



Clinical trial results:

An Exploratory Study to Evaluate the Kinetics of Viral Load Decline with Ombitasvir/ABT-450/Ritonavir (Ombitasvir/ABT-450/r) and Dasabuvir Therapy with Low Dose Ribavirin (RBV), Full Dose RBV or RBV Add-On in Treatment-Naïve Adults with Genotype 1a Chronic Hepatitis C Virus (HCV) Infection

Summary

EudraCT number	2014-001478-32
Trial protocol	FR
Global end of trial date	06 December 2016

Results information

Result version number	v1 (current)
This version publication date	15 October 2017
First version publication date	15 October 2017

Trial information

Trial identification

Sponsor protocol code	M14-242
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02493855
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 011 800-633-9110, eu-clinical-trials@abbvie.com
Scientific contact	Emily Dumas, PhD, AbbVie, emily.dumas@abbvie.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	06 December 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of ribavirin on second phase plasma hepatitis C virus (HCV) ribonucleic acid (RNA) decline in participants who receive ombitasvir/ABT-450/ritonavir and dasabuvir with full dose ribavirin, low dose ribavirin or without ribavirin for 2 weeks in treatment-naïve HCV genotype (GT) 1a-infected adults.

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2015
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	United States: 29
Country: Number of subjects enrolled	France: 17
Worldwide total number of subjects	46
EEA total number of subjects	17

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)	46
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at one clinic in France and one clinic in the United States. Participants were treatment-naïve adults with hepatitis C virus (HCV) genotype (GT)1a infection without cirrhosis.

Pre-assignment

Screening details:

Participants were randomized to Arms A or B in a 1:1 ratio first, and once those arms fully enrolled, Arm C was enrolled. Randomization to Arms A and B was stratified by site.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Ribavirin Full Dose for Last 10 Weeks

Arm description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) for 12 weeks and weight-based ribavirin (1000 mg or 1200 mg split BID) for the last 10 weeks.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir/ABT-450/Ritonavir
Investigational medicinal product code	
Other name	ABT-267/ABT-450/ritonavir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ombitasvir/ABT-450/ritonavir combination tablets taken once daily

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	ABT-333
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dasabuvir 250 mg tablets taken twice daily

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

Dosage and administration details:

Ribavirin 200 mg tablets: subjects weighing < 75 kg received 2 tablets in the morning and 3 tablets in the evening (1000 mg total daily dose); subjects weighing ≥ 75 kg received 3 tablets in the morning and 3 tablets in the evening (1200 mg total daily dose).

Arm title	Arm B: Ribavirin Full Dose for 12 Weeks
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Arm description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and weight-based ribavirin (1000 mg or 1200 mg split BID) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir/ABT-450/Ritonavir
Investigational medicinal product code	
Other name	ABT-267/ABT-450/ritonavir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ombitasvir/ABT-450/ritonavir combination tablets taken once daily

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	ABT-333
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dasabuvir 250 mg tablets taken twice daily

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

Dosage and administration details:

Ribavirin 200 mg tablets: subjects weighing < 75 kg received 2 tablets in the morning and 3 tablets in the evening (1000 mg total daily dose); subjects weighing ≥ 75 kg received 3 tablets in the morning and 3 tablets in the evening (1200 mg total daily dose).

Arm title	Arm C: Ribavirin Low-dose for 12 Weeks
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Arm description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and 600 mg ribavirin once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir/ABT-450/Ritonavir
Investigational medicinal product code	
Other name	ABT-267/ABT-450/ritonavir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ombitasvir/ABT-450/ritonavir combination tablets taken once daily

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	ABT-333
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dasabuvir 250 mg tablets taken twice daily

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

Dosage and administration details:

Ribavirin 200 mg tablets taken orally as 3 tablets once daily (total 600 mg QD)

Number of subjects in period 1	Arm A: Ribavirin Full Dose for Last 10 Weeks	Arm B: Ribavirin Full Dose for 12 Weeks	Arm C: Ribavirin Low-dose for 12 Weeks
Started	21	19	6
Completed	19	18	6
Not completed	2	1	0
Consent withdrawn by subject	1	-	-
Non-compliance	1	-	-
Adverse event	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Ribavirin Full Dose for Last 10 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) for 12 weeks and weight-based ribavirin (1000 mg or 1200 mg split BID) for the last 10 weeks.	
Reporting group title	Arm B: Ribavirin Full Dose for 12 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and weight-based ribavirin (1000 mg or 1200 mg split BID) for 12 weeks.	
Reporting group title	Arm C: Ribavirin Low-dose for 12 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and 600 mg ribavirin once daily for 12 weeks.	

Reporting group values	Arm A: Ribavirin Full Dose for Last 10 Weeks	Arm B: Ribavirin Full Dose for 12 Weeks	Arm C: Ribavirin Low-dose for 12 Weeks
Number of subjects	21	19	6
Age categorical Units: Subjects			
< 55 years	17	14	5
≥ 55 - 65 years	4	5	1
≥ 65 years	0	0	0
Age continuous Units: years			
arithmetic mean	44.9	46	36.7
standard deviation	± 11.96	± 12.78	± 15.79
Gender categorical Units: Subjects			
Female	11	12	4
Male	10	7	2
Race Units: Subjects			
White	16	14	4
Black or African American	4	3	1
Asian	0	0	0
American Indian or Alaskan Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Multi-race	1	2	1

Reporting group values	Total		
Number of subjects	46		
Age categorical Units: Subjects			
< 55 years	36		
≥ 55 - 65 years	10		
≥ 65 years	0		

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	27		
Male	19		
Race Units: Subjects			
White	34		
Black or African American	8		
Asian	0		
American Indian or Alaskan Native	0		
Native Hawaiian or Other Pacific Islander	0		
Multi-race	4		

End points

End points reporting groups

Reporting group title	Arm A: Ribavirin Full Dose for Last 10 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) for 12 weeks and weight-based ribavirin (1000 mg or 1200 mg split BID) for the last 10 weeks.	
Reporting group title	Arm B: Ribavirin Full Dose for 12 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and weight-based ribavirin (1000 mg or 1200 mg split BID) for 12 weeks.	
Reporting group title	Arm C: Ribavirin Low-dose for 12 Weeks
Reporting group description: Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and 600 mg ribavirin once daily for 12 weeks.	

Primary: Slope of the Second Phase Decline in Plasma HCV Ribonucleic Acid (RNA) Levels During Treatment

End point title	Slope of the Second Phase Decline in Plasma HCV Ribonucleic Acid (RNA) Levels During Treatment
End point description: HCV viral kinetics in plasma during therapy were modeled through non-linear mixed effect models, including a rapid first phase of initial decline and a slower second phase decline. The slope of the second phase decline was estimated for each treatment arm. Participants with evaluable HCV RNA to calculate the slope of the second phase were included in the analysis. Three participants were excluded due to algorithm non-convergence in the non-linear modeling process.	
End point type	Primary
End point timeframe: From Week 0 to Week 2	

End point values	Arm A: Ribavirin Full Dose for Last 10 Weeks	Arm B: Ribavirin Full Dose for 12 Weeks	Arm C: Ribavirin Low- dose for 12 Weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	17	6	
Units: 1/day				
median (full range (min-max))	0.0036 (0.0006 to 0.0128)	0.0046 (-0.0003 to 0.0155)	0.0051 (0.0031 to 0.0076)	

Statistical analyses

Statistical analysis title	Comparison of Slope
Statistical analysis description: This study was an exploratory study to evaluate the effect of ribavirin on the slope of the second phase	

of HCV RNA decline in participants who received the 3-direct-acting antiviral agent regimen.

Comparison groups	Arm B: Ribavirin Full Dose for 12 Weeks v Arm A: Ribavirin Full Dose for Last 10 Weeks
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.311
Method	Wilcoxon Rank Sum Test

Statistical analysis title	Comparison of Slope
Statistical analysis description:	
This study was an exploratory study to evaluate the effect of ribavirin on the slope of the second phase of HCV RNA decline in participants who received the 3-direct-acting antiviral agent regimen.	
Comparison groups	Arm B: Ribavirin Full Dose for 12 Weeks v Arm C: Ribavirin Low-dose for 12 Weeks
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.561
Method	Wilcoxon Rank Sum Test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until 30 days after last dose; up to 16 weeks.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Arm A: Ribavirin Full Dose for Last 10 Weeks
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Reporting group description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) for 12 weeks and weight-based ribavirin (1000 mg or 1200 mg split BID) for the last 10 weeks.

Reporting group title	Arm B: Ribavirin Full Dose for 12 Weeks
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Reporting group description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and weight-based ribavirin (1000 mg or 1200 mg split BID) for 12 weeks.

Reporting group title	Arm C: Ribavirin Low-dose for 12 Weeks
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Reporting group description:

Participants received ombitasvir/ABT-450/ritonavir 25 mg/150 mg/100 mg once daily (QD) + dasabuvir 250 mg twice daily (BID) and 600 mg ribavirin once daily for 12 weeks.

Serious adverse events	Arm A: Ribavirin Full Dose for Last 10 Weeks	Arm B: Ribavirin Full Dose for 12 Weeks	Arm C: Ribavirin Low-dose for 12 Weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 6 (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
Drug Dependence			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 6 (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

Non-serious adverse events	Arm A: Ribavirin Full Dose for Last 10 Weeks	Arm B: Ribavirin Full Dose for 12 Weeks	Arm C: Ribavirin Low-dose for 12 Weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	16 / 19 (84.21%)	6 / 6 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 21 (14.29%)	3 / 19 (15.79%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Fatigue			
subjects affected / exposed	5 / 21 (23.81%)	7 / 19 (36.84%)	2 / 6 (33.33%)
occurrences (all)	5	7	2
Feeling Abnormal			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Polymenorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1

Oropharyngeal Pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Respiratory Tract Congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinus Congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Confusional State			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Depressed Mood			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	3 / 21 (14.29%)	2 / 19 (10.53%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Emotional Distress			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	3 / 21 (14.29%)	3 / 19 (15.79%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Irritability			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Mood Swings			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Sleep Disorder			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Body Temperature Fluctuation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Glucose Urine Present			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemoglobin Decreased			
subjects affected / exposed	1 / 21 (4.76%)	3 / 19 (15.79%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
International Normalised Ratio Increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Prothrombin Level Increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Limb Injury			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Procedural Headache			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Procedural Pain			
subjects affected / exposed	7 / 21 (33.33%)	5 / 19 (26.32%)	5 / 6 (83.33%)
occurrences (all)	9	6	10
Cardiac disorders			

Palpitations subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Nervous system disorders			
Amnesia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	2 / 19 (10.53%) 2	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	4 / 21 (19.05%) 4	4 / 19 (21.05%) 5	0 / 6 (0.00%) 0
Memory Impairment subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	3 / 19 (15.79%) 3	0 / 6 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	4 / 21 (19.05%) 6	4 / 19 (21.05%) 7	2 / 6 (33.33%) 2
Increased Tendency To Bruise subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	2 / 19 (10.53%) 2	0 / 6 (0.00%) 0
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders			
Abdominal Discomfort subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Abdominal Pain subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 4	3 / 19 (15.79%) 4	1 / 6 (16.67%) 1
Abdominal Pain Upper subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Diarrhoea subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Dry Mouth subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	1 / 19 (5.26%) 1	2 / 6 (33.33%) 2
Dyspepsia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	2 / 19 (10.53%) 2	3 / 6 (50.00%) 3
Haematochezia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Nausea subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 4	3 / 19 (15.79%) 3	2 / 6 (33.33%) 2
Rectal Haemorrhage subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 19 (5.26%) 1	0 / 6 (0.00%) 0
Vomiting			

subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 5	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	2 / 6 (33.33%)
occurrences (all)	4	0	5
Hypertransaminasaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Angioedema			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dermatitis Contact			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dry Skin			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	3 / 21 (14.29%)	6 / 19 (31.58%)	1 / 6 (16.67%)
occurrences (all)	4	6	1
Rash			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Rash Generalised			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysuria			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 19 (0.00%) 0	1 / 6 (16.67%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	2 / 6 (33.33%)
occurrences (all)	3	1	2
Flank Pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle Tightness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Myalgia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fungal Skin Infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral Candidiasis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 6 (16.67%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2015	<p>The purpose of this amendment was as follows:</p> <ul style="list-style-type: none">• Update Introduction to remove language detailing effects of ABT-450/ritonavir, ABT-267 (and its major, inactive human metabolites) and ABT-333 on embryo-fetal development.• Update Introduction to refer Investigators to locally approved labels for preclinical toxicology (including reproductive and developmental toxicology), metabolism, pharmacokinetics and drug-drug interactions in countries that have received marketing approval.• Decrease the duration of RBV-free treatment in Arm A from 4 to 2 weeks.• Update Contraindicated Medication list in Synopsis and Exclusion 3 (Amendment 1, Table 4) and refer Investigators to local labels for the AbbVie product containing the regimen for this study.• Modify the time points of FNA of the liver and peripheral blood mononuclear cell (PBMC) samples in subjects at the specified site in the United States.• Clarify that virologic failures will be offered retreatment with 3-DAA + sofosbuvir + RBV.• Address inconsistencies throughout the protocol.
11 October 2016	<p>The purpose of this amendment was to accomplish the following:</p> <ul style="list-style-type: none">• Clarify that virologic failures will be offered retreatment with ABT-493/ABT-530 + sofosbuvir + RBV.• Update Section 6.0, Complaints, to incorporate new protocol template language.• Update Section 5.3.1, Table 5, Activities Table, and Section 6.1.4, Adverse Event Collection Period, to incorporate collection of serious adverse events after 30 days following the last dose of study drug.• To incorporate administrative changes made throughout for clarity as well as to update study personnel titles, study contact information, and to document the new study Medical Director.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported