Clinical trial results:
A multicenter, randomized, open label, parallel-group phase IIB study on the efficacy and safety of oral regimens of DEB025 alone or in combination with ribavirin versus Standard of Care (peg-IFN2a plus ribavirin) in treatment-naïve hepatitis C genotype 2 and 3 patients

Summary

EudraCT number	2010-020034-26
Trial protocol	DE PL GB BE IT
Global end of trial date	15 May 2012

Results information

Result version number	v1 (current)
This version publication date	18 June 2016
First version publication date	18 June 2016

Trial information

Trial identification

Sponsor protocol code	CDEB025A2211

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01215643
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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	15 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the proportion of patients who achieve RVR with DEB025 600mg QD plus RBV 400 mg BID, DEB025 800 mg QD plus RBV 400 mg BID and DEB025 1000 mg QD treatment groups, in treatment-naïve chronic hepatitis C genotype 2/3 patients.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 33
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	India: 60
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Taiwan: 29
Country: Number of subjects enrolled	Thailand: 44
Worldwide total number of subjects	340
EEA total number of subjects	121

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)	337
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Approximately 400 patients were planned to be randomized in a 2:2:2:1:1 ratio. Due to higher screen failure rate and difficulties in enrollment, the targeted sample size was not reached within the targeted time frame. The recruitment was stopped after 340 patients were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DEB025 1000 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DEB025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

200 mg soft gel capsules taken orally.

Arm title	DEB025 600 mg + RBV

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DEB025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

200 mg soft gel capsules taken orally.

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

Dosage and administration details:

200 mg tablets or capsules taken orally.

Arm title	DEB025 800 mg +RBV

Arm description: -

Arm type	Experimental

Investigational medicinal product name	DEB025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:
200 mg soft gel capsules taken orally.

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

Dosage and administration details:
200 mg tablets or capsules taken orally.

Arm title	DEB025 600 mg +PEG

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DEB025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:
200 mg soft gel capsules taken orally.

Investigational medicinal product name	PEG
Investigational medicinal product code	
Other name	Peg-IFN alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Syringes containing 180 µg/0.5 mL Peg-IFNα2a for s.c. injection.

Arm title	PEG + RBV

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	PEG
Investigational medicinal product code	
Other name	Peg-IFN alfa-2a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Syringes containing 180 µg/0.5 mL Peg-IFNα2a for s.c. injection.

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

Dosage and administration details:
200 mg tablets or capsules taken orally.

Number of subjects in period 1	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV
Started	83	84	94
Treated	82	84	94
Completed	73	78	85
Not completed	10	6	9
Abnormal laboratory value(s)	1	-	-
Consent withdrawn by subject	2	-	1
Adverse event, non-fatal	2	2	3
Unsatisfactory therapeutic effect	2	2	2
Non-compliance	1	2	-
Lost to follow-up	-	-	3
Protocol deviation	2	-	-

Number of subjects in period 1	DEB025 600 mg +PEG	PEG + RBV
Started	39	40
Treated	39	37
Completed	35	33
Not completed	4	7
Abnormal laboratory value(s)	-	-
Consent withdrawn by subject	-	3
Adverse event, non-fatal	3	-
Unsatisfactory therapeutic effect	1	-
Non-compliance	-	-
Lost to follow-up	-	3
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	DEB025 1000 mg
Reporting group description: -	
Reporting group title	DEB025 600 mg + RBV
Reporting group description: -	
Reporting group title	DEB025 800 mg +RBV
Reporting group description: -	
Reporting group title	DEB025 600 mg +PEG
Reporting group description: -	
Reporting group title	PEG + RBV
Reporting group description: -	

Reporting group values	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV
Number of subjects	83	84	94
Age categorical Units: Subjects			
Adults (18-64 years)	83	82	94
From 65-84 years	0	2	0
Age continuous Units: years			
arithmetic mean	40.2	42.8	42.6
standard deviation	± 11.27	± 11.77	± 11
Gender categorical Units: Subjects			
Female	32	28	33
Male	51	56	61

Reporting group values	DEB025 600 mg +PEG	PEG + RBV	Total
Number of subjects	39	40	340
Age categorical Units: Subjects			
Adults (18-64 years)	38	40	337
From 65-84 years	1	0	3
Age continuous Units: years			
arithmetic mean	43.2	39.9	
standard deviation	± 10.56	± 11.2	-
Gender categorical Units: Subjects			
Female	14	16	123
Male	25	24	217

End points

End points reporting groups

Reporting group title	DEB025 1000 mg
Reporting group description: -	
Reporting group title	DEB025 600 mg + RBV
Reporting group description: -	
Reporting group title	DEB025 800 mg +RBV
Reporting group description: -	
Reporting group title	DEB025 600 mg +PEG
Reporting group description: -	
Reporting group title	PEG + RBV
Reporting group description: -	

Primary: Percentage of patients who achieve Rapid Viral Response (RVR)

End point title	Percentage of patients who achieve Rapid Viral Response

End point description:

Defined as serum Hepatitis C Virus (HCV) RNA undetectable (by Limit of quantification (LOQ)) after 4 weeks of treatment.

End point type	Primary

End point timeframe:

week 4

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: No statistical analyses have been performed for this primary end point.

End point values	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV	DEB025 600 mg +PEG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81[2]	84[3]	93[4]	39[5]
Units: percent				
number (not applicable)	28.4	36.9	41.9	84.6

Notes:

[2] - Full Analysis Set (FAS) - all subjects to whom study treatment had been assigned

[3] - Full Analysis Set (FAS)

[4] - Full Analysis Set (FAS)

[5] - Full Analysis Set (FAS)

End point values	PEG + RBV			
Subject group type	Reporting group			
Number of subjects analysed	40[6]			
Units: percent				
number (not applicable)	72.5			

Notes:

[6] - Full Analysis Set (FAS)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with RVR on interferon free treatment who achieve Sustained Viral Response (SVR24) at Week 24

End point title	Percentage of patients with RVR on interferon free treatment who achieve Sustained Viral Response (SVR24) at Week 24

End point description:

defined as serum HCV RNA undetectable (by LOD) after 24 weeks of treatment.

End point type	Secondary

End point timeframe:

24 weeks

End point values	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV	DEB025 600 mg +PEG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81[7]	84[8]	93[9]	39[10]
Units: percent				
number (not applicable)	80.2	84.5	80.6	79.5

Notes:

[7] - Full Analysis Set (FAS) - all subjects to whom study treatment had been assigned

[8] - Full Analysis Set (FAS)

[9] - Full Analysis Set (FAS)

[10] - Full Analysis Set (FAS)

End point values	PEG + RBV			
Subject group type	Reporting group			
Number of subjects analysed	40[11]			
Units: percent				
number (not applicable)	57.5			

Notes:

[11] - Full Analysis Set (FAS)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with cEVR, ETR (week 24), SVR12 and SVR24 measured at the level of quantification (LOQ)

End point title	Percentage of participants with cEVR, ETR (week 24), SVR12 and SVR24 measured at the level of quantification (LOQ)

End point description:

End point type	Secondary

End point timeframe:

Week 12 and 24

End point values	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV	DEB025 600 mg +PEG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81[12]	84[13]	93[14]	39[15]
Units: percent				
number (not applicable)				
RVR4LOQ (=RVR)	28.4	36.9	41.9	84.6
EVR12LOQ (=EVR)	93.8	95.2	91.4	97.4
pEVR	0	0	1.1	2.6
cEVR12LOQ	93.8	95.2	90.3	94.9
ETR24LOQ	95.1	96.4	95.7	94.9
SVR12LOQ	81.5	84.5	80.6	76.9
SVR24LOQ	80.2	84.5	80.6	79.5

Notes:

[12] - Full Analysis Set (FAS): all participants that study treatment had been assigned.

[13] - FAS

[14] - FAS

[15] - FAS

End point values	PEG + RBV			
Subject group type	Reporting group			
Number of subjects analysed	40[16]			
Units: percent				
number (not applicable)				
RVR4LOQ (=RVR)	72.5			
EVR12LOQ (=EVR)	85			
pEVR	0			
cEVR12LOQ	85			
ETR24LOQ	87.5			
SVR12LOQ	62.5			
SVR24LOQ	57.5			

Notes:

[16] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with SVR12LOQ and SVR24LOQ by actual genotype and screening HCV RNA

End point title	Percentage of participants with SVR12LOQ and SVR24LOQ by actual genotype and screening HCV RNA

End point description:

End point type	Secondary

End point timeframe:

Week 12 and 24

End point values	DEB025 1000 mg	DEB025 600 mg + RBV	DEB025 800 mg +RBV	DEB025 600 mg +PEG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81[17]	84[18]	93[19]	39[20]
Units: percent				
number (not applicable)				
SVR12LOQ - Genotype 2	78.3	76.7	76.9	72.7
SVR12LOQ - Genotype 3	82.8	88.9	82.1	78.6
SVR12LOQ - Screening HCV RNA ≥ 800,000 IU/mL	88	85.5	81.8	73.1
SVR12LOQ - Screening HCV RNA < 800,000 IU/mL	73.3	82.8	78.9	84.6
SVR24LOQ - Genotype 2	78.3	76.7	76.9	72.7
SVR24LOQ - Genotype 3	81	88.9	82.1	82.1
SVR24LOQ - Screening HCV RNA ≥ 800,000 IU/mL	88	85.5	81.8	73.1
SVR24LOQ - Screening HCV RNA < 800,000 IU/mL	70	82.8	78.9	92.3

Notes:

[17] - FAS: n/N = 18/23; 48/58; 44/50; 22/30

[18] - FAS: n/N = 23/30; 48/54; 47/55; 24/29

[19] - FAS: n/N = 8/11; 22/28; 19/26; 11/13

[20] - FAS: n/N = 18/13; 17/27; 18/27; 7/13

End point values	PEG + RBV			
Subject group type	Reporting group			
Number of subjects analysed	40[21]			
Units: percent				
number (not applicable)				
SVR12LOQ - Genotype 2	61.5			
SVR12LOQ - Genotype 3	63			
SVR12LOQ - Screening HCV RNA ≥ 800,000 IU/mL	66.7			
SVR12LOQ - Screening HCV RNA < 800,000 IU/mL	53.8			
SVR24LOQ - Genotype 2	53.8			
SVR24LOQ - Genotype 3	59.3			
SVR24LOQ - Screening HCV RNA ≥ 800,000 IU/mL	59.3			
SVR24LOQ - Screening HCV RNA < 800,000 IU/mL	53.8			

Notes:

[21] - FAS: n/N = 8/13; 17/27; 18/27; 7/13

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	DEB025 1000 mg
Reporting group description:	
DEB025 1000 mg	
Reporting group title	DEB025 600mg+RBV
Reporting group description:	
DEB025 600mg+RBV	
Reporting group title	DEB025 800mg+RBV
Reporting group description:	
DEB025 800mg+RBV	
Reporting group title	DEB025 600mg+PEG
Reporting group description:	
DEB025 600mg+PEG	
Reporting group title	PEG+RBV
Reporting group description:	
PEG+RBV	

Serious adverse events	DEB025 1000 mg	DEB025 600mg+RBV	DEB025 800mg+RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 82 (4.88%)	1 / 84 (1.19%)	9 / 94 (9.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinopathy			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 82 (1.22%)	0 / 84 (0.00%)	0 / 94 (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
Abdominal pain upper			

subjects affected / exposed	1 / 82 (1.22%)	0 / 84 (0.00%)	0 / 94 (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
Diarrhoea			
subjects affected / exposed	1 / 82 (1.22%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 82 (1.22%)	0 / 84 (0.00%)	0 / 94 (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
Vomiting			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperventilation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
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			
Erythema nodosum			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Homicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 82 (0.00%)	1 / 84 (1.19%)	0 / 94 (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 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle abscess			
subjects affected / exposed	1 / 82 (1.22%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DEB025 600mg+PEG	PEG+RBV	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 39 (10.26%)	2 / 37 (5.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Maternal exposure during pregnancy			

subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 39 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinopathy			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Homicidal ideation			

subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle abscess			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 37 (2.70%)	
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 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DEB025 1000 mg	DEB025 600mg+RBV	DEB025 800mg+RBV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 82 (78.05%)	69 / 84 (82.14%)	76 / 94 (80.85%)
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 82 (10.98%)	10 / 84 (11.90%)	8 / 94 (8.51%)
occurrences (all)	9	11	8
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 82 (12.20%)	7 / 84 (8.33%)	11 / 94 (11.70%)
occurrences (all)	10	7	12
Chills			
subjects affected / exposed	5 / 82 (6.10%)	3 / 84 (3.57%)	5 / 94 (5.32%)
occurrences (all)	5	3	5
Fatigue			
subjects affected / exposed	21 / 82 (25.61%)	23 / 84 (27.38%)	30 / 94 (31.91%)
occurrences (all)	22	24	33
Feeling cold			

subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	2 / 94 (2.13%)
occurrences (all)	0	0	2
Influenza like illness			
subjects affected / exposed	8 / 82 (9.76%)	6 / 84 (7.14%)	9 / 94 (9.57%)
occurrences (all)	9	6	9
Injection site erythema			
subjects affected / exposed	2 / 82 (2.44%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences (all)	2	0	0
Irritability			
subjects affected / exposed	2 / 82 (2.44%)	5 / 84 (5.95%)	8 / 94 (8.51%)
occurrences (all)	2	5	8
Malaise			
subjects affected / exposed	2 / 82 (2.44%)	3 / 84 (3.57%)	0 / 94 (0.00%)
occurrences (all)	2	3	0
Pain			
subjects affected / exposed	3 / 82 (3.66%)	3 / 84 (3.57%)	5 / 94 (5.32%)
occurrences (all)	3	3	5
Pyrexia			
subjects affected / exposed	14 / 82 (17.07%)	16 / 84 (19.05%)	15 / 94 (15.96%)
occurrences (all)	17	20	18
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	2 / 94 (2.13%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 82 (13.41%)	13 / 84 (15.48%)	12 / 94 (12.77%)
occurrences (all)	12	13	12
Dyspnoea			
subjects affected / exposed	3 / 82 (3.66%)	6 / 84 (7.14%)	3 / 94 (3.19%)
occurrences (all)	3	6	4
Dyspnoea exertional			
subjects affected / exposed	1 / 82 (1.22%)	6 / 84 (7.14%)	4 / 94 (4.26%)
occurrences (all)	1	6	4
Oropharyngeal pain			

subjects affected / exposed	5 / 82 (6.10%)	2 / 84 (2.38%)	5 / 94 (5.32%)
occurrences (all)	5	2	6
Productive cough			
subjects affected / exposed	0 / 82 (0.00%)	1 / 84 (1.19%)	1 / 94 (1.06%)
occurrences (all)	0	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 82 (9.76%)	9 / 84 (10.71%)	5 / 94 (5.32%)
occurrences (all)	8	10	5
Depressed mood			
subjects affected / exposed	2 / 82 (2.44%)	2 / 84 (2.38%)	3 / 94 (3.19%)
occurrences (all)	2	2	3
Depression			
subjects affected / exposed	12 / 82 (14.63%)	7 / 84 (8.33%)	9 / 94 (9.57%)
occurrences (all)	12	7	9
Insomnia			
subjects affected / exposed	11 / 82 (13.41%)	12 / 84 (14.29%)	14 / 94 (14.89%)
occurrences (all)	11	12	15
Sleep disorder			
subjects affected / exposed	2 / 82 (2.44%)	4 / 84 (4.76%)	3 / 94 (3.19%)
occurrences (all)	2	4	3
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 82 (1.22%)	1 / 84 (1.19%)	1 / 94 (1.06%)
occurrences (all)	1	1	1
Neutrophil count decreased			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	1 / 94 (1.06%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 82 (1.22%)	3 / 84 (3.57%)	2 / 94 (2.13%)
occurrences (all)	1	3	2
Weight decreased			
subjects affected / exposed	4 / 82 (4.88%)	2 / 84 (2.38%)	4 / 94 (4.26%)
occurrences (all)	4	2	4
Injury, poisoning and procedural complications			

Wound			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 82 (0.00%)	2 / 84 (2.38%)	6 / 94 (6.38%)
occurrences (all)	0	2	7
Tachycardia			
subjects affected / exposed	2 / 82 (2.44%)	2 / 84 (2.38%)	4 / 94 (4.26%)
occurrences (all)	2	3	5
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 82 (3.66%)	1 / 84 (1.19%)	4 / 94 (4.26%)
occurrences (all)	3	1	4
Dizziness			
subjects affected / exposed	6 / 82 (7.32%)	11 / 84 (13.10%)	16 / 94 (17.02%)
occurrences (all)	6	13	16
Dysgeusia			
subjects affected / exposed	4 / 82 (4.88%)	3 / 84 (3.57%)	3 / 94 (3.19%)
occurrences (all)	4	3	4
Headache			
subjects affected / exposed	19 / 82 (23.17%)	18 / 84 (21.43%)	27 / 94 (28.72%)
occurrences (all)	21	30	30
Hypoaesthesia			
subjects affected / exposed	0 / 82 (0.00%)	2 / 84 (2.38%)	1 / 94 (1.06%)
occurrences (all)	0	2	1
Memory impairment			
subjects affected / exposed	1 / 82 (1.22%)	1 / 84 (1.19%)	2 / 94 (2.13%)
occurrences (all)	1	2	2
Paraesthesia			
subjects affected / exposed	1 / 82 (1.22%)	1 / 84 (1.19%)	3 / 94 (3.19%)
occurrences (all)	1	4	3
Somnolence			
subjects affected / exposed	2 / 82 (2.44%)	1 / 84 (1.19%)	1 / 94 (1.06%)
occurrences (all)	2	1	1
Syncope			

subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 82 (9.76%)	11 / 84 (13.10%)	10 / 94 (10.64%)
occurrences (all)	8	12	10
Leukopenia			
subjects affected / exposed	3 / 82 (3.66%)	2 / 84 (2.38%)	2 / 94 (2.13%)
occurrences (all)	3	3	2
Neutropenia			
subjects affected / exposed	9 / 82 (10.98%)	8 / 84 (9.52%)	13 / 94 (13.83%)
occurrences (all)	10	10	16
Thrombocytopenia			
subjects affected / exposed	0 / 82 (0.00%)	5 / 84 (5.95%)	3 / 94 (3.19%)
occurrences (all)	0	5	3
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 82 (1.22%)	1 / 84 (1.19%)	1 / 94 (1.06%)
occurrences (all)	1	1	1
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 82 (0.00%)	0 / 84 (0.00%)	0 / 94 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 82 (3.66%)	5 / 84 (5.95%)	6 / 94 (6.38%)
occurrences (all)	3	6	7
Abdominal pain			
subjects affected / exposed	6 / 82 (7.32%)	4 / 84 (4.76%)	7 / 94 (7.45%)
occurrences (all)	9	4	7
Abdominal pain upper			
subjects affected / exposed	6 / 82 (7.32%)	6 / 84 (7.14%)	7 / 94 (7.45%)
occurrences (all)	6	7	9
Constipation			

subjects affected / exposed	5 / 82 (6.10%)	5 / 84 (5.95%)	8 / 94 (8.51%)
occurrences (all)	5	5	9
Diarrhoea			
subjects affected / exposed	13 / 82 (15.85%)	6 / 84 (7.14%)	10 / 94 (10.64%)
occurrences (all)	17	7	12
Dry mouth			
subjects affected / exposed	3 / 82 (3.66%)	2 / 84 (2.38%)	3 / 94 (3.19%)
occurrences (all)	3	2	3
Dyspepsia			
subjects affected / exposed	7 / 82 (8.54%)	8 / 84 (9.52%)	7 / 94 (7.45%)
occurrences (all)	8	10	7
Gastritis			
subjects affected / exposed	0 / 82 (0.00%)	2 / 84 (2.38%)	0 / 94 (0.00%)
occurrences (all)	0	2	0
Mouth ulceration			
subjects affected / exposed	5 / 82 (6.10%)	0 / 84 (0.00%)	3 / 94 (3.19%)
occurrences (all)	6	0	4
Nausea			
subjects affected / exposed	17 / 82 (20.73%)	15 / 84 (17.86%)	23 / 94 (24.47%)
occurrences (all)	19	16	26
Vomiting			
subjects affected / exposed	7 / 82 (8.54%)	7 / 84 (8.33%)	7 / 94 (7.45%)
occurrences (all)	8	8	13
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 82 (3.66%)	2 / 84 (2.38%)	5 / 94 (5.32%)
occurrences (all)	3	2	6
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 82 (12.20%)	8 / 84 (9.52%)	4 / 94 (4.26%)
occurrences (all)	10	8	4
Dry skin			
subjects affected / exposed	8 / 82 (9.76%)	5 / 84 (5.95%)	6 / 94 (6.38%)
occurrences (all)	9	5	7
Eczema			

subjects affected / exposed	2 / 82 (2.44%)	0 / 84 (0.00%)	2 / 94 (2.13%)
occurrences (all)	2	0	2
Erythema			
subjects affected / exposed	0 / 82 (0.00%)	1 / 84 (1.19%)	2 / 94 (2.13%)
occurrences (all)	0	1	2
Pruritus			
subjects affected / exposed	14 / 82 (17.07%)	14 / 84 (16.67%)	12 / 94 (12.77%)
occurrences (all)	16	17	15
Rash			
subjects affected / exposed	11 / 82 (13.41%)	9 / 84 (10.71%)	14 / 94 (14.89%)
occurrences (all)	14	9	20
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 82 (1.22%)	2 / 84 (2.38%)	1 / 94 (1.06%)
occurrences (all)	1	2	1
Hypothyroidism			
subjects affected / exposed	2 / 82 (2.44%)	1 / 84 (1.19%)	3 / 94 (3.19%)
occurrences (all)	2	1	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 82 (10.98%)	2 / 84 (2.38%)	15 / 94 (15.96%)
occurrences (all)	10	2	16
Back pain			
subjects affected / exposed	5 / 82 (6.10%)	4 / 84 (4.76%)	10 / 94 (10.64%)
occurrences (all)	5	4	10
Muscle spasms			
subjects affected / exposed	4 / 82 (4.88%)	3 / 84 (3.57%)	3 / 94 (3.19%)
occurrences (all)	4	3	3
Musculoskeletal pain			
subjects affected / exposed	5 / 82 (6.10%)	3 / 84 (3.57%)	0 / 94 (0.00%)
occurrences (all)	5	3	0
Myalgia			
subjects affected / exposed	10 / 82 (12.20%)	7 / 84 (8.33%)	13 / 94 (13.83%)
occurrences (all)	10	7	15
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	5 / 82 (6.10%)	4 / 84 (4.76%)	5 / 94 (5.32%)
occurrences (all)	6	4	5
Upper respiratory tract infection			
subjects affected / exposed	2 / 82 (2.44%)	3 / 84 (3.57%)	4 / 94 (4.26%)
occurrences (all)	2	6	4
Urinary tract infection			
subjects affected / exposed	5 / 82 (6.10%)	1 / 84 (1.19%)	1 / 94 (1.06%)
occurrences (all)	5	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	15 / 82 (18.29%)	14 / 84 (16.67%)	14 / 94 (14.89%)
occurrences (all)	17	14	16

Non-serious adverse events	DEB025 600mg+PEG	PEG+RBV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 39 (94.87%)	30 / 37 (81.08%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 39 (12.82%)	1 / 37 (2.70%)	
occurrences (all)	5	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 39 (7.69%)	8 / 37 (21.62%)	
occurrences (all)	3	9	
Chills			
subjects affected / exposed	4 / 39 (10.26%)	1 / 37 (2.70%)	
occurrences (all)	4	1	
Fatigue			
subjects affected / exposed	18 / 39 (46.15%)	10 / 37 (27.03%)	
occurrences (all)	20	10	
Feeling cold			
subjects affected / exposed	0 / 39 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Influenza like illness			

subjects affected / exposed	8 / 39 (20.51%)	4 / 37 (10.81%)	
occurrences (all)	9	4	
Injection site erythema			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Irritability			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Malaise			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	3	2	
Pain			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Pyrexia			
subjects affected / exposed	12 / 39 (30.77%)	9 / 37 (24.32%)	
occurrences (all)	16	13	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 39 (2.56%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 39 (7.69%)	4 / 37 (10.81%)	
occurrences (all)	3	4	
Dyspnoea			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Dyspnoea exertional			
subjects affected / exposed	1 / 39 (2.56%)	3 / 37 (8.11%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Productive cough			

subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 39 (2.56%)	5 / 37 (13.51%)	
occurrences (all)	1	6	
Depressed mood			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	3 / 39 (7.69%)	3 / 37 (8.11%)	
occurrences (all)	4	3	
Insomnia			
subjects affected / exposed	4 / 39 (10.26%)	6 / 37 (16.22%)	
occurrences (all)	4	8	
Sleep disorder			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	3	1	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Neutrophil count decreased			
subjects affected / exposed	2 / 39 (5.13%)	3 / 37 (8.11%)	
occurrences (all)	2	3	
Platelet count decreased			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Weight decreased			
subjects affected / exposed	3 / 39 (7.69%)	4 / 37 (10.81%)	
occurrences (all)	3	4	
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			

Palpitations			
subjects affected / exposed	1 / 39 (2.56%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Dizziness			
subjects affected / exposed	5 / 39 (12.82%)	4 / 37 (10.81%)	
occurrences (all)	5	4	
Dysgeusia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	16 / 39 (41.03%)	7 / 37 (18.92%)	
occurrences (all)	20	16	
Hypoaesthesia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Memory impairment			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Somnolence			
subjects affected / exposed	4 / 39 (10.26%)	1 / 37 (2.70%)	
occurrences (all)	4	3	
Syncope			
subjects affected / exposed	3 / 39 (7.69%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 39 (10.26%)	3 / 37 (8.11%)	
occurrences (all)	4	4	
Leukopenia			
subjects affected / exposed	2 / 39 (5.13%)	3 / 37 (8.11%)	
occurrences (all)	2	4	
Neutropenia			
subjects affected / exposed	10 / 39 (25.64%)	4 / 37 (10.81%)	
occurrences (all)	15	5	
Thrombocytopenia			
subjects affected / exposed	6 / 39 (15.38%)	2 / 37 (5.41%)	
occurrences (all)	6	4	
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 39 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Vertigo			
subjects affected / exposed	0 / 39 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	4	
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 39 (7.69%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	3 / 39 (7.69%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Diarrhoea			

subjects affected / exposed	9 / 39 (23.08%)	1 / 37 (2.70%)	
occurrences (all)	11	2	
Dry mouth			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Mouth ulceration			
subjects affected / exposed	4 / 39 (10.26%)	2 / 37 (5.41%)	
occurrences (all)	5	2	
Nausea			
subjects affected / exposed	9 / 39 (23.08%)	5 / 37 (13.51%)	
occurrences (all)	9	5	
Vomiting			
subjects affected / exposed	2 / 39 (5.13%)	2 / 37 (5.41%)	
occurrences (all)	4	2	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	4	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 39 (23.08%)	7 / 37 (18.92%)	
occurrences (all)	9	7	
Dry skin			
subjects affected / exposed	3 / 39 (7.69%)	3 / 37 (8.11%)	
occurrences (all)	3	3	
Eczema			
subjects affected / exposed	0 / 39 (0.00%)	3 / 37 (8.11%)	
occurrences (all)	0	4	
Erythema			

subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	7 / 39 (17.95%)	6 / 37 (16.22%)	
occurrences (all)	9	8	
Rash			
subjects affected / exposed	2 / 39 (5.13%)	3 / 37 (8.11%)	
occurrences (all)	2	5	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 39 (5.13%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Hypothyroidism			
subjects affected / exposed	4 / 39 (10.26%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 39 (25.64%)	5 / 37 (13.51%)	
occurrences (all)	11	7	
Back pain			
subjects affected / exposed	4 / 39 (10.26%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Muscle spasms			
subjects affected / exposed	2 / 39 (5.13%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	8 / 39 (20.51%)	8 / 37 (21.62%)	
occurrences (all)	11	8	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed	4 / 39 (10.26%)	3 / 37 (8.11%)	
occurrences (all)	5	3	
Urinary tract infection			
subjects affected / exposed	0 / 39 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 39 (25.64%)	9 / 37 (24.32%)	
occurrences (all)	10	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2010	The major changes that were made to the protocol with Amendment 1 were as follows: Exclusion criteria 11 and 13 were changed to make sure women of child-bearing potential use highly effective contraception i.e. total abstinence, sterilization, male partner sterilization, or a combination of two specified contraceptive methods. A rationale for birth control to be used in this study was added. Substrates of cytochrome P450 3A for which a potentially clinically important interaction was expected and not yet investigated (e.g., hormonal contraceptives, etc.) was added to the list of prohibited treatment .
15 December 2010	The major changes that were made to the protocol with Amendment 2 were as follows: • Inclusion criteria 2 were changed to allow patients up to 70 years of age to participate in the study. • Inclusion criteria 4 were changed to clarify the definition of chronic hepatitis C. • Exclusion criteria were added to exclude patients with hyperbilirubinemia or Gilbert's disease, or use of illicit drugs. • The algorithm for DEB025 dose adjustments and interruptions in response to DEB025-induced hyperbilirubinemia was changed. DEB025 dosing was adjusted or interrupted, if no decrease in total bilirubin level was observed in a repeat bilirubin test one week later. • The list of prohibited treatment was updated. • Text was added to clarify that patients who experienced a confirmed viral breakthrough and null non-responders were discontinued from study medication but continued follow up in the study. Partial non-responders should have continued study medication and study. • Correction of the Treatment Satisfaction Questionnaire for Medication (TSQM) modified version 1.4 into TSQM version. • Editorial changes throughout the document.
22 December 2010	Canada only: • The definition of post-menopausal in exclusion criterion 13 was changed to require 12 months of spontaneous amenorrhea. • Cap and sponge were removed from the list of highly effective contraception in exclusion criterion .
06 June 2011	To adapt the requirement to discontinue study treatment for patients with a confirmed viral breakthrough if this occurs in the first 12 weeks of study treatment. Viral load variations in the first four weeks of the study should have not been construed to be viral breakthrough. If the patient's viral load was still positive at week 4 (> LOQ), then the patient should have been allowed to receive intensification to triple therapy (DEB025 600 mg QD and Peg-IFNα2a/RBV) for sufficient time to benefit from treatment, instead of being discontinued from study treatment because of a variable early response to treatment. The study design ensured that all patients received sufficient treatment before they may have been considered as treatment failures, and discontinued from the study. In addition, a correction in the documentation was needed in case male partner sterilization was implemented. Further, the interim analysis plan was adapted to include additional time points for interim analyses at 12 weeks and 24 weeks treatment as well as the final sample size was adapted.

28 February 2012	The corrections in the Viral Response Definitions table to better align the definitions with AASLD guidelines The addition of the exploratory objectives related to the pharmacokinetic of RBV (Ribavirin). Some cross-references to the Viral Response Definitions table. Limited changes to allow the measurement of RBV plasma level concentrations on the DEB025 PK samples already collected. Editorial changes throughout the document .

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported