotic (NC) treatment group 2
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Arm description:

Matching placebo to DBV, Matching placebo to FDV and Matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to DBV for 8 weeks followed by 600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in non-cirrhotic patients for 16 weeks.

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

Dosage and administration details:

Matching placebo to RBV for 8 weeks followed by 500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in non-cirrhotic patients for 16 weeks.

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

Dosage and administration details:

Matching placebo to FDV for 8 weeks followed by 120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily for 16 weeks.

Arm title	24-wk cirrhotic (CR) treatment group 3
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Arm description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.

Arm type	Experimental
Investigational medicinal product name	deleobuvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg deleobuvir (DBV) tablet was administered twice daily for a total daily dose of 1200 mg in cirrhotic patients for 24 weeks.

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

Dosage and administration details:

120 mg faldaprevir (FDV) Soft gelatin capsule was administered once daily mg in cirrhotic patients for 24 weeks.

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

Dosage and administration details:

500 mg or 600 mg ribavirin (RBV) tablet twice daily for a total daily dose of 1000 mg (<75 kg body weight) or 1200 mg (≥ 75 kg body weight) in cirrhotic patients for 24 weeks.

Number of subjects in period 3	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Started	211	213	72
Completed	172	176	57
Not completed	39	37	15
Consent withdrawn by subject	9	5	2
Adverse Event (Placebo Period)	-	1	-

Adverse event, non-fatal	15	16	5
Lack of efficacy	14	11	7
Other than stated above	1	3	1
Protocol Violation (Placebo Period)	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	24-wk non-cirrhotic (NC) treatment group 1
Reporting group description:	24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.
Reporting group title	16-wk non-cirrhotic (NC) treatment group 2
Reporting group description:	Matching placebo to DBV, matching placebo to FDV and matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.
Reporting group title	24-wk cirrhotic (CR) treatment group 3
Reporting group description:	24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.

Reporting group values	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Number of subjects	211	213	72
Age categorical			
Units: Subjects			

Age Continuous			
Full Analysis Set (FAS): This analysis set includes all randomized patients who were dispensed study medication and were documented to have taken at least one dose of any study medication, either active or placebo.			
Units: years			
arithmetic mean	50.3	50.5	58
standard deviation	± 12.5	± 12.3	± 8.8
Gender, Male/Female			
Units: Participants			
Female	108	120	27
Male	103	93	45

Reporting group values	Total		
Number of subjects	496		
Age categorical			
Units: Subjects			

Age Continuous			
Full Analysis Set (FAS): This analysis set includes all randomized patients who were dispensed study medication and were documented to have taken at least one dose of any study medication, either active or placebo.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: Participants			
Female	255		
Male	241		

End points

End points reporting groups

Reporting group title	24-wk non-cirrhotic (NC) treatment group 1
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.	
Reporting group title	16-wk non-cirrhotic (NC) treatment group 2
Reporting group description: Matching placebo to DBV, matching placebo to FDV and matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.	
Reporting group title	24-wk cirrhotic (CR) treatment group 3
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.	
Reporting group title	24-wk non-cirrhotic (NC) treatment group 1
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.	
Reporting group title	16-wk non-cirrhotic (NC) treatment group 2
Reporting group description: Matching placebo to DBV, matching placebo to FDV and Matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.	
Reporting group title	24-wk cirrhotic (CR) treatment group 3
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.	
Reporting group title	24-wk non-cirrhotic (NC) treatment group 1
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.	
Reporting group title	16-wk non-cirrhotic (NC) treatment group 2
Reporting group description: Matching placebo to DBV, Matching placebo to FDV and Matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.	
Reporting group title	24-wk cirrhotic (CR) treatment group 3
Reporting group description: 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.	
Subject analysis set title	24-wk non-cirrhotic (NC)+24-wk Cirrhotic (CR) treatment group
Subject analysis set type	Full analysis
Subject analysis set description: The subject analysis type is infact Modified full analysis set (mFAS). 24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic and cirrhotic patients.	
Subject analysis set title	16-wk non-cirrhotic (NC)+24-wk cirrhotic (CR) treatment group
Subject analysis set type	Full analysis
Subject analysis set description: The subject analysis type is infact Modified full analysis set (mFAS). This is the combination of 16 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients and for 24 weeks in cirrhotic patients	

Primary: SVR12 rates with historical control

End point title	SVR12 rates with historical control ^[1]
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End point description:

Sustained Virologic Response at Week 12 post-treatment (SVR12): Plasma Hepatitis C virus (HCV) RNA (Ribonucleic acid) level <25 IU/mL (international Unit/ milliliter) at 12 weeks after end of treatment (EOT). SVR12, was assessed based on the observed HCV RNA result taken at least 10 weeks after treatment discontinuation. This definition was also applied to patients who discontinued treatment early: if the patient had HCV RNA undetected at least 10 weeks after stopping all treatment, they were considered a responder in the primary analysis. This is the primary analyses of the primary endpoint. The Number of Participants Analyzed are actually Adjusted Number of Participant Analyzed. Modified full analysis set (mFAS): included patients in the full analysis set (FAS) who received at least one dose of active treatment.

End point type	Primary
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End point timeframe:

12 Week (post-treatment)

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 Primary outcome measure reporting statistical analysis for one group are defined and analysed for trial 1241.36, however due to the platform limitations those could not be provided. Results can be found on CT.gov study number: NCT01728324.

End point values	24-wk non-cirrhotic (NC)+24-wk Cirrhotic (CR) treatment group	16-wk non-cirrhotic (NC)+24-wk cirrhotic (CR) treatment group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	283 ^[2]	283 ^[3]		
Units: percentage of participants				
number (not applicable)				
PegIFN eligible	79.95	76.68		
PegIFN ineligible	88.28	70.78		

Notes:

[2] - Modified full analysis set (mFAS)

[3] - Modified full analysis set (mFAS)

Statistical analyses

No statistical analyses for this end point

Primary: Comparisons of SVR12 rates across treatment arms

End point title	Comparisons of SVR12 rates across treatment arms
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End point description:

Sustained Virologic Response rates across treatment arms at Week 12 post-treatment (SVR12). This is the secondary analyses of the primary endpoint.

End point type	Primary
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End point timeframe:

12 Week (post-treatment)

End point values	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	211 ^[4]	213 ^[5]	72 ^[6]	
Units: Percentage of participants				
number (confidence interval 95%)	82 (76.8 to 87.2)	75.6 (69.8 to 81.4)	73.6 (63.4 to 83.8)	

Notes:

[4] - FAS

[5] - FAS

[6] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Koch's stratum-adjusted Mantel Haenszel methods were used to compare durations, adjusting for stratification factors.	
Comparison groups	16-wk non-cirrhotic (NC) treatment group 2 v 24-wk non-cirrhotic (NC) treatment group 1
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0532 ^[7]
Method	Koch's method
Parameter estimate	SVR12 Rates difference
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	14.2

Notes:

[7] - Adjusted for PegIFN eligibility using Koch's method, with continuity correction.

Secondary: SVR4: Plasma HCV RNA level <25 IU/mL at 4 weeks after EOT.

End point title	SVR4: Plasma HCV RNA level <25 IU/mL at 4 weeks after EOT.
End point description:	
SVR4: Plasma HCV RNA level <25 IU/mL at 4 weeks after EOT.	
End point type	Secondary
End point timeframe:	
4 weeks (after End Of Treatment)	

End point values	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	211 ^[8]	213 ^[9]	72 ^[10]	
Units: percentage of participants				
number (confidence interval)	83.9 (78.9 to 88.8)	80.3 (74.9 to 85.6)	77.8 (68.2 to 87.4)	

Notes:

[8] - FAS

[9] - FAS

[10] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Koch's stratum-adjusted Mantel Haenszel methods were used to compare durations, adjusting for stratification factors.	
Comparison groups	24-wk non-cirrhotic (NC) treatment group 1 v 16-wk non-cirrhotic (NC) treatment group 2
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1671 ^[11]
Method	Koch's method
Parameter estimate	SVR4 Rates difference
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	10.9

Notes:

[11] - Adjusted for PegIFN eligibility using Koch's method, with continuity correction.

Secondary: SVR24: Plasma HCV RNA level <25 IU/mL at 24 weeks after EOT.

End point title	SVR24: Plasma HCV RNA level <25 IU/mL at 24 weeks after EOT.
End point description:	
SVR24: Plasma HCV RNA level <25 IU/mL at 24 weeks after EOT.	
End point type	Secondary
End point timeframe:	
4 weeks (after End Of Treatment)	

End point values	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	211 ^[12]	213 ^[13]	72 ^[14]	
Units: percentage of participants				
number (confidence interval 95%)	81 (75.8 to 86.3)	74.2 (68.3 to 80.1)	72.2 (61.9 to 82.6)	

Notes:

[12] - FAS

[13] - FAS

[14] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Koch's stratum-adjusted Mantel Haenszel methods were used to compare durations, adjusting for stratification factors.	
Comparison groups	24-wk non-cirrhotic (NC) treatment group 1 v 16-wk non-cirrhotic (NC) treatment group 2
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0447 ^[15]
Method	Koch's method
Parameter estimate	SVR24 Rates difference
Point estimate	-6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	1.1

Notes:

[15] - Adjusted for PegIFN eligibility using Koch's method, with continuity correction.

Secondary: Prognostic value of SVR12 predicting SVR24

End point title	Prognostic value of SVR12 predicting SVR24
End point description:	
The positive predictive value of SVR12 predicting SVR24 are the patients with an SVR12 (=YES) and the SVR24 was assessed.	
End point type	Secondary
End point timeframe:	
24 Week (post-treatment)	

End point values	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	211 ^[16]	213 ^[17]	72 ^[18]	
Units: Percentage of participants				
number (not applicable)	99	99	98	

Notes:

[16] - FAS

[17] - FAS

[18] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first drug administration until 28 days after the last drug administration.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	24-wk non-cirrhotic (NC) treatment group 1
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Reporting group description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in non-cirrhotic patients.

Reporting group title	16-wk non-cirrhotic (NC) treatment group 2
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Reporting group description:

Matching placebo to DBV, matching placebo to FDV and matching placebo to RBV for 8 weeks followed by 600mg BID DBV in combination with 120mg FDV plus RBV for 16 weeks in non-cirrhotic patients.

Reporting group title	24-wk cirrhotic (CR) treatment group 3
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Reporting group description:

24 weeks of treatment with 600mg BID deleobuvir (DBV) in combination with 120mg QD faldaprevir (FDV) plus ribavirin (RBV) in cirrhotic patients.

Serious adverse events	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 211 (3.32%)	12 / 213 (5.63%)	8 / 72 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Malaise			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Psychiatric disorders			
Bipolar I disorder			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Depression			
subjects affected / exposed	1 / 211 (0.47%)	2 / 213 (0.94%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			

subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Suicide attempt			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Jaw fracture			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 211 (0.47%)	2 / 213 (0.94%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytosis			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 211 (0.00%)	2 / 213 (0.94%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
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 haemorrhage			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Portal hypertensive gastropathy			

subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 211 (0.00%)	2 / 213 (0.94%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	0 / 72 (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
Photosensitivity reaction			
subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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
Renal failure acute			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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			
Cellulitis			

subjects affected / exposed	0 / 211 (0.00%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 211 (0.47%)	0 / 213 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 211 (0.00%)	1 / 213 (0.47%)	0 / 72 (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

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

Non-serious adverse events	24-wk non-cirrhotic (NC) treatment group 1	16-wk non-cirrhotic (NC) treatment group 2	24-wk cirrhotic (CR) treatment group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	198 / 211 (93.84%)	202 / 213 (94.84%)	66 / 72 (91.67%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	43 / 211 (20.38%)	34 / 213 (15.96%)	18 / 72 (25.00%)
occurrences (all)	45	34	20
Fatigue			
subjects affected / exposed	74 / 211 (35.07%)	73 / 213 (34.27%)	26 / 72 (36.11%)
occurrences (all)	79	82	26
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 211 (6.64%)	20 / 213 (9.39%)	7 / 72 (9.72%)
occurrences (all)	15	22	7
Dyspnoea			
subjects affected / exposed	18 / 211 (8.53%)	11 / 213 (5.16%)	6 / 72 (8.33%)
occurrences (all)	19	12	6
Psychiatric disorders			
Anxiety			

subjects affected / exposed occurrences (all)	8 / 211 (3.79%) 8	21 / 213 (9.86%) 21	6 / 72 (8.33%) 6
Depression subjects affected / exposed occurrences (all)	16 / 211 (7.58%) 16	9 / 213 (4.23%) 9	4 / 72 (5.56%) 4
Insomnia subjects affected / exposed occurrences (all)	35 / 211 (16.59%) 37	25 / 213 (11.74%) 25	10 / 72 (13.89%) 10
Irritability subjects affected / exposed occurrences (all)	8 / 211 (3.79%) 8	8 / 213 (3.76%) 8	4 / 72 (5.56%) 4
Investigations Weight decreased subjects affected / exposed occurrences (all)	19 / 211 (9.00%) 19	11 / 213 (5.16%) 11	6 / 72 (8.33%) 6
Injury, poisoning and procedural complications Sunburn subjects affected / exposed occurrences (all)	13 / 211 (6.16%) 13	14 / 213 (6.57%) 14	3 / 72 (4.17%) 3
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	19 / 211 (9.00%) 22	21 / 213 (9.86%) 22	6 / 72 (8.33%) 6
Dysgeusia subjects affected / exposed occurrences (all)	14 / 211 (6.64%) 15	8 / 213 (3.76%) 8	5 / 72 (6.94%) 6
Headache subjects affected / exposed occurrences (all)	33 / 211 (15.64%) 36	46 / 213 (21.60%) 52	5 / 72 (6.94%) 6
Paraesthesia subjects affected / exposed occurrences (all)	15 / 211 (7.11%) 17	17 / 213 (7.98%) 17	3 / 72 (4.17%) 3
Tremor subjects affected / exposed occurrences (all)	2 / 211 (0.95%) 2	2 / 213 (0.94%) 2	5 / 72 (6.94%) 5
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	26 / 211 (12.32%) 26	22 / 213 (10.33%) 23	13 / 72 (18.06%) 15
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	8 / 211 (3.79%) 8	6 / 213 (2.82%) 6	5 / 72 (6.94%) 5
Eye disorders Ocular icterus subjects affected / exposed occurrences (all)	27 / 211 (12.80%) 30	16 / 213 (7.51%) 16	2 / 72 (2.78%) 2
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	6 / 211 (2.84%) 8	8 / 213 (3.76%) 9	7 / 72 (9.72%) 7
Abdominal pain subjects affected / exposed occurrences (all)	16 / 211 (7.58%) 17	16 / 213 (7.51%) 17	4 / 72 (5.56%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	26 / 211 (12.32%) 28	19 / 213 (8.92%) 20	7 / 72 (9.72%) 8
Constipation subjects affected / exposed occurrences (all)	22 / 211 (10.43%) 22	16 / 213 (7.51%) 17	12 / 72 (16.67%) 12
Diarrhoea subjects affected / exposed occurrences (all)	59 / 211 (27.96%) 73	54 / 213 (25.35%) 63	24 / 72 (33.33%) 28
Dyspepsia subjects affected / exposed occurrences (all)	26 / 211 (12.32%) 27	26 / 213 (12.21%) 29	13 / 72 (18.06%) 14
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	9 / 211 (4.27%) 10	5 / 213 (2.35%) 5	4 / 72 (5.56%) 4
Nausea subjects affected / exposed occurrences (all)	129 / 211 (61.14%) 153	121 / 213 (56.81%) 139	41 / 72 (56.94%) 45
Vomiting			

subjects affected / exposed occurrences (all)	69 / 211 (32.70%) 91	64 / 213 (30.05%) 84	25 / 72 (34.72%) 40
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	8 / 211 (3.79%)	6 / 213 (2.82%)	7 / 72 (9.72%)
occurrences (all)	8	6	7
Jaundice			
subjects affected / exposed	27 / 211 (12.80%)	15 / 213 (7.04%)	18 / 72 (25.00%)
occurrences (all)	31	16	19
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	15 / 211 (7.11%)	3 / 213 (1.41%)	3 / 72 (4.17%)
occurrences (all)	15	3	3
Dry skin			
subjects affected / exposed	18 / 211 (8.53%)	12 / 213 (5.63%)	5 / 72 (6.94%)
occurrences (all)	18	12	5
Erythema			
subjects affected / exposed	33 / 211 (15.64%)	39 / 213 (18.31%)	10 / 72 (13.89%)
occurrences (all)	36	41	13
Photosensitivity reaction			
subjects affected / exposed	38 / 211 (18.01%)	26 / 213 (12.21%)	6 / 72 (8.33%)
occurrences (all)	42	27	6
Pruritus			
subjects affected / exposed	47 / 211 (22.27%)	47 / 213 (22.07%)	23 / 72 (31.94%)
occurrences (all)	50	52	24
Rash			
subjects affected / exposed	43 / 211 (20.38%)	39 / 213 (18.31%)	10 / 72 (13.89%)
occurrences (all)	63	52	11
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 211 (4.74%)	6 / 213 (2.82%)	6 / 72 (8.33%)
occurrences (all)	10	6	6
Muscle spasms			
subjects affected / exposed	11 / 211 (5.21%)	8 / 213 (3.76%)	2 / 72 (2.78%)
occurrences (all)	11	8	2
Myalgia			

subjects affected / exposed occurrences (all)	7 / 211 (3.32%) 7	11 / 213 (5.16%) 11	1 / 72 (1.39%) 1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 211 (5.21%)	9 / 213 (4.23%)	2 / 72 (2.78%)
occurrences (all)	11	10	2
Upper respiratory tract infection			
subjects affected / exposed	8 / 211 (3.79%)	4 / 213 (1.88%)	5 / 72 (6.94%)
occurrences (all)	8	4	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	34 / 211 (16.11%)	27 / 213 (12.68%)	14 / 72 (19.44%)
occurrences (all)	34	27	14
Vitamin D deficiency			
subjects affected / exposed	8 / 211 (3.79%)	5 / 213 (2.35%)	8 / 72 (11.11%)
occurrences (all)	8	5	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2012	1) Excluded patients with GT1a IL28b CC. 2) Removed stratification by sub-GT and IL-28b. 3) Extended safety data collection at rescue to 4 weeks. 4) Removed protein electrophoresis at screening. 5) Revised sample size to 210 patients for Group 1, 210 patients for Group 2 and 50-70 patients for Group 3, based on exclusion of GT1a patients.
28 June 2013	1) Redefined the minimum historical target SVR12 rates from a point estimate of 71% for the lower bound of the CI (original protocol) to a weighted average of 66% (PegIFN-eligible) and 50% (PegIFN-ineligible), where 1/2 CI is approximately 6%. 2) Specified a hierarchical order for the comparisons to the historical control. Clarified that one-sided tests with $\alpha=0.025$ were to be performed. 3) Added power calculations for comparison to the historical control. 4) Added increased ECG monitoring based on preliminary results from 1241.25. 5) Added monitoring for appearance of systemic symptoms of DRESS and criteria for treatment discontinuation in case of potentially life threatening skin reactions. 6) Added second confirmation in case of virologic breakthrough; clarified the confirmation process. 7) Clarified procedures related to rescue medication. 8) Revised SAE reporting processes based on updated sponsor SOP.
24 September 2013	1) Changed the order of primary and secondary objectives. 2) Re-defined the minimum historical target SVR12 rates. Specified a hierarchical order for primary and secondary objective testing. 3) Updated power calculation for the primary analysis based on the proposed sample size. 4) Specified collection of all SAEs with onset date after 28 days post-EOT until EOO. Defined residual effect period. Extended safety reporting during follow-up period.
31 October 2013	1) Added potential risk of agranulocytosis/neutropenia. 2) Added discontinuation of patients with $ANC \leq 500$ cells/mm ³ . 3) Clarified SAE reporting requirements. 4) Treatment phase cut-off revised to 7 days after last treatment for laboratory values.
08 April 2014	1) Due to termination of the DBV program, the FU period was reduced to 24 weeks for patients who achieved SVR12 and to 48 weeks for non-responders provided they had not started an alternative HCV treatment. 2) Follow-up of rescue treatment was reduced to RFU1 at REOT+12 weeks. 3) FU3 snapshot was removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 April 2014	Clinical development of the DBV was terminated, thus this trial was prematurely discontinued.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Primary outcome measure 1 reporting statistical analysis for one group are defined and analysed for trial 1241.36, however due to the platform limitations those could not be provided. Results can be found on CT.gov study number: NCT01728324.

Notes: