



Clinical trial results:

A phase IIb open label study of BI 207127 in combination with faldaprevir and ribavirin in patients with moderate hepatic impairment (Child-Pugh B) with genotype 1b chronic hepatitis C infection

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	2012-003534-17
Trial protocol	ES DE GB IT IE FR
Global end of trial date	21 October 2014

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	1241.30
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01830127
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 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	04 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2014
Global end of trial reached?	Yes
Global end of trial date	21 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of Cohort A was to evaluate the safety and pharmacokinetic (PK) profile of deleobuvir (DBV) in combination with 120 mg once daily (QD) faldaprevir (FDV) and weight-based ribavirin (RBV) in a small group of patients with moderate hepatic impairment (Child-Pugh B [CPB]) compared to patients with mild hepatic impairment (Child-Pugh A [CPA]). The objective of this study related to Cohort B from the original protocol (to assess the efficacy, safety, and PK of 24-week treatment with the DBV dose selected in Cohort A in combination with FDV and RBV in a larger group of chronically infected HCV GT1b patients with moderate hepatic impairment [CPB]) was removed in Global Amendment 3 due to the sponsor decision to halt the development of the DBV drug program.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were 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. In addition, for safety reasons first cohort of each dose level was treated with fixed treatment sequence and investigator could decide at any time to discontinue dosing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2013
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	Germany: 25
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	64
EEA total number of subjects	48

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)	51
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

35 patients were enrolled and treated with Deleobuvir (DBV) / Faldaprevir (FDV) / Ribavirin (RBV): 18 patients with Child-Pugh A (mild hepatic impairment) and 17 patients with Child-Pugh B (moderate hepatic impairment).

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 allocated to trial treatment if any one of the specific entry criteria were violated.

Period 1

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

Blinding implementation details:

This was a randomised and open-label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm1: Child-Pugh A

Arm description:

Arm 1 (genotype 1b) - 600mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

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:

600mg Deleobuvir (DBV) tablet taken orally twice daily (BID) for 24 weeks.

Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

120mg Faldaprevir (FDV) capsule taken orally once daily (QD) 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:

Ribavirin (RBV) tablet taken orally twice daily for 24 weeks.

Arm title	Arm2: Child-Pugh B
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Arm description:

Arm 2 (genotype 1b) - 400mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

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:

400mg Deleobuvir (DBV) tablet taken orally twice daily (BID) for 24 weeks.

Investigational medicinal product name	Faldaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

120mg Faldaprevir (FDV) capsule taken orally once daily (QD) 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:

Ribavirin (RBV) tablet taken orally twice daily for 24 weeks.

Number of subjects in period 1^[1]	Arm1: Child-Pugh A	Arm2: Child-Pugh B
Started	18	17
Completed	13	8
Not completed	5	9
Other reason not defined	-	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	6
Lack of efficacy	3	-

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 randomized after successfully completing the screening period and received at least one of the trial medication.

Baseline characteristics

Reporting groups

Reporting group title	Arm1: Child-Pugh A
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Reporting group description:

Arm 1 (genotype 1b) - 600mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

Reporting group title	Arm2: Child-Pugh B
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Reporting group description:

Arm 2 (genotype 1b) - 400mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

Reporting group values	Arm1: Child-Pugh A	Arm2: Child-Pugh B	Total
Number of subjects	18	17	35
Age categorical Units: Subjects			

Age Continuous			
Treated Set (TS) All patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment, regardless of randomization.			
Units: years			
arithmetic mean	57.8	56.6	
standard deviation	± 8.8	± 9.7	-
Gender, Male/Female Units: Participants			
Female	8	7	15
Male	10	10	20

End points

End points reporting groups

Reporting group title	Arm1: Child-Pugh A
Reporting group description: Arm 1 (genotype 1b) - 600mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.	
Reporting group title	Arm2: Child-Pugh B
Reporting group description: Arm 2 (genotype 1b) - 400mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.	

Primary: SVR12: Plasma HCV RNA level less than 25 IU/mL at 12 weeks after End of Treatment (EOT)

End point title	SVR12: Plasma HCV RNA level less than 25 IU/mL at 12 weeks after End of Treatment (EOT) ^[1]
End point description: Sustained virologic response (SVR) at Week 12 post-treatment (SVR12): Plasma Hepatitis C virus Ribonucleic acid (HCV RNA) level <25 IU/mL (international units per millilitre) at 12 weeks after EOT. SVR12 was analyzed in a descriptive manner using percentage.	
End point type	Primary
End point timeframe: 12 weeks after End of 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 endpoint was evaluated only descriptively. Thus, no statistical hypothesis test was tested.

End point values	Arm1: Child-Pugh A	Arm2: Child-Pugh B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18 ^[2]	17 ^[3]		
Units: Percentage of participants				
number (confidence interval 95%)	61.1 (38.6 to 83.6)	52.9 (29.2 to 76.7)		

Notes:

[2] - TS

[3] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: SVR4: Plasma HCV RNA level less than 25 IU/mL at 4 weeks after End of Treatment (EOT)

End point title	SVR4: Plasma HCV RNA level less than 25 IU/mL at 4 weeks after End of Treatment (EOT)
End point description: Sustained virologic response (SVR) at Week 4 post-treatment (SVR4): Plasma Hepatitis C virus Ribonucleic acid (HCV RNA) level <25 IU/mL at 4 weeks after EOT. SVR4 was analyzed in a descriptive manner using percentage.	
End point type	Secondary

End point timeframe:
4 weeks after End of Treatment

End point values	Arm1: Child-Pugh A	Arm2: Child-Pugh B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18 ^[4]	17 ^[5]		
Units: Percentage of participants				
number (confidence interval 95%)	72.2 (51.5 to 92.9)	76.5 (56.3 to 96.6)		

Notes:

[4] - TS

[5] - TS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first drug administration until last drug administration plus 28 days, up to 28 weeks.

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	Arm1: Child-Pugh A
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Reporting group description:

Arm 1 (genotype 1b) - 600mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

Reporting group title	Arm2: Child-Pugh B
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Reporting group description:

Arm 2 (genotype 1b) - 400mg DBV tablet taken orally twice daily (BID) plus 120mg FDV capsule taken orally once daily (QD) plus RBV tablet taken orally twice daily for 24 weeks.

Serious adverse events	Arm1: Child-Pugh A	Arm2: Child-Pugh B	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	9 / 17 (52.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 18 (0.00%)	4 / 17 (23.53%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Peritonitis bacterial			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm1: Child-Pugh A	Arm2: Child-Pugh B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	17 / 17 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Vasospasm			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	7 / 18 (38.89%) 8	7 / 17 (41.18%) 7	
Fatigue subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	3 / 17 (17.65%) 3	
Chills subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Gait disturbance subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	2 / 17 (11.76%) 2	
Mucosal dryness subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Oedema subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 2	
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	5 / 17 (29.41%) 7	
Pyrexia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 2	
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Breast pain			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	
occurrences (all)	0	3	
Dyspnoea exertional			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Nasal dryness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Bradyphrenia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Depressed mood			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Disorientation			
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	3	
Insomnia			

subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	4 / 17 (23.53%) 4	
Libido increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Nightmare subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Investigations			
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Hepatic enzyme increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Hepatitis C RNA increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Lipase increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 2	
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Weight decreased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 17 (5.88%) 1	
Waist circumference increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Weight increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 17 (17.65%) 3	

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Injury			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Limb injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Muscle injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Disturbance in attention			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	5 / 17 (29.41%)	
occurrences (all)	1	6	

Dysgeusia		
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)
occurrences (all)	2	1
Encephalopathy		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Headache		
subjects affected / exposed	1 / 18 (5.56%)	2 / 17 (11.76%)
occurrences (all)	1	2
Hepatic encephalopathy		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Hyperaesthesia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0
Hypertonia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0
Memory impairment		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Migraine		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Parosmia		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Paraesthesia		
subjects affected / exposed	2 / 18 (11.11%)	1 / 17 (5.88%)
occurrences (all)	3	1
Presyncope		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Sensory loss		
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0

Restless legs syndrome subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Somnolence subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Tremor subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Syncope subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 17 (5.88%) 2	
Anaemia subjects affected / exposed occurrences (all)	6 / 18 (33.33%) 8	8 / 17 (47.06%) 10	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Erythema of eyelid subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Ocular icterus subjects affected / exposed occurrences (all)	6 / 18 (33.33%) 7	3 / 17 (17.65%) 3	
Photophobia			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 7	1 / 17 (5.88%) 2	
Abdominal pain subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	2 / 17 (11.76%) 3	
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	3 / 17 (17.65%) 3	
Aphthous stomatitis subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Ascites subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	7 / 17 (41.18%) 9	
Constipation subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	3 / 17 (17.65%) 3	
Cheilitis subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	0 / 17 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	9 / 18 (50.00%) 14	9 / 17 (52.94%) 13	
Dry mouth subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Dyspepsia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	2 / 17 (11.76%) 2	
Faeces soft subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	

Flatulence			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Hiatus hernia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	13 / 18 (72.22%)	13 / 17 (76.47%)	
occurrences (all)	16	16	
Melaena			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Portal hypertensive gastropathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	9 / 18 (50.00%)	6 / 17 (35.29%)	
occurrences (all)	20	9	
Varices oesophageal			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Gallbladder disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hepatomegaly			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			

subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 10	4 / 17 (23.53%) 4	
Jaundice subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 5	8 / 17 (47.06%) 9	
Skin and subcutaneous tissue disorders			
Blister subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	
Dry skin subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 17 (5.88%) 1	
Eczema subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 17 (5.88%) 1	
Erythema subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 4	2 / 17 (11.76%) 3	
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Night sweats subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Onychalgia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1	
Photosensitivity reaction subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	1 / 17 (5.88%) 1	
Pruritus subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 10	5 / 17 (29.41%) 5	
Rash subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 4	1 / 17 (5.88%) 1	

Pruritus generalised subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 2	
Rash papular subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Skin exfoliation subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Renal and urinary disorders			
Chromaturia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0	
Proteinuria subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 17 (5.88%) 2	
Renal colic subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Renal failure subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 17 (11.76%) 2	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	0 / 17 (0.00%) 0	
Monarthritis			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Muscle tightness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 18 (27.78%)	2 / 17 (11.76%)	
occurrences (all)	6	2	
Hyperglycaemia			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0
Hypernatraemia		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Hypertriglyceridaemia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0
Hyperuricaemia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	1	0
Hypoalbuminaemia		
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	4
Hypocalcaemia		
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	5
Hypokalaemia		
subjects affected / exposed	0 / 18 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	3
Hypoglycaemia		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1
Hyponatraemia		
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2013	Added the deleobuvir name for BI 207127. Phase of trial changed from Ib/Iib to Iib/III. Amendment was based on the trial 1241.25 preliminary results suggesting a QTc increase and, regardless of its methodological shortcomings, increased frequency of electrocardiogram measurements. Removed ondansetron as a recommended treatment of vomiting because of its QTc prolongation potential per updated List of Restricted and Use with Caution Concomitant Drugs, Version 3.0 in investigator site file. Added clarification that additional ECGs could have been collected by the investigator for safety reasons. Added that electrocardiograms could have been sent to the electrocardiogram laboratory to undergo central assessment. Added clarification that serum pregnancy tests would be performed for females of childbearing potential only at all marked visits on the Flow Chart. Added clarification that urine pregnancy tests would be performed at Visit 2 for all females as part of eligibility assessment. Added that DRESS had been reported in the faldaprevir program at 120 and 240 mg QD doses. Referred to Appendix 10.2.3 for treatment discontinuation in case of potentially life-threatening skin reactions. Added DRESS to potentially life threatening reaction examples. Added that patients needed to be monitored for the appearance of systemic symptoms. Added clarification of definitions of treatment experienced patients eligible to enter the trial. Clarified exclusion of patients that had taken direct acting antiviral agent. Clarified that Child-Pugh C patients were to be excluded Modification of entry criteria to be more adapted to the Child-Pugh B patient population. Added clarification for treatment discontinuation if a female patient became pregnant and added guidance if a female partner of a male patient became pregnant.
13 November 2013	Potential risk of agranulocytosis/neutropenia was added. Deleted text that referenced dose reduction instructions. Added treatment discontinuation if absolute neutrophil count was ≤ 500 cells/mm ³ . To record all SAEs with onset date after 28 days post-end-of-treatment (EOT) until end-of-observation (EOO), to define residual effect period, and to clarify SAE reporting requirements after trial completion. Updated text on the management of gastrointestinal events.
11 June 2014	Removed Arm 3 and Cohort B from the trial design as well as all supporting text intended only for these treatment groups. Week 16 intensive pharmacokinetic (PK) sampling and analysis removed. PK parameters edited. Protein binding sampling and analysis removed. Follow up period shortened from 96 to 12 weeks. Analyses for all endpoints to be done after last patient last visit. Revised wording on reporting pregnancy for a female partner of a male patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Because the company decided to stop the DBV development program, analyses for this trial were limited to the basic requirement for efficacy, and only the primary endpoint and secondary endpoint were analyzed.

Notes: