Clinical trial results:
A Randomized, Double-Blind Study to Evaluate the Safety and Antiviral Activity of IDX184 in Combination with Pegylated Interferon and Ribavirin for 12 Weeks in Treatment-Naïve Subjects with Genotype 1 Chronic Hepatitis C Infection

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-001878-25
Trial protocol	BG
Global end of trial date	31 October 2014

Results information

Result version number	v1 (current)
This version publication date	23 April 2016
First version publication date	23 April 2016

Trial information

Trial identification

Sponsor protocol code	2355-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01371604
WHO universal trial number (UTN)	-
Other trial identifiers	Idenix Protocol Number: IDX-08C-005

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	31 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety and tolerability of MK-2355 (IDX184) in combination with peg-interferon alfa-2a (Peg-IFN) and ribavirin (RBV), and to evaluate antiviral activity of MK-2355 in combination with Peg-IFN/RBV at Week 12.

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	15 November 2011
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	Bulgaria: 4
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	United States: 56
Worldwide total number of subjects	68
EEA total number of subjects	4

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)	68
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adult (18 to 65 years of age) treatment-naive (TN) participants infected with hepatitis C virus (HCV) genotype (GT) 1 and compensated liver disease were enrolled.

Pre-assignment

Screening details:

The screening period was up to 49 days (from Day -56 to Day -7). Two of the 70 screened participants were considered screen failures; a total of 68 participants were randomized into Period 1.

Period 1

Period 1 title	Period 1: MK-2355 + Peg-IFN/RBV
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	MK-2355 50 mg + Peg-IFN/RBV

Arm description:

TN participants with HCV GT1 took 1 MK-2355 50 mg tablet and 1 matching placebo tablet q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 50 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Arm type	Experimental
Investigational medicinal product name	MK-2355
Investigational medicinal product code	
Other name	IDX-184
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-2355 was taken as either 1 or 2 50 mg tablet(s) once daily (q.d.) for 12 weeks.

Investigational medicinal product name	Peg-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN (180 µg) was administered once weekly via subcutaneous injection.

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

Dosage and administration details:

RBV (200 mg tablets) was taken twice daily (b.i.d.) by mouth with food at a total daily dose dependent on body weight (<75 kilograms [kg] = 1000 mg/day or ≥75 kg = 1200 mg/day).

Arm title	MK-2355 100 mg + Peg-IFN/RBV

Arm description:

TN participants with HCV GT1 took 2 MK-2355 50 mg tablets q.d. in combination with Peg-IFN and RBV

for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 100 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Arm type	Experimental
Investigational medicinal product name	MK-2355
Investigational medicinal product code	
Other name	IDX-184
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two 50 mg tablets (100 mg) q.d. for 12 weeks

Investigational medicinal product name	Peg-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN (180 µg) was administered weekly via subcutaneous injection.

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

Dosage and administration details:

RBV (200 mg tablets) was taken b.i.d. by mouth with food at a total daily dose dependent on body weight (<75 kilograms [kg] = 1000 mg/day or ≥75 kg = 1200 mg/day).

Number of subjects in period 1	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV
Started	34	34
Completed	19	23
Not completed	15	11
Consent withdrawn by subject	6	-
Adverse event, non-fatal	4	-
Lost to follow-up	-	3
Lack of efficacy	5	6
Protocol deviation	-	2

Period 2

Period 2 title	Period 2: Peg-IFN/RBV
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind

Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Peg-IFN/RBV (eRVR+) 24 Weeks

Arm description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and showed extended Rapid Virologic Response (eRVR; HCV viral ribonucleic acid [RNA] levels <25 IU/mL at Weeks 4 and 12) were pooled and randomized a second time to continue taking Peg-IFN/RBV for an additional 12 weeks (total treatment duration = 24 weeks).

Arm type	Experimental
Investigational medicinal product name	Peg-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN (180 µg) was administered weekly via subcutaneous injection.

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

Dosage and administration details:

RBV (200 mg tablets) was taken by mouth with food twice daily (b.i.d.) at a total daily dose dependent on body weight (<75 kilograms [kg] = 1000 mg/day or ≥75 kg = 1200 mg/day).

Arm title	Peg-IFN/RBV (eRVR+) 48 Weeks

Arm description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and showed eRVR were pooled and randomized a second time to continue taking Peg-IFN/RBV for an additional 36 weeks (total treatment duration = 48 weeks).

Arm type	Experimental
Investigational medicinal product name	Peg-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN (180 µg) was administered weekly via subcutaneous injection.

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

Dosage and administration details:

RBV (200 mg tablets) was taken by mouth with food twice daily (b.i.d.) at a total daily dose dependent on body weight (<75 kilograms [kg] = 1000 mg/day or ≥75 kg = 1200 mg/day).

Arm title	Peg-IFN/RBV (eRVR-) 48 Weeks

Arm description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and did not show eRVR continued to take Peg-IFN/RBV for an additional 36 weeks (total treatment duration = 48 weeks).

Arm type	Experimental

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

Dosage and administration details:

RBV (200 mg tablets) was taken by mouth with food twice daily (b.i.d.) at a total daily dose dependent on body weight (<75 kilograms [kg] = 1000 mg/day or ≥75 kg = 1200 mg/day).

Investigational medicinal product name	Peg-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN (180 µg) was administered weekly via subcutaneous injection.

Number of subjects in period 2[1]	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks
Started	16	15	2
Completed	16	15	2

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: Of the total 68 participants who were randomized, 42 completed 24 weeks of treatment with MK-2355 and peg-IFN/RBV. Of those 42 participants, a total of 33 continued in study in the eRVR (+/-)-designated groups for up to an additional 24 weeks of peg-IFN/RBV treatment (48 total weeks of study treatment).

Baseline characteristics

Reporting groups	
Reporting group title	MK-2355 50 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 1 MK-2355 50 mg tablet and 1 matching placebo tablet q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 50 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Reporting group title	MK-2355 100 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 2 MK-2355 50 mg tablets q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 100 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Reporting group values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV	Total
Number of subjects	34	34	68
Age Categorical Units: Subjects			
Adults (18-64 years)	34	34	68
Age Continuous Units: years			
arithmetic mean	48.1	48.4	
standard deviation	± 11.3	± 9.4	-
Gender Categorical Units: Subjects			
Female	12	10	22
Male	22	24	46

End points

End points reporting groups

Reporting group title	MK-2355 50 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 1 MK-2355 50 mg tablet and 1 matching placebo tablet q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 50 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Reporting group title	MK-2355 100 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 2 MK-2355 50 mg tablets q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered weekly via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 100 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Reporting group title	Peg-IFN/RBV (eRVR+) 24 Weeks

Reporting group description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and showed extended Rapid Virologic Response (eRVR; HCV viral ribonucleic acid [RNA] levels <25 IU/mL at Weeks 4 and 12) were pooled and randomized a second time to continue taking Peg-IFN/RBV for an additional 12 weeks (total treatment duration = 24 weeks).

Reporting group title	Peg-IFN/RBV (eRVR+) 48 Weeks

Reporting group description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and showed eRVR were pooled and randomized a second time to continue taking Peg-IFN/RBV for an additional 36 weeks (total treatment duration = 48 weeks).

Reporting group title	Peg-IFN/RBV (eRVR-) 48 Weeks

Reporting group description:

Participants that completed 12 weeks of treatment with MK-2355 in combination with Peg-IFN/RBV and did not show eRVR continued to take Peg-IFN/RBV for an additional 36 weeks (total treatment duration = 48 weeks).

Subject analysis set title	Period 2: Other
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes participants who received at least 1 dose of study drug but discontinued prior to Week 20 and were not randomized or assigned to a treatment regimen in Period 2.

Primary: Percentage of participants experiencing a serious adverse event (SAE) during treatment (Periods 1 and 2)

End point title	Percentage of participants experiencing a serious adverse event (SAE) during treatment (Periods 1 and 2)[1]

End point description:

An SAE is any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

End point type	Primary

End point timeframe:

Up to Week 24 or Week 48

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: Per protocol, only descriptive statistics are presented.

End point values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: Percentage of participants	3	6		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants experiencing an adverse event (AE) during MK-2355 treatment (Period 1)

End point title	Percentage of participants experiencing an adverse event (AE) during MK-2355 treatment (Period 1)[2]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product, and that does not necessarily have a causal relationship with the study drug(s).

End point type	Primary

End point timeframe:

Up to 12 weeks

Notes:

[2] - 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: Per protocol, only descriptive statistics are presented.

End point values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: Percentage of participants	91	88		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants experiencing a Grade 1-4 laboratory abnormality (Periods 1 and 2)

End point title	Number of participants experiencing a Grade 1-4 laboratory abnormality (Periods 1 and 2)[3]

End point description:

End point type	Primary

End point timeframe:

Up to 16 weeks

Notes:

[3] - 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: Per protocol, only descriptive statistics are presented.

End point values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Number of participants				

Notes:

[4] - Laboratory abnormality results were reported as change from baseline per measure (not shown here).

[5] - Laboratory abnormality results were reported as change from baseline per measure (not shown here).

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with undetectable HCV ribonucleic acid (RNA) viral levels at Week 12 (Period 1)

End point title	Percentage of participants with undetectable HCV ribonucleic acid (RNA) viral levels at Week 12 (Period 1)[6]

End point description:

HCV viral RNA levels were measured after completing 12 weeks of MK-2355 and Peg-IFN/RBV therapy. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Primary

End point timeframe:

Week 12

Notes:

[6] - 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: Per protocol, only descriptive statistics are presented.

End point values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[7]	31[8]		
Units: Percentage of participants	77	79		

Notes:

[7] - Data for 5 participants was unavailable.

[8] - Data for 3 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with undetectable HCV RNA viral levels at Week 4 (Period 1)

End point title	Percentage of participants with undetectable HCV RNA viral levels at Week 4 (Period 1)

End point description:

HCV viral RNA levels were measured after completing 4 weeks of MK-2355 and Peg-IFN/RBV therapy. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 4

End point values	MK-2355 50 mg + Peg-IFN/RBV	MK-2355 100 mg + Peg-IFN/RBV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33[9]	31[10]		
Units: Percentage of participants	53	56		

Notes:

[9] - Data for 1 participant was unavailable.

[10] - Data for 5 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with undetectable HCV RNA viral levels at end of treatment (EOT) (Period 1 or 2)

End point title	Percentage of participants with undetectable HCV RNA viral levels at end of treatment (EOT) (Period 1 or 2)

End point description:

HCV viral RNA levels were determined after completing all study therapy (Week 24 or Week 48). HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 24 or Week 48

End point values	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks	Period 2: Other
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	2	31[11]
Units: Percentage of participants	100	100	100	17

Notes:

[11] - Data for 4 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve sustained viral response (SVR) (Period 2)

End point title	Percentage of participants who achieve sustained viral response (SVR) (Period 2)

End point description:

SVR was defined as undetectable HCV viral RNA 24 weeks after the last dose of study drug. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

24 weeks after last dose (Week 48 or Week 72)

End point values	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks	Period 2: Other
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	2	27[12]
Units: Percentage of participants	56	100	100	26

Notes:

[12] - Data for 8 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants (in Period 2) with HCV RNA levels below the lower limit of quantification (LLoQ) at Week 4

End point title	Percentage of participants (in Period 2) with HCV RNA levels below the lower limit of quantification (LLoQ) at Week 4

End point description:

The percentage of participants with HCV viral RNA <LLoQ at Week 4 is presented according to Period 2 arms. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 4

End point values	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks	Period 2: Other
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	2	31[13]
Units: Percentage of participants	100	100	0	40

Notes:

[13] - Data for 4 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve HCV RNA <LLoQ at EOT (Period 2)

End point title	Percentage of participants who achieve HCV RNA <LLoQ at EOT (Period 2)

End point description:

The percentage of participants with HCV RNA <LLoQ at EOT is presented according to Period 2 arms. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 24 or 48

End point values	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks	Period 2: Other
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	2	26[14]
Units: Percentage of participants	100	100	100	40

Notes:

[14] - Data for nine participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve HCV RNA <LLoQ at follow-up (Period 2)

End point title	Percentage of participants who achieve HCV RNA <LLoQ at follow-up (Period 2)

End point description:

The percentage of participants with HCV RNA <LLoQ at follow-up (24 weeks after completing study therapy) is presented according to Period 2 arms. HCV viral RNA was measured with a commercial laboratory assay which had a LLoQ of 25 IU/mL.

End point type	Secondary

End point timeframe:

Week 48 or 72

End point values	Peg-IFN/RBV (eRVR+) 24 Weeks	Peg-IFN/RBV (eRVR+) 48 Weeks	Peg-IFN/RBV (eRVR-) 48 Weeks	Period 2: Other
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	2	27[15]
Units: Percentage of participants	56	100	100	51

Notes:

[15] - Data for 8 participants was unavailable.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 52 weeks for AEs and up to 72 weeks for SAEs

Adverse event reporting additional description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product, and that does not necessarily have a causal relationship with the study drug(s).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	MK-2355 100 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 2 MK-2355 50 mg tablets q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered q.w. via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 100 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Reporting group title	MK-2355 50 mg + Peg-IFN/RBV

Reporting group description:

TN participants with HCV GT1 took 1 MK-2355 50 mg tablet and 1 matching placebo tablet q.d. in combination with Peg-IFN and RBV for 12 weeks. Peg-IFN was administered q.w. via subcutaneous injection and RBV was taken b.i.d. by mouth with food at a total daily dose of 1000 mg/day or 1200 mg/day. After completing the 12-week MK-2355 50 mg regimen, participants took Peg-IFN and RBV for an additional 12 or 36 weeks based on treatment response.

Serious adverse events	MK-2355 100 mg + Peg-IFN/RBV	MK-2355 50 mg + Peg-IFN/RBV	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	MK-2355 100 mg + Peg-IFN/RBV	MK-2355 50 mg + Peg-IFN/RBV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 34 (88.24%)	32 / 34 (94.12%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Chills			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	18 / 34 (52.94%)	16 / 34 (47.06%)	
occurrences (all)	19	17	
Influenza like illness			
subjects affected / exposed	2 / 34 (5.88%)	5 / 34 (14.71%)	
occurrences (all)	2	5	
Injection site erythema			
subjects affected / exposed	1 / 34 (2.94%)	3 / 34 (8.82%)	
occurrences (all)	1	4	
Non-cardiac chest pain			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Pain			

subjects affected / exposed	1 / 34 (2.94%)	7 / 34 (20.59%)	
occurrences (all)	1	7	
Pyrexia			
subjects affected / exposed	7 / 34 (20.59%)	3 / 34 (8.82%)	
occurrences (all)	7	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 34 (5.88%)	5 / 34 (14.71%)	
occurrences (all)	2	5	
Dyspnoea			
subjects affected / exposed	4 / 34 (11.76%)	3 / 34 (8.82%)	
occurrences (all)	4	3	
Epistaxis			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Rhinorrhoea			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	3	
Sinus congestion			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 34 (11.76%)	2 / 34 (5.88%)	
occurrences (all)	4	3	
Depression			
subjects affected / exposed	6 / 34 (17.65%)	7 / 34 (20.59%)	
occurrences (all)	7	7	
Insomnia			
subjects affected / exposed	6 / 34 (17.65%)	11 / 34 (32.35%)	
occurrences (all)	6	12	
Mood altered			

subjects affected / exposed	4 / 34 (11.76%)	1 / 34 (2.94%)	
occurrences (all)	4	2	
Mood swings			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Investigations			
Weight decreased			
subjects affected / exposed	3 / 34 (8.82%)	3 / 34 (8.82%)	
occurrences (all)	4	3	
White blood cell count decreased			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Hand fracture			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 34 (5.88%)	4 / 34 (11.76%)	
occurrences (all)	3	4	
Dysgeusia			
subjects affected / exposed	3 / 34 (8.82%)	1 / 34 (2.94%)	
occurrences (all)	3	1	
Headache			
subjects affected / exposed	9 / 34 (26.47%)	11 / 34 (32.35%)	
occurrences (all)	9	14	
Memory impairment			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 34 (20.59%)	7 / 34 (20.59%)	
occurrences (all)	18	11	

Leukopenia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	3	0	
Neutropenia			
subjects affected / exposed	5 / 34 (14.71%)	5 / 34 (14.71%)	
occurrences (all)	9	32	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 34 (2.94%)	3 / 34 (8.82%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	1 / 34 (2.94%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	5 / 34 (14.71%)	1 / 34 (2.94%)	
occurrences (all)	7	1	
Dyspepsia			
subjects affected / exposed	4 / 34 (11.76%)	0 / 34 (0.00%)	
occurrences (all)	4	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 34 (2.94%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	8 / 34 (23.53%)	13 / 34 (38.24%)	
occurrences (all)	10	15	
Vomiting			
subjects affected / exposed	4 / 34 (11.76%)	4 / 34 (11.76%)	
occurrences (all)	4	4	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	4 / 34 (11.76%)	3 / 34 (8.82%)	
occurrences (all)	4	3	
Dry skin			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Night sweats			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	5 / 34 (14.71%)	9 / 34 (26.47%)	
occurrences (all)	5	9	
Rash			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Rash generalised			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Rash macular			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	
occurrences (all)	3	2	
Rash pruritic			
subjects affected / exposed	6 / 34 (17.65%)	5 / 34 (14.71%)	
occurrences (all)	7	7	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 34 (17.65%)	5 / 34 (14.71%)	
occurrences (all)	6	5	

Back pain			
subjects affected / exposed	5 / 34 (14.71%)	1 / 34 (2.94%)	
occurrences (all)	7	1	
Muscle spasms			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	3	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 34 (2.94%)	5 / 34 (14.71%)	
occurrences (all)	1	5	
Musculoskeletal pain			
subjects affected / exposed	2 / 34 (5.88%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	6 / 34 (17.65%)	5 / 34 (14.71%)	
occurrences (all)	7	5	
Pain in extremity			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
occurrences (all)	2	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	4	
Dermatophytosis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Oral herpes			
subjects affected / exposed	4 / 34 (11.76%)	1 / 34 (2.94%)	
occurrences (all)	4	1	
Upper respiratory tract infection			
subjects affected / exposed	3 / 34 (8.82%)	1 / 34 (2.94%)	
occurrences (all)	3	1	
Urinary tract infection			

subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Viral infection			
subjects affected / exposed	1 / 34 (2.94%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 34 (8.82%)	5 / 34 (14.71%)	
occurrences (all)	4	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2013	Amendment 3 included the additional cardiac assessments that were completed as part of the partial clinical hold, as well as the follow-up plan, that was recommended by U.S. FDA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
15 August 2012	The program was placed on Partial Clinical Hold by the U.S. FDA on 15-Aug-2012; the program was electively discontinued for non-safety reasons on 04-Feb-2013.	-

Notes:

Limitations and caveats

None reported