



Clinical trial results:

A Phase III Randomized Clinical Trial to Study the Efficacy and Safety of the Combination Regimen of MK-5172/MK-8742 in Treatment-Naïve Subjects with Chronic HCV GT1, GT4, and GT6 Infection.

Summary

EudraCT number	2014-000137-22
Trial protocol	CZ SE DE
Global end of trial date	06 September 2015

Results information

Result version number	v1 (current)
This version publication date	11 September 2016
First version publication date	11 September 2016

Trial information

Trial identification

Sponsor protocol code	MK-5172-060
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02105467
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 September 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was an efficacy and safety study of grazoprevir (MK-5172) in combination with elbasvir (MK-8742) in treatment-naïve participants with chronic hepatitis C virus (HCV) genotype (GT) 1, 4, or 6 infection. Participants were randomly assigned (3:1 ratio) to immediate treatment or deferred treatment (placebo control).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2014
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	Australia: 17
Country: Number of subjects enrolled	Czech Republic: 28
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Korea, Republic of: 31
Country: Number of subjects enrolled	Sweden: 24
Country: Number of subjects enrolled	Taiwan: 25
Country: Number of subjects enrolled	United States: 205
Country: Number of subjects enrolled	Israel: 22
Worldwide total number of subjects	421
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)	374
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

For Subject Disposition, Period 1 covers Day 1 through Week 12 for both treatment groups. Period 2 covers Week 12 through Week 36 for the Immediate Treatment Group (ITG) and Week 12 through Week 28 for the Deferred Treatment Group (DTG). Period 3 covers Week 28 through Week 52 for the DTG; the ITG completed the study with Period 2.

Pre-assignment

Screening details:

A total of 469 participants were screened and 421 were randomized.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Treatment Group

Arm description:

Participants received blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet orally once daily for 12 weeks (Period 1), followed by a 24-week follow-up period (Period 2)

Arm type	Experimental
Investigational medicinal product name	grazoprevir 100 mg / elbasvir 50 mg FDC
Investigational medicinal product code	
Other name	MK-5172A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet once daily by mouth for 12 weeks beginning on Day 1 (Period 1)

Arm title	Deferred Treatment Group
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Arm description:

Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).

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

Dosage and administration details:

Blinded placebo tablet once daily by mouth for 12 weeks beginning on Day 1 (Period 1)

Number of subjects in period 1	Immediate Treatment Group	Deferred Treatment Group
Started	316	105
Completed	314	105
Not completed	2	0
Death	1	-
Lost to follow-up	1	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Treatment Group

Arm description:

Participants received blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet orally once daily for 12 weeks (Period 1) followed by a 24-week follow-up period (Period 2).

Arm type	Experimental
Investigational medicinal product name	grazoprevir 100 mg / elbasvir 50 mg FDC
Investigational medicinal product code	
Other name	MK-5172A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet once daily by mouth for 12 weeks beginning on Day 1 (Period 1). No study drug was administered during Period 2.

Arm title	Deferred Treatment Group
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Arm description:

Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).

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

Dosage and administration details:

Blinded placebo tablet once daily by mouth for 12 weeks beginning on Day 1 (Period 1)

Investigational medicinal product name	grazoprevir 100 mg / elbasvir 50 mg FDC
Investigational medicinal product code	
Other name	MK-5172A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet once daily by mouth for 12 weeks beginning at Week 16 (Period 2)

Number of subjects in period 2^[1]	Immediate Treatment Group	Deferred Treatment Group
Started	314	104
Completed	312	102
Not completed	2	2
Consent withdrawn by subject	-	2
Death	1	-
Lost to follow-up	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One participant proceeded directly to Period 3

Period 3

Period 3 title	Period 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Deferred Treatment Group
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Arm description:

Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).

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

Dosage and administration details:

Blinded placebo tablet once daily by mouth for 12 weeks beginning on Day 1 (Period 1)

Investigational medicinal product name	grazoprevir 100 mg / elbasvir 50 mg FDC
Investigational medicinal product code	
Other name	MK-5172A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet once daily by

mouth for 12 weeks beginning at Week 16 (Period 2). No study drug was administered during Period 3.

Number of subjects in period 3^[2]	Deferred Treatment Group
Started	103
Completed	102
Not completed	1
Lost to follow-up	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One participant proceeded directly to Period 3

Baseline characteristics

Reporting groups

Reporting group title	Immediate Treatment Group
Reporting group description:	
Participants received blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet orally once daily for 12 weeks (Period 1), followed by a 24-week follow-up period (Period 2)	
Reporting group title	Deferred Treatment Group
Reporting group description:	
Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	

Reporting group values	Immediate Treatment Group	Deferred Treatment Group	Total
Number of subjects	316	105	421
Age Categorical			
Units: Subjects			
Adults (18-64 years)	287	87	374
From 65-84 years	29	18	47
Age Continuous			
Units: years			
arithmetic mean	52.2	53.8	
standard deviation	± 11.1	± 11.2	-
Gender Categorical			
Units: Subjects			
Female	145	49	194
Male	171	56	227
HCV Genotype			
HCV genotype was determined for each participant at Screening			
Units: Subjects			
Genotype 1a	157	54	211
Genotype 1b	131	40	171
Genotype 4	18	8	26
Genotype 6	10	3	13

End points

End points reporting groups

Reporting group title	Immediate Treatment Group
Reporting group description: Participants received blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet orally once daily for 12 weeks (Period 1), followed by a 24-week follow-up period (Period 2)	
Reporting group title	Deferred Treatment Group
Reporting group description: Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	
Reporting group title	Immediate Treatment Group
Reporting group description: Participants received blinded grazoprevir 100 mg / elbasvir 50 mg fixed-dose combination (FDC) tablet orally once daily for 12 weeks (Period 1) followed by a 24-week follow-up period (Period 2).	
Reporting group title	Deferred Treatment Group
Reporting group description: Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	
Reporting group title	Deferred Treatment Group
Reporting group description: Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	
Subject analysis set title	Deferred Treatment Group (Blinded Treatment Period 1)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	
Subject analysis set title	Deferred Treatment Group (Open-label Treatment Period 2)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received blinded placebo tablet orally once daily for 12 weeks (Period 1), followed by a 4-week unblinding/washout period and 12 weeks of open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily (Period 2), followed by a 24-week follow-up period (Period 3).	

Primary: Percentage of Participants Achieving Sustained Virologic Response at 12 Weeks After the End of Treatment (SVR12)

End point title	Percentage of Participants Achieving Sustained Virologic Response at 12 Weeks After the End of Treatment (SVR12) ^{[1][2]}
End point description: Hepatitis C virus ribonucleic acid (RNA) was measured using the Roche COBAS® Taqman® HCV Test, v2.0 assay. SVR12 was defined as HCV RNA <Lower Limit of Quantification (<15 IU/mL) 12 weeks after the end of all study therapy. The Full Analysis Set included randomized participants who received at least one dose of study treatment. This endpoint applied only to the Immediate Treatment group.	
End point type	Primary
End point timeframe: Week 24 (12 weeks after the end of treatment)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was conducted for this endpoint comparing treatment groups in the study

[2] - 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: This endpoint applied only to the Immediate Treatment group

End point values	Immediate Treatment Group			
Subject group type	Reporting group			
Number of subjects analysed	316			
Units: Percentage of participants				
number (confidence interval 95%)	94.6 (91.5 to 96.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing at Least One Adverse Event

End point title	Percentage of Participants Experiencing at Least One Adverse Event
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End point description:

An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign(including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an adverse event. The All Subjects as Treated population included randomized participants who received at least one dose of study treatment. This endpoint applied only to the blinded treatment period.

End point type	Primary
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End point timeframe:

Up to Week 14 (14 days after blinded treatment was completed)

End point values	Immediate Treatment Group	Deferred Treatment Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	105		
Units: Percentage of participants				
number (not applicable)	67.4	68.6		

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
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Statistical analysis description:

Between-treatment difference (Immediate Treatment Group - Deferred Treatment Group) was analyzed using the Miettinen and Nurminen method.

Comparison groups	Immediate Treatment Group v Deferred Treatment Group
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Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	9.6

Primary: Percentage of Participants Discontinued from Study Treatment Because of an Adverse Event

End point title	Percentage of Participants Discontinued from Study Treatment Because of an Adverse Event
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End point description:

An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an adverse event. The All Subjects as Treated population included randomized participants who received at least one dose of study treatment. This endpoint applied only to the blinded treatment period.

End point type	Primary
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End point timeframe:

Up to Week 12 (end of blinded treatment)

End point values	Immediate Treatment Group	Deferred Treatment Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	316	105		
Units: Percentage of participants				
number (not applicable)	0.9	1		

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
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Statistical analysis description:

Between-treatment difference (Immediate Treatment Group - Deferred Treatment Group) was analyzed using the Miettinen and Nurminen method.

Comparison groups	Immediate Treatment Group v Deferred Treatment Group
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Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	2

Secondary: Percentage of Participants Achieving Sustained Virologic Response at 24 Weeks After the End of Treatment (SVR24)

End point title	Percentage of Participants Achieving Sustained Virologic Response at 24 Weeks After the End of Treatment (SVR24) ^[3]
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End point description:

Hepatitis C virus RNA was measured using the Roche COBAS® Taqman® HCV Test, v2.0 assay. SVR24 was defined as HCV RNA <Lower Limit of Quantification (<15 IU/mL) 24 weeks after the end of all study therapy. The Full Analysis Set included randomized participants who received at least one dose of study treatment. This endpoint applied only to the Immediate Treatment group.

End point type	Secondary
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End point timeframe:

Week 36 (24 weeks after the end of treatment)

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: This endpoint applied only to the Immediate Treatment group

End point values	Immediate Treatment Group			
Subject group type	Reporting group			
Number of subjects analysed	316			
Units: Percentage of participants				
number (confidence interval 95%)	94.3 (91.1 to 96.6)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Achieving Sustained Virologic Response at 4 Weeks After the End of Treatment (SVR4)

End point title	Percentage of Participants Achieving Sustained Virologic Response at 4 Weeks After the End of Treatment (SVR4) ^[4]
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End point description:

Hepatitis C virus RNA was measured using the Roche COBAS® Taqman® HCV Test, v2.0 assay. SVR4 was defined as HCV RNA <Lower Limit of Quantification (<15 IU/mL) 4 weeks after the end of all study therapy. The Full Analysis Set included randomized participants who received at least one dose of study treatment. This endpoint applied only to the Immediate Treatment group.

End point type	Other pre-specified
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End point timeframe:

Week 16 (4 weeks after the end of treatment)

Notes:

[4] - 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: This endpoint applied only to the Immediate Treatment group

End point values	Immediate Treatment Group			
Subject group type	Reporting group			
Number of subjects analysed	316			
Units: Percentage of participants				
number (confidence interval 95%)	97.2 (94.7 to 98.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Immediate Treatment Group: Up to Week 36; Deferred Treatment Group (Blinded Treatment): Up to Week 16; Deferred Treatment Group (Open-label Treatment): Week 16 to Week 52

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0, 18.0

Reporting groups

Reporting group title	Immediate Treatment Group
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Reporting group description:

Participants received blinded grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily for 12 weeks. Follow-up was for an additional 24 weeks.

Reporting group title	Deferred Treatment Group (Blinded Treatment)
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Reporting group description:

Participants received blinded placebo tablet orally once daily for 12 weeks; after a 4-week unblinding/washout period participants received open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily for 12 weeks. Follow-up was for an additional 24 weeks. Time frame for AE assessment was up to 36 weeks for one participant who did not receive open-label treatment but remained in follow-up.

Reporting group title	Deferred Treatment Group (Open-label Treatment)
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Reporting group description:

Participants received blinded placebo tablet orally once daily for 12 weeks; after a 4-week unblinding/washout period participants received open label grazoprevir 100 mg / elbasvir 50 mg FDC tablet orally once daily for 12 weeks. Follow-up was for an additional 24 weeks.

Serious adverse events	Immediate Treatment Group	Deferred Treatment Group (Blinded Treatment)	Deferred Treatment Group (Open-label Treatment)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 316 (4.75%)	4 / 105 (3.81%)	3 / 103 (2.91%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Bladder cancer			
subjects affected / exposed	0 / 316 (0.00%)	0 / 105 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancreatic carcinoma			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Prostate cancer			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Multiple fractures			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 316 (0.00%)	0 / 105 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 316 (0.32%)	1 / 105 (0.95%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			

subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Chest pain			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	0 / 316 (0.00%)	1 / 105 (0.95%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Hiatus hernia strangulated			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Pancreatitis acute			

subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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
Osteoarthritis			
subjects affected / exposed	0 / 316 (0.00%)	1 / 105 (0.95%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 316 (0.00%)	1 / 105 (0.95%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Peritoneal abscess			
subjects affected / exposed	0 / 316 (0.00%)	0 / 105 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			

subjects affected / exposed	1 / 316 (0.32%)	0 / 105 (0.00%)	0 / 103 (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

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

Non-serious adverse events	Immediate Treatment Group	Deferred Treatment Group (Blinded Treatment)	Deferred Treatment Group (Open-label Treatment)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	147 / 316 (46.52%)	60 / 105 (57.14%)	42 / 103 (40.78%)
Nervous system disorders			
Headache			
subjects affected / exposed	51 / 316 (16.14%)	18 / 105 (17.14%)	17 / 103 (16.50%)
occurrences (all)	61	19	19
Dizziness			
subjects affected / exposed	9 / 316 (2.85%)	7 / 105 (6.67%)	0 / 103 (0.00%)
occurrences (all)	9	9	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	49 / 316 (15.51%)	18 / 105 (17.14%)	12 / 103 (11.65%)
occurrences (all)	53	19	13
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	14 / 316 (4.43%)	7 / 105 (6.67%)	5 / 103 (4.85%)
occurrences (all)	15	7	5
Nausea			
subjects affected / exposed	29 / 316 (9.18%)	8 / 105 (7.62%)	8 / 103 (7.77%)
occurrences (all)	32	8	8
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 316 (2.22%)	8 / 105 (7.62%)	1 / 103 (0.97%)
occurrences (all)	7	9	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 316 (1.90%)	6 / 105 (5.71%)	3 / 103 (2.91%)
occurrences (all)	6	6	3
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	20 / 316 (6.33%)	6 / 105 (5.71%)	3 / 103 (2.91%)
occurrences (all)	22	6	3
Back pain			
subjects affected / exposed	10 / 316 (3.16%)	3 / 105 (2.86%)	7 / 103 (6.80%)
occurrences (all)	10	3	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	20 / 316 (6.33%)	7 / 105 (6.67%)	7 / 103 (6.80%)
occurrences (all)	23	8	8
Upper respiratory tract infection			
subjects affected / exposed	17 / 316 (5.38%)	2 / 105 (1.90%)	5 / 103 (4.85%)
occurrences (all)	18	2	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2014	The primary reason for Protocol Amendment 1 was to add urinalysis assessments.
25 September 2014	The primary reason for Protocol Amendment 2 was to make participants infected with HCV GT5 no longer eligible for enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported