



Clinical trial results:

A Phase II, Randomized, Open-Label Clinical Trial to Study the Efficacy and Safety of the Combination Regimen of MK-3682B (MK-5172 + MK-3682 + MK-8408 Fixed Dose Combination (FDC)) in Subjects with Chronic HCV GT1 or GT3 Infection who have failed a Direct Acting Antiviral Regimen

Summary

EudraCT number	2015-001483-19
Trial protocol	SE DE ES
Global end of trial date	25 September 2017

Results information

Result version number	v1 (current)
This version publication date	24 March 2018
First version publication date	24 March 2018

Trial information

Trial identification

Sponsor protocol code	3682-021
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02613403
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-3682-021

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	27 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a randomized, multicenter, 2-part, open-label trial to evaluate the efficacy of the fixed-dose combination (FDC) regimen of grazoprevir (GZR; MK-5172), uprifosbuvir (UPR; MK-3682) and ruzasvir (RZR; MK-8408), referred to as MK-3682B, +/- ribavirin (RBV) in cirrhotic (C) or non-cirrhotic (NC) participants infected with hepatitis C virus (HCV) previously failing a direct-acting antiviral (DAA) regimen. In Part A, C or NC participants with HCV genotype (GT) 1 infection previously failing a DAA regimen of sofosbuvir (SOF)/ledipasvir (LDV) [Arms 1 and 2] or elbasvir (EBR)/GZR [Arms 3 and 4] receive: 1) MK-3682B + RBV for 16 weeks [Arms 1 and 3]; or 2) MK-3682B for 24 weeks [Arms 2 and 4]. In Part B, C or NC participants with HCV GT1-6 infection previously failing any all-oral DAA regimen (GT1-6) or SOF/pegylated interferon and ribavirin (PR) regimen (GT3 only) were to receive MK-3682B for 16 weeks. However, the trial was terminated prior to participant enrollment for Part B.

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	10 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United States: 75
Worldwide total number of subjects	94
EEA total number of subjects	19

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)	76
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part A randomized 94 C/NC participants with chronic HCV GT1 failing a DAA regimen; 1 participant withdrew prior to treatment. Part B was to evaluate MK-3682B in C/NC HCV GT1-6 participants failing any all-oral DAA (GT1-6) or PR (GT 3) regimen, enrolling after Part A completed. Part A completed as planned; trial terminated before Part B enrollment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV

Arm description:

C or NC HCV GT1 participants previously failing a DAA regimen of sofosbuvir (SOF)/ledipasvir (LDV) receive MK-3682B, a fixed dose combination (FDC) of grazoprevir (GZR; MK-5172 [50 mg]) + uprifosbuvir (UPR; MK-3682 [225 mg]) + ruzasvir (RZR; MK-8408 [30 mg]), administered as 2 tablets once daily in combination with ribavirin (RBV) twice daily for 16 weeks.

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

Dosage and administration details:

Ribavirin 200 mg capsules, taken twice daily by mouth as part of a weight-based dosing regimen. Depending on participant body weight, total daily dose of Ribavirin may be 800, 1000, 1200 or 1400 mg per day.

Investigational medicinal product name	MK-3682B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two MK-3682B 1,136 mg FDC tablets each containing 50 mg MK-5172 (GZR), 225 mg MK-3682 (UPR, formerly IDX21437), and 30 mg MK-8408 (RZR) taken once daily by mouth.

Arm title	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B
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Arm description:

C or NC HCV GT1 participants previously failing a DAA regimen of SOF/LDV receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.

Arm type	Experimental
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Investigational medicinal product name	MK-3682B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two MK-3682B 1,136 mg FDC tablets each containing 50 mg MK-5172 (GZR), 225 mg MK-3682 (UPR, formerly IDX21437), and 30 mg MK-8408 (RZR) taken once daily by mouth.

Arm title	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
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Arm description:

C or NC HCV GT1 participants previously failing a DAA regimen of GZR/elbasvir (EBR) (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily in combination with RBV twice daily for 16 weeks.

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

Dosage and administration details:

Ribavirin 200 mg capsules, taken twice daily by mouth as part of a weight-based dosing regimen. Depending on participant body weight, total daily dose of Ribavirin may be 800, 1000, 1200 or 1400 mg per day.

Investigational medicinal product name	MK-3682B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two MK-3682B 1,136 mg FDC tablets each containing 50 mg MK-5172 (GZR), 225 mg MK-3682 (UPR, formerly IDX21437), and 30 mg MK-8408 (RZR) taken once daily by mouth.

Arm title	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B
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Arm description:

C or NC HCV GT1 participants previously failing a DAA regimen of GZR/EBR (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	MK-3682B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two MK-3682B 1,136 mg FDC tablets each containing 50 mg MK-5172 (GZR), 225 mg MK-3682 (UPR, formerly IDX21437), and 30 mg MK-8408 (RZR) taken once daily by mouth.

Number of subjects in period 1	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Started	36	36	9
Treated	35	36	9
Completed	34	35	9
Not completed	2	1	0
Consent withdrawn by subject	2	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B
Started	13
Treated	13
Completed	13
Not completed	0
Consent withdrawn by subject	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of sofosbuvir (SOF)/ledipasvir (LDV) receive MK-3682B, a fixed dose combination (FDC) of grazoprevir (GZR; MK-5172 [50 mg]) + uprifosbuvir (UPR; MK-3682 [225 mg]) + ruzasvir (RZR; MK-8408 [30 mg]), administered as 2 tablets once daily in combination with ribavirin (RBV) twice daily for 16 weeks.	
Reporting group title	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of SOF/LDV receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.	
Reporting group title	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of GZR/elbasvir (EBR) (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily in combination with RBV twice daily for 16 weeks.	
Reporting group title	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of GZR/EBR (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.	

Reporting group values	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Number of subjects	36	36	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	27	30	8
From 65-84 years	9	6	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	59.2	58.9	57.3
standard deviation	± 8.3	± 6.6	± 8.5
Sex: Female, Male Units: Subjects			
Female	4	2	3
Male	32	34	6
Reporting group values	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B	Total	

Number of subjects	13	94	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	76	
From 65-84 years	2	18	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	53.9		
standard deviation	± 11.0	-	
Sex: Female, Male			
Units: Subjects			
Female	4	13	
Male	9	81	

End points

End points reporting groups

Reporting group title	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of sofosbuvir (SOF)/ledipasvir (LDV) receive MK-3682B, a fixed dose combination (FDC) of grazoprevir (GZR; MK-5172 [50 mg]) + uprifosbuvir (UPR; MK-3682 [225 mg]) + ruzasvir (RZR; MK-8408 [30 mg]), administered as 2 tablets once daily in combination with ribavirin (RBV) twice daily for 16 weeks.	
Reporting group title	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of SOF/LDV receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.	
Reporting group title	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of GZR/elbasvir (EBR) (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily in combination with RBV twice daily for 16 weeks.	
Reporting group title	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B
Reporting group description: C or NC HCV GT1 participants previously failing a DAA regimen of GZR/EBR (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.	

Primary: Percentage of Participants Achieving Sustained Virologic Response 12 Weeks After The End of Study Therapy (SVR12)

End point title	Percentage of Participants Achieving Sustained Virologic Response 12 Weeks After The End of Study Therapy (SVR12) ^[1]
End point description: The percentage of participants achieving SVR12 was determined, defined as having a plasma HCV ribonucleic acid (RNA) level below the lower limit of quantification (LLOQ) 12 weeks after the end of study therapy. Plasma HCV RNA level was measured using the Roche COBAS™ AmpliPrep/COBAS™ Taqman™ HCV Test, v2.0 ® assay with a LLOQ of 15 IU/mL. The analysis population includes all randomized participants in Part A receiving ≥1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.	
End point type	Primary
End point timeframe: 12 weeks following final dose of study treatment ([MK-3682B + RBV Groups]: Study Week 28; [MK-3682B Groups]: Study Week 36)	

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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Percentage				
number (confidence interval 95%)	97.1 (85.1 to 99.9)	100.0 (90.3 to 100.0)	100.0 (66.4 to 100.0)	100.0 (75.3 to 100.0)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced an Adverse Event

End point title	Number of Participants Who Experienced an Adverse Event ^[2]
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End point description:

The number of participants experiencing an adverse event (AE) was assessed. An AE is any unfavorable and unintended medical occurrence, symptom, or disease witnessed in a participant, regardless of whether or not a causal relationship with the study treatment can be demonstrated. Further, any worsening of a preexisting condition that is temporally associated with the use of the study treatment is also considered an AE. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	31	27	9	12

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued Study Drug Due to an Adverse Event

End point title	Number of Participants Who Discontinued Study Drug Due to an Adverse Event ^[3]
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End point description:

The number of participants discontinuing study drug due to an AE was assessed. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Serious Adverse Event

End point title	Number of Participants Who Experienced a Serious Adverse Event ^[4]
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End point description:

The number of participants experiencing a serious adverse event (SAE) was assessed. An SAE is an adverse event that: results in death; is life threatening; results in persistent or significant disability or incapacity; results in or prolongs a hospitalization; is a congenital anomaly or birth defect; is a cancer; or may jeopardize the participant, potentially require medical or surgical intervention. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Notes:

[4] - 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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	3	4	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Drug-Related Adverse Event

End point title	Number of Participants Who Experienced a Drug-Related Adverse Event ^[5]
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End point description:

The number of participants experiencing a drug-related AE was assessed. A drug-related AE was an AE thought to be possibly, probably, or definitely related to the study drug as determined by the investigator. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Notes:

[5] - 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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	23	18	9	5

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Serious and Drug-Related Adverse Event

End point title	Number of Participants Who Experienced a Serious and Drug-Related Adverse Event ^[6]
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End point description:

The number of participants experiencing a serious and drug-related AE was assessed. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced an Accidental or Intentional Overdose Without Adverse Effect

End point title	Number of Participants Who Experienced an Accidental or Intentional Overdose Without Adverse Effect ^[7]
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End point description:

The number of participants experiencing an accidental or intentional overdose without adverse effect was determined. Per study protocol, any occurrence of a participant receiving either MK-3682B or RBV at any dose higher than prescribed was considered an overdose. If this definition of overdose was met without any associated clinical symptoms or abnormal laboratory results, this occurrence of overdose was reported as an accidental or intentional overdose without adverse effect. The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Notes:

[7] - 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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants				
Overdose	1	3	2	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Non-Overdose Event of Clinical Interest

End point title	Number of Participants Who Experienced a Non-Overdose Event of Clinical Interest ^[8]
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End point description:

The number of participants experiencing a non-overdose event of clinical interest (ECI) was determined. Non-overdose ECIs, assessed from initiation of study therapy through 14 days following study treatment cessation, included the following: 1) aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >500 IU/L; or 2) AST or ALT $>3\times$ nadir value and $>3\times$ upper limit normal (ULN). The analysis population includes all randomized participants in Part A receiving ≥ 1 dose of study treatment. Part B was terminated prior to participant enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Notes:

[8] - 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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	9	13
Units: Participants	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced AST/ALT >5x Upper Limit Normal (ULN)

End point title	Number of Participants Who Experienced AST/ALT >5x Upper Limit Normal (ULN) ^[9]
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End point description:

The number of participants experiencing AST / ALT >5 times ULN from study week 4 until 2 weeks following completion of study therapy was determined. All randomized participants in Part A receiving ≥1 dose of study treatment with ≥1 AST/ALT measurement subsequent to study week 4. One participant with prior SOF/LDV failure receiving MK-3682B + RBV withdrew from study before study week 4 and was excluded from analysis. Part B terminated prior to enrollment and was not included for analysis.

End point type	Primary
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End point timeframe:

From Study Week 4 up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Notes:

[9] - 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 study protocol, statistical analysis was not planned for this endpoint.

End point values	[Part A, Arm 1] Prior SOF/LDV Failure: MK- 3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK- 3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK- 3682B + RBV	[Part A, Arm 4] Prior GZR/EBR Failure: MK- 3682B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	9	13
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2 weeks following cessation of study treatment ([MK-3682B + RBV Groups]: Up to Week 18; [MK-3682B Groups]: Up to Week 26)

Adverse event reporting additional description:

Includes only randomized participants in Study Part A receiving ≥ 1 dose of study treatment. The trial was terminated prior to participant enrollment for study Part B.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV
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Reporting group description:

C or NC HCV GT1 participants previously failing a DAA regimen of SOF/LDV receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily in combination with RBV twice daily for 16 weeks.

Reporting group title	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B
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Reporting group description:

C or NC HCV GT1 participants previously failing a DAA regimen of SOF/LDV receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.

Reporting group title	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
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Reporting group description:

C or NC HCV GT1 participants previously failing a DAA regimen of GZR/EBR (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily in combination with RBV twice daily for 16 weeks.

Reporting group title	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B
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Reporting group description:

C or NC HCV GT1 participants previously failing a DAA regimen of GZR/EBR (MK-5172/MK-8742) receive MK-3682B, an FDC of GZR (MK-5172 [50 mg]) + UPR (MK-3682 [225 mg]) + RZR (MK-8408 [30 mg]), administered as 2 tablets once daily for 24 weeks.

Serious adverse events	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 35 (8.57%)	4 / 36 (11.11%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 9 (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

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 9 (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
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 9 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (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			
Pancreatitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Bone cyst			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (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

Serious adverse events	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)		
number of deaths (all causes)	0		
number of deaths resulting from	0		

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone cyst			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	[Part A, Arm 1] Prior SOF/LDV Failure: MK-3682B + RBV	[Part A, Arm 2] Prior SOF/LDV Failure: MK-3682B	[Part A, Arm 3] Prior GZR/EBR Failure: MK-3682B + RBV
Total subjects affected by non-serious adverse events subjects affected / exposed	29 / 35 (82.86%)	25 / 36 (69.44%)	9 / 9 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	15 / 35 (42.86%)	7 / 36 (19.44%)	6 / 9 (66.67%)
occurrences (all)	17	7	10
Influenza like illness			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Malaise			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 35 (2.86%)	3 / 36 (8.33%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	2 / 36 (5.56%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	1 / 9 (11.11%)
occurrences (all)	2	4	1
Dyspnoea			
subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	2 / 9 (22.22%)
occurrences (all)	2	2	2
Dyspnoea exertional			
subjects affected / exposed	3 / 35 (8.57%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Epistaxis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Emotional disorder			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Irritability			
subjects affected / exposed	2 / 35 (5.71%)	1 / 36 (2.78%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Mood altered			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervousness			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Stress subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 36 (0.00%) 0	0 / 9 (0.00%) 0
Investigations Haemoglobin decreased subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	0 / 36 (0.00%) 0	0 / 9 (0.00%) 0
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) Subcutaneous haematoma subjects affected / exposed occurrences (all) Wound subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1 0 / 35 (0.00%) 0 0 / 35 (0.00%) 0	3 / 36 (8.33%) 3 0 / 36 (0.00%) 0 0 / 36 (0.00%) 0	2 / 9 (22.22%) 2 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1 1 / 35 (2.86%) 1	0 / 36 (0.00%) 0 0 / 36 (0.00%) 0	1 / 9 (11.11%) 2 0 / 9 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Lethargy	1 / 35 (2.86%) 1 1 / 35 (2.86%) 1 1 / 35 (2.86%) 1	2 / 36 (5.56%) 2 0 / 36 (0.00%) 0 5 / 36 (13.89%) 5	3 / 9 (33.33%) 3 1 / 9 (11.11%) 1 5 / 9 (55.56%) 7

subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 36 (0.00%) 0	1 / 9 (11.11%) 1
Sciatica subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	0 / 36 (0.00%) 0	0 / 9 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 36 (0.00%) 0	1 / 9 (11.11%) 1
Tremor subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 36 (0.00%) 0	1 / 9 (11.11%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	0 / 36 (0.00%) 0	1 / 9 (11.11%) 1
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	0 / 36 (0.00%) 0	0 / 9 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	1 / 36 (2.78%) 1	1 / 9 (11.11%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 36 (0.00%) 0	1 / 9 (11.11%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	1 / 36 (2.78%) 1	1 / 9 (11.11%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	3 / 36 (8.33%) 3	0 / 9 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 3	3 / 36 (8.33%) 4	2 / 9 (22.22%) 2
Dry mouth			

subjects affected / exposed	3 / 35 (8.57%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Flatulence			
subjects affected / exposed	2 / 35 (5.71%)	1 / 36 (2.78%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Gastritis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Large intestine polyp			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Proctitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	4 / 35 (11.43%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	6	0	1

Rash			
subjects affected / exposed	6 / 35 (17.14%)	2 / 36 (5.56%)	0 / 9 (0.00%)
occurrences (all)	8	2	0
Skin lesion			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	1 / 9 (11.11%)
occurrences (all)	2	2	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)	3 / 36 (8.33%)	0 / 9 (0.00%)
occurrences (all)	2	4	0
Sinusitis			
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
Tooth abscess			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Urinary tract infection			

subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Diabetes mellitus			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	[Part A, Arm 4] Prior GZR/EBR Failure: MK-3682B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	5 / 13 (38.46%)		
occurrences (all)	5		
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

Oedema peripheral subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Dyspnoea subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Respiratory tract congestion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Emotional disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Insomnia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Irritability			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mood altered</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nervousness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Stress</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 13 (7.69%)</p> <p>1</p> <p>0 / 13 (0.00%)</p> <p>0</p> <p>0 / 13 (0.00%)</p> <p>0</p> <p>1 / 13 (7.69%)</p> <p>1</p>		
<p>Investigations</p> <p>Haemoglobin decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 13 (0.00%)</p> <p>0</p>		
<p>Injury, poisoning and procedural complications</p> <p>Accidental overdose</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Subcutaneous haematoma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Wound</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 13 (7.69%)</p> <p>1</p> <p>1 / 13 (7.69%)</p> <p>1</p> <p>1 / 13 (7.69%)</p> <p>1</p>		
<p>Cardiac disorders</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 13 (0.00%)</p> <p>0</p> <p>1 / 13 (7.69%)</p> <p>1</p>		
<p>Nervous system disorders</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 13 (0.00%)</p> <p>0</p>		

Dysgeusia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Lethargy subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Sciatica subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Syncope subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Tremor subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 2 / 13 (15.38%) 2		

Constipation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Large intestine polyp			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Proctitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

<p>Skin and subcutaneous tissue disorders</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Skin lesion</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>1 / 13 (7.69%)</p> <p>occurrences (all)</p> <p>1</p> <p>Arthritis</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Muscle spasms</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Infections and infestations</p> <p>Conjunctivitis</p> <p>subjects affected / exposed</p> <p>0 / 13 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Cystitis</p> <p>subjects affected / exposed</p> <p>1 / 13 (7.69%)</p> <p>occurrences (all)</p> <p>2</p> <p>Lower respiratory tract infection</p> <p>subjects affected / exposed</p> <p>1 / 13 (7.69%)</p> <p>occurrences (all)</p> <p>1</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>1 / 13 (7.69%)</p> <p>occurrences (all)</p> <p>1</p>			

Sinusitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2015	Amendment 01: Primary reasons for amendment were: 1) to delay enrollment of GT3-infected participants until the supportive efficacy and safety results from MK-3682-012 Part B are available; and 2) to include an interim analysis for the primary efficacy endpoint in GT1 participants.
10 June 2016	Amendment 02: Primary reason for amendment was to add statements indicating that the relevant regulatory authority/agency will be notified if: 1) the decision is made to proceed with enrollment of GT3-infected participants; or 2) if study enrollment is paused / stopped based on safety or virologic concerns.
02 September 2016	Amendment 03: Primary reason for amendment was to indicate that participants considered virologic failures from MK-3682-021 will be eligible for the long term follow up study MK-5172-017.
19 July 2017	Amendment 04: Primary reason for amendment was to revise the trial to add a Part B, evaluating the safety and efficacy of a 16-week treatment regimen of MK-3682B in C or NC participants with chronic HCV GT1-6 infection (with or without HIV infection) previously failing a DAA regimen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 September 2017	Trial was terminated early before participant enrollment in study Part B.	-

Notes:

Limitations and caveats

None reported