Clinical trial results:
A Long-Term Follow-up Study of Subjects Who Participated in a Clinical Trial in Which Asunaprevir (BMS-650032) and/or Daclatasvir (BMS-790052) was Administered for the Treatment of Chronic Hepatitis C

Summary

EudraCT number	2011-005287-21
Trial protocol	DE IE SE IT GB DK ES
Global end of trial date	16 March 2018

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	AI444-046

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01492504
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	03 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the durability of virologic response in subjects previously treated with asunaprevir and/or daclatasvir who achieved Sustained Virologic Response (SVR12) in the previous study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2012
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	Argentina: 54
Country: Number of subjects enrolled	Australia: 54
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Canada: 110
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	France: 270
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Ireland: 12
Country: Number of subjects enrolled	Italy: 50
Country: Number of subjects enrolled	Japan: 246
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Puerto Rico: 18
Country: Number of subjects enrolled	Spain: 74
Country: Number of subjects enrolled	Sweden: 23
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 628

Worldwide total number of subjects	1706
EEA total number of subjects	508

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)	1426
From 65 to 84 years	280
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1706 participants completed the follow up period from the parent study and were eligible for AI444046

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DCV 3DAA +/- R

Arm description:

Daclatasvir (DCV) in combination with asunaprevir (ASV) and beclabuvir (BCV), BMS-791325, NS5B Polymerase Inhibitor) with or without ribavirin (RBV).

(Parent studies AI443014, AI443102, AI443113, and AI443123)

Arm type	No Intervention
Investigational medicinal product name	No Intervention
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

No intervention - System limitation pharmaceutical form and route of administration must be filled in below. Capsule and oral administration used as placeholder.

Arm title	DCV + ASV

Arm description:

Daclatasvir (DCV) in combination with asunaprevir (ASV).

(Parent studies AI444026, AI447011, AI447017, AI447026, and AI447028)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	DCV + ASV + P/R

Arm description:

Daclatasvir/asunaprevir (DCV/ASV) plus peginterferon a-2a (pegIFNa-2a)/ ribavirin (RBV).

(Parent study AI444026, AI447011, and AI447029); includes DCV/ASV plus RBV (Group B3 in parent study AI447011, N = 4)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	DCV + SOF +/- R

Arm description:

Daclatasvir (DCV) in combination with sofosbuvi (SOF) (with or without ribavirin (RBV))

(Parent study AI444040, AI444215, AI444216, and AI444218)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	DCV + P/R

Arm description:

Daclatasvir (DCV) plus pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444026, AI444031, AI444038, AI444042, AI444043, and AI444052)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	ASV + P/R

Arm description:

Asunaprevir (ASV) plus pegIFNa-2a/ribavirin (RBV)

(Parent study AI447016)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Comparator + P/R

Arm description:

Comparator/pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444031, AI444042, and AI447016) Comparator includes placebo (PBO) or telaprevir (TVR)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Rescue/Re-trt

Arm description:

Rescue therapy (daclatasvir/asunaprevir (DCV/ASV) plus pegIFNa-2a or pegIFNa-2b/ribavirin (RBV) after virologic non-response to DCV/ASV.

(Parent studies AI444040, AI447011, AI447026, and AI447028 or DCV/ASV/RBV [Group B3 in parent study AI447011, N = 3] therapy administered for a subset of subjects.)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R
Started	265	389	199
Completed	196	351	158
Not completed	69	38	41
Participant No Longer Meets Study Criteria	3	6	7
Other Reasons	13	2	2
Death	2	7	2
Lost to follow-up	21	10	9
Participant Withdrew Consent	29	13	21
Administrative Reason by Sponsor	1	-	-

Number of subjects in period 1	DCV + SOF +/- R	DCV + P/R	ASV + P/R
Started	263	410	94

Completed	177	294	76
Not completed	86	116	18
Participant No Longer Meets Study Criteria	9	43	4
Other Reasons	5	7	1
Death	4	5	2
Lost to follow-up	25	33	9
Participant Withdrew Consent	23	28	2
Administrative Reason by Sponsor	20	-	-

Number of subjects in period 1	Comparator + P/R	Rescue/Re-trt
Started	63	23
Completed	44	13
Not completed	19	10
Participant No Longer Meets Study Criteria	2	4
Other Reasons	5	2
Death	-	-
Lost to follow-up	6	-
Participant Withdrew Consent	6	1
Administrative Reason by Sponsor	-	3

Baseline characteristics

Reporting groups	
Reporting group title	DCV 3DAA +/- R
Reporting group description:	
Daclatasvir (DCV) in combination with asunaprevir (ASV) and beclabuvir (BCV), BMS-791325, NS5B Polymerase Inhibitor) with or without ribavirin (RBV). (Parent studies AI443014, AI443102, AI443113, and AI443123)	
Reporting group title	DCV + ASV
Reporting group description:	
Daclatasvir (DCV) in combination with asunaprevir (ASV). (Parent studies AI444026, AI447011, AI447017, AI447026, and AI447028)	
Reporting group title	DCV + ASV + P/R
Reporting group description:	
Daclatasvir/asunaprevir (DCV/ASV) plus peginterferon a-2a (pegIFNa-2a)/ ribavirin (RBV). (Parent study AI444026, AI447011, and AI447029); includes DCV/ASV plus RBV (Group B3 in parent study AI447011, N = 4)	
Reporting group title	DCV + SOF +/- R
Reporting group description:	
Daclatasvir (DCV) in combination with sofosbuvi (SOF) (with or without ribavirin (RBV)) (Parent study AI444040, AI444215, AI444216, and AI444218)	
Reporting group title	DCV + P/R
Reporting group description:	
Daclatasvir (DCV) plus pegIFNa-2a/ribavirin (RBV) (Parent studies AI444010, AI444011, AI444014, AI444026, AI444031, AI444038, AI444042, AI444043, and AI444052)	
Reporting group title	ASV + P/R
Reporting group description:	
Asunaprevir (ASV) plus pegIFNa-2a/ribavirin (RBV) (Parent study AI447016)	
Reporting group title	Comparator + P/R
Reporting group description:	
Comparator/pegIFNa-2a/ribavirin (RBV) (Parent studies AI444010, AI444011, AI444014, AI444031, AI444042, and AI447016) Comparator includes placebo (PBO) or telaprevir (TVR)	
Reporting group title	Rescue/Re-trt
Reporting group description:	
Rescue therapy (daclatasvir/asunaprevir (DCV/ASV) plus pegIFNa-2a or pegIFNa-2b/ribavirin (RBV) after virologic non-response to DCV/ASV. (Parent studies AI444040, AI447011, AI447026, and AI447028 or DCV/ASV/RBV [Group B3 in parent study AI447011, N = 3] therapy administered for a subset of subjects.)	

Reporting group values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R
Number of subjects	265	389	199
Age Categorical Units: Subjects			
Adults (18-64 years)	229	239	180

From 65-84 years	36	150	19

Age Continuous			
Units: years			
arithmetic mean	55.8	60.3	53.7
standard deviation	± 9.16	± 10.88	± 8.94
Gender Categorical			
Units: Subjects			
Female	85	235	60
Male	180	154	139
Race			
Units: Subjects			
White	229	103	162
Black/African American	28	11	22
Asian Indian	0	0	0
Chinese	1	15	0
Japanese	0	238	0
Korean	0	15	14
Asian Other	3	3	0
American Indian/ Alaskan Native	2	0	0
Native Hawaiian/ Other Pacific	1	0	0
Other	1	4	1
Ethnicity			
Units: Subjects			
Hispanic/ Latino	26	5	16
Not Hispanic/ Latino	235	348	178
Not Reported	4	36	5

Reporting group values	DCV + SOF +/- R	DCV + P/R	ASV + P/R
Number of subjects	263	410	94
Age Categorical			
Units: Subjects			
Adults (18-64 years)	230	383	84
From 65-84 years	33	27	10
Age Continuous			
Units: years			
arithmetic mean	55.9	51.4	50.8
standard deviation	± 9.22	± 9.38	± 10.18
Gender Categorical			
Units: Subjects			
Female	88	143	30
Male	175	267	64
Race			
Units: Subjects			
White	216	352	83
Black/African American	34	30	6
Asian Indian	3	2	0
Chinese	0	3	0
Japanese	0	1	0
Korean	1	0	0

Asian Other	4	8	2
American Indian/ Alaskan Native	1	1	0
Native Hawaiian/ Other Pacific	1	0	0
Other	3	13	3
Ethnicity Units: Subjects			
Hispanic/ Latino	54	55	24
Not Hispanic/ Latino	209	350	65
Not Reported	0	5	5

Reporting group values	Comparator + P/R	Rescue/Re-trt	Total
Number of subjects	63	23	1706
Age Categorical Units: Subjects			
Adults (18-64 years)	60	21	1426
From 65-84 years	3	2	280
Age Continuous Units: years			
arithmetic mean	51.3	57.7	
standard deviation	± 8.23	± 7.37	-
Gender Categorical Units: Subjects			
Female	21	11	673
Male	42	12	1033
Race Units: Subjects			
White	58	11	1214
Black/African American	3	4	138
Asian Indian	0	0	5
Chinese	0	0	19
Japanese	0	8	247
Korean	0	0	30
Asian Other	1	0	21
American Indian/ Alaskan Native	1	0	5
Native Hawaiian/ Other Pacific	0	0	2
Other	0	0	25
Ethnicity Units: Subjects			
Hispanic/ Latino	9	2	191
Not Hispanic/ Latino	47	21	1453
Not Reported	7	0	62

End points

End points reporting groups

Reporting group title	DCV 3DAA +/- R

Reporting group description:

Daclatasvir (DCV) in combination with asunaprevir (ASV) and beclabuvir (BCV), BMS-791325, NS5B Polymerase Inhibitor) with or without ribavirin (RBV).

(Parent studies AI443014, AI443102, AI443113, and AI443123)

Reporting group title	DCV + ASV

Reporting group description:

Daclatasvir (DCV) in combination with asunaprevir (ASV).

(Parent studies AI444026, AI447011, AI447017, AI447026, and AI447028)

Reporting group title	DCV + ASV + P/R

Reporting group description:

Daclatasvir/asunaprevir (DCV/ASV) plus peginterferon a-2a (pegIFNa-2a)/ ribavirin (RBV).

(Parent study AI444026, AI447011, and AI447029); includes DCV/ASV plus RBV (Group B3 in parent study AI447011, N = 4)

Reporting group title	DCV + SOF +/- R

Reporting group description:

Daclatasvir (DCV) in combination with sofosbuvi (SOF) (with or without ribavirin (RBV))

(Parent study AI444040, AI444215, AI444216, and AI444218)

Reporting group title	DCV + P/R

Reporting group description:

Daclatasvir (DCV) plus pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444026, AI444031, AI444038, AI444042, AI444043, and AI444052)

Reporting group title	ASV + P/R

Reporting group description:

Asunaprevir (ASV) plus pegIFNa-2a/ribavirin (RBV)

(Parent study AI447016)

Reporting group title	Comparator + P/R

Reporting group description:

Comparator/pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444031, AI444042, and AI447016) Comparator includes placebo (PBO) or telaprevir (TVR)

Reporting group title	Rescue/Re-trt

Reporting group description:

Rescue therapy (daclatasvir/asunaprevir (DCV/ASV) plus pegIFNa-2a or pegIFNa-2b/ribavirin (RBV) after virologic non-response to DCV/ASV.

(Parent studies AI444040, AI447011, AI447026, and AI447028 or DCV/ASV/RBV [Group B3 in parent study AI447011, N = 3] therapy administered for a subset of subjects.)

Primary: Durability of Virologic Response

End point title	Durability of Virologic Response[1]

End point description:

The durability of virologic response, as assessed by the time to loss of virologic response among BMS-treated subjects who achieved a sustained virologic Response at post-treatment at week 12 (SVR12) in

the previous study. The principal analysis of this endpoint is estimating the probability of maintaining a durable virologic response through long-term follow-up using the Kaplan-Meier approach.

Subjects are considered to be in response until a hepatitis C virus (HCV) RNA >/= limit of quantitation (LOQ) (confirmed or last available) is observed. Eligible subjects who achieved SVR12 and who discontinue from the long-term study before having an event will be censored at the time of the latest HCV RNA. Eligible subjects who achieved SVR12 and have not had the event at the time of an analysis will be censored at the time of the last HCV RNA.

End point type	Primary

End point timeframe:

Up to 144 weeks following SVR12 in parent study

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: Only summary statistics planned for this endpoint

End point values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R	DCV + SOF +/- R
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	3	0[2]
Units: Years				
median (full range (min-max))	0.39 (0.23 to 1.196)	0.52 (0.52 to 0.52)	0.23 (0.23 to 0.747)	(to)

Notes:

[2] - No eligible subjects with relapse

End point values	DCV + P/R	ASV + P/R	Comparator + P/R	Rescue/Re-trt
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	1	2
Units: Years				
median (full range (min-max))	0.23 (0.23 to 1.175)	0.42 (0.23 to 0.474)	0.60 (0.60 to 0.60)	0.23 (0.23 to 0.233)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Viral Genotypic Substitutions

End point title	Frequency of Viral Genotypic Substitutions[3]

End point description:

The number of viral genotypic substitutions at analysis intervals among subjects previously treated with asunaprevir and/or daclatasvir who did not achieve or did not maintain a sustained virologic response at post-treatment at week 12 (SVR12) in the previous study.

End point type	Secondary

End point timeframe:

Screening/ Day 1 participation up to 144 weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to participants previously treated with asunaprevir and/or daclatasvir. Missing arm is comprised of participants not previously treated with asunaprevir and/or daclatasvir

End point values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R	DCV + SOF +/- R
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	389	199	263
Units: Genotypic Substitutions				
Week 24	9	35	11	0
Week 48	6	35	12	0
Week 72	1	5	3	0
Week 96	4	25	2	1
Week 120	0	0	0	0
Week 144	3	25	2	0

End point values	DCV + P/R	ASV + P/R	Rescue/Re-trt	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	410	94	23	
Units: Genotypic Substitutions				
Week 24	101	11	12	
Week 48	87	11	12	
Week 72	40	5	2	
Week 96	73	8	12	
Week 120	10	2	4	
Week 144	45	4	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Hepatic Disease Progression

End point title	Frequency of Hepatic Disease Progression

End point description:

The number of hepatic disease progression events diagnosed after end of therapy. (events include: hepatic cirrhosis, esophageal varices, bleeding esophageal varices, ascites, hepatic encephalopathy, hepatocellular carcinoma, spontaneous bacterial peritonitis, gastric varices, bleeding gastric varices, hepatorenal syndrome, liver transplant)

End point type	Secondary

End point timeframe:

Screening/ Day 1 participation up to 144 weeks

End point values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R	DCV + SOF +/- R
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	389	199	263
Units: Events	19	17	9	8

End point values	DCV + P/R	ASV + P/R	Comparator + P/R	Rescue/Re-trt
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	410	94	63	23
Units: Events	18	2	2	3

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants that Died During the Long Term Follow Up

End point title	The Number of Participants that Died During the Long Term Follow Up

End point description:

The number of participants that died during the long term follow up

End point type	Secondary

End point timeframe:

Screening/ Day 1 participation up to 144 weeks

End point values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R	DCV + SOF +/- R
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	389	199	263
Units: Participants	3	7	2	4

End point values	DCV + P/R	ASV + P/R	Comparator + P/R	Rescue/Re-trt
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	410	94	63	23
Units: Participants	5	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Liver-Related Death During the Long Term Follow Up

End point title	The Number of Participants with Liver-Related Death During the Long Term Follow Up

End point description:

The number of participants with liver-related death during the long term follow Up

End point type	Secondary

End point timeframe:

Screening/ Day 1 participation up to 144 weeks

End point values	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R	DCV + SOF +/- R
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	389	199	263
Units: Participants	0	2	1	0

End point values	DCV + P/R	ASV + P/R	Comparator + P/R	Rescue/Re-trt
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	410	94	63	23
Units: Participants	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From screening/ Day 1 participation up to 144 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	DCV 3DAA +/- R

Reporting group description:

Daclatasvir (DCV) in combination with asunaprevir (ASV) and beclabuvir (BCV), BMS-791325, NS5B Polymerase Inhibitor) with or without ribavirin (RBV).

(Parent studies AI443014, AI443102, AI443113, and AI443123)

Reporting group title	DCV + ASV

Reporting group description:

Daclatasvir (DCV) in combination with asunaprevir (ASV).

(Parent studies AI444026, AI447011, AI447017, AI447026, and AI447028)

Reporting group title	DCV + ASV + P/R

Reporting group description:

Daclatasvir/asunaprevir (DCV/ASV) plus peginterferon a-2a (pegIFNa-2a)/ ribavirin (RBV).

(Parent study AI444026, AI447011, and AI447029); includes DCV/ASV plus RBV (Group B3 in parent study AI447011, N = 4)

Reporting group title	DCV + SOF +/- RBV

Reporting group description:

Daclatasvir (DCV) in combination with sofosbuvi (SOF) (with or without ribavirin (RBV))

(Parent study AI444040, AI444215, AI444216, and AI444218)

Reporting group title	DCV + P/R

Reporting group description:

Daclatasvir (DCV) plus pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444026, AI444031, AI444038, AI444042, AI444043, and AI444052)

Reporting group title	ASV + P/R

Reporting group description:

Asunaprevir (ASV) plus pegIFNa-2a/ribavirin (RBV)

(Parent study AI447016)

Reporting group title	COMPARATOR + P/R

Reporting group description:

Comparator/pegIFNa-2a/ribavirin (RBV)

(Parent studies AI444010, AI444011, AI444014, AI444031, AI444042, and AI447016) Comparator includes placebo (PBO) or telaprevir (TVR)

Reporting group title	RESCUE/RE-TRT

Reporting group description:

Rescue therapy (daclatasvir/asunaprevir (DCV/ASV) plus pegIFNa-2a or pegIFNa-2b/ribavirin (RBV) after virologic non-response to DCV/ASV.

(Parent studies AI444040, AI447011, AI447026, and AI447028 or DCV/ASV/RBV [Group B3 in parent study AI447011, N = 3] therapy administered for a subset of subjects.)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: SAEs not related to the BMS product under study and non-serious AEs will not be reported as part of this study.

Serious adverse events	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 265 (0.38%)	3 / 389 (0.77%)	1 / 199 (0.50%)
number of deaths (all causes)	1	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Hepatic cancer			
subjects affected / exposed	0 / 265 (0.00%)	1 / 389 (0.26%)	0 / 199 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Malignant melanoma			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Neoplasm malignant			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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

Overdose			
subjects affected / exposed	1 / 265 (0.38%)	0 / 389 (0.00%)	0 / 199 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	1 / 199 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Sudden death			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 265 (0.00%)	1 / 389 (0.26%)	0 / 199 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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			

Chronic kidney disease			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (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
Infections and infestations			
Septic shock			
subjects affected / exposed	0 / 265 (0.00%)	1 / 389 (0.26%)	0 / 199 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	DCV + SOF +/- RBV	DCV + P/R	ASV + P/R
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 263 (1.52%)	5 / 410 (1.22%)	2 / 94 (2.13%)
number of deaths (all causes)	4	5	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 410 (0.24%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic cancer			
subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 410 (0.24%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 263 (0.38%)	0 / 410 (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 / 1	0 / 0	0 / 0
Neoplasm malignant			

subjects affected / exposed	1 / 263 (0.38%)	0 / 410 (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 / 1	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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 / 1
Overdose			
subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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			
Cardiac arrest			
subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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 / 1
Myocardial infarction			
subjects affected / exposed	0 / 263 (0.00%)	1 / 410 (0.24%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 263 (0.00%)	1 / 410 (0.24%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sudden death			
subjects affected / exposed	1 / 263 (0.38%)	0 / 410 (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 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			

subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 263 (0.38%)	0 / 410 (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 / 1	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 263 (0.00%)	1 / 410 (0.24%)	0 / 94 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Septic shock			
subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (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

Serious adverse events	COMPARATOR + P/R	RESCUE/RE-TRT	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			

subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (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 / 63 (0.00%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (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			
Septic shock			
subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (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	DCV 3DAA +/- R	DCV + ASV	DCV + ASV + P/R
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 265 (0.00%)	0 / 389 (0.00%)	0 / 199 (0.00%)

Non-serious adverse events	DCV + SOF +/- RBV	DCV + P/R	ASV + P/R
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 263 (0.00%)	0 / 410 (0.00%)	0 / 94 (0.00%)

Non-serious adverse events	COMPARATOR + P/R	RESCUE/RE-TRT	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 63 (0.00%)	0 / 23 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2012	Implements changes to the target patient population
05 April 2012	Implements reporting of serious adverse events (SAEs) related to the BMS product under study and clarifies the inclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported