Clinical trial results:
A Phase IIa, open-label trial to evaluate the safety, tolerability and efficacy of a 12 weeks combination therapy of TMC647055 and TMC435, with and without GSK2336805 (JNJ-569148745), with a pharmacokinetic enhancer with and without ribavirin in chronic genotype 1 hepatitis C infected patients

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	2012-002555-42
Trial protocol	BE DE
Global end of trial date	16 December 2014

Results information

Result version number	v1 (current)
This version publication date	10 June 2016
First version publication date	10 June 2016

Trial information

Trial identification

Sponsor protocol code	TMC647055HPC2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01724086
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development Ireland
Sponsor organisation address	Eastgate Village, Little Island, Cork, Ireland,
Public contact	Clinical Registry Group, Janssen Research & Development Ireland, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development Ireland, clinicaltrialsEU@its.jnj.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	16 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to evaluate the pharmacokinetics, safety and tolerability of a 12 weeks dosing regimen containing TMC647055/simeprevir(SMV)/ritonavir(RTV) and JNJ-56914845 once daily at selected doses with and without ribavirin (RBV) (2 daily doses) in treatment naïve/prior relapser chronic hepatitis C virus (HCV) genotype1 (GT1)-infected subjects and to evaluate the efficacy of a 12 weeks combination therapy of TMC647055/SMV/RTV once daily at selected doses with RBV (2 daily doses) in treatment-naïve/prior relapser chronic HCV GT1-infected subjects and in treatment-naïve/prior relapser chronic HCV GT1b-infected subjects.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations included monitoring of adverse events (AEs), clinical laboratory tests (Hematology, Serum chemistry, Urinalysis) vital signs, electrocardiograms (ECG) and physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 81
Country: Number of subjects enrolled	Germany: 9
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	88
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted from 12 Sep 2012 to 16 Dec 2014 and included 90 subjects in 4 panels: Panel 1 and 2 included 31 subjects, Panel 3 included 15 subjects and Panel 4 included 44 subjects.

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	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin

Arm description:

Subjects (chronic HCV genotype 1a (GT1a) or 1b (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq: 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) administered once daily for 12 weeks

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily for 12 weeks.

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

Dosage and administration details:

Subjects received ribavirin (RBV) 5 or 6 tablet (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks.

Arm title	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Arm description:

Subjects (chronic HCV genotype (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily without RBV for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) administered once daily for 12 weeks

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily for 12 weeks.

Arm title	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin

Arm description:

Subjects (chronic HCV GT1a infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) administered once daily for 12 weeks

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily for 12 weeks.

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

Dosage and administration details:

Subjects received ribavirin (RBV) 5 or 6 tablet (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks.

Arm title	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Arm description:

Subjects (chronic HCV GT1b infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily without ribavirin (RBV) for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) adminstered once daily for 12 weeks

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily for 12 weeks.

Arm title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg

Arm description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 30 mg oral tablet (1 x 30mg) once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) administered once daily for 12 weeks

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily for 12 weeks.

Investigational medicinal product name	JNJ-56914845
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-56914845 30 mg oral tablet (1 x 30mg) given orally once daily for 12 weeks

Arm title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg

Arm description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 60 mg tablet (2 x 30mg) once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	TMC647055
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily for 12 weeks.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received simeprevir (TMC435) 75 mg capsule (1 x 75 mg) adminstered once daily for 12 weeks	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
Subjects received ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily for 12 weeks.	
Investigational medicinal product name	JNJ-56914845
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received JNJ-56914845 60 mg tablet (2 x 30mg) given orally once daily for 12 weeks	

Number of subjects in period 1	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin
Started	22	9	7
Completed	21	8	7
Not completed	1	1	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	1	1	-

Number of subjects in period 1	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg
Started	8	22	22
Completed	7	21	22
Not completed	1	1	0
Consent withdrawn by subject	-	1	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin
Reporting group description:	
Subjects (chronic HCV genotype 1a (GT1a) or 1b (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq: 200 mg/tablet) per day, divided in 2 doses for 12 weeks	
Reporting group title	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin
Reporting group description:	
Subjects (chronic HCV genotype (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily without RBV for 12 weeks	
Reporting group title	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin
Reporting group description:	
Subjects (chronic HCV GT1a infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks	
Reporting group title	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin
Reporting group description:	
Subjects (chronic HCV GT1b infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily without ribavirin (RBV) for 12 weeks	
Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Reporting group description:	
Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 30 mg oral tablet (1 x 30mg) once daily for 12 weeks	
Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg
Reporting group description:	
Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 60 mg tablet (2 x 30mg) once daily for 12 weeks	

Reporting group values	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin
Number of subjects	22	9	7
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	9	7
From 65 to 84 years	0	0	0
85 years and over	0	0	0

Title for AgeContinuous Units: years			
median	47	37	44
full range (min-max)	29 to 62	18 to 64	28 to 58
Title for Gender Units: subjects			
Female	10	2	0
Male	12	7	7

Reporting group values	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg
Number of subjects	8	22	22
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	21	22
From 65 to 84 years	1	1	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	48.5	50.5	48
full range (min-max)	43 to 66	24 to 70	27 to 58
Title for Gender Units: subjects			
Female	5	6	5
Male	3	16	17

Reporting group values	Total		
Number of subjects	90		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	88		
From 65 to 84 years	2		
85 years and over	0		
Title for AgeContinuous Units: years median full range (min-max)	-		
Title for Gender Units: subjects			
Female	28		
Male	62		

End points

End points reporting groups

Reporting group title	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin

Reporting group description:

Subjects (chronic HCV genotype 1a (GT1a) or 1b (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq: 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Reporting group title	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Reporting group description:

Subjects (chronic HCV genotype (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily without RBV for 12 weeks

Reporting group title	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin

Reporting group description:

Subjects (chronic HCV GT1a infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Reporting group title	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Reporting group description:

Subjects (chronic HCV GT1b infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily without ribavirin (RBV) for 12 weeks

Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg

Reporting group description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 30 mg oral tablet (1 x 30mg) once daily for 12 weeks

Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg

Reporting group description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 60 mg tablet (2 x 30mg) once daily for 12 weeks

Subject analysis set title	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (chronic HCV genotype 1a (GT1a) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablet (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Subject analysis set title	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (chronic HCV genotype 1b (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablet (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Primary: Number of Subjects With a Sustained Virologic Response (SVR) 12 Weeks After the Actual end of Treatment

End point title	Number of Subjects With a Sustained Virologic Response (SVR) 12 Weeks After the Actual end of Treatment[1][2]

End point description:

SVR12 is defined as undetectable Hepatitis C Virus at the actual end of treatment and HCV RNA less than 25 IU/mL at 12 Weeks after the actual end of treatment. Intent-to-treat (ITT) analysis set included all subjects who received at least one dose of TMC647055, Simeprevir (SMV), Ritonavir (RTV), or JNJ-56914845.

End point type	Primary

End point timeframe:

Week 24 (Up to 12 weeks after end-of treatment visit)

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: Descriptive statistical analysis was performed for this endpoint.

[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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Proportion				
number (confidence interval 95%)	44.4 (17.7 to 74.9)	85.7 (41.9 to 98)	50 (20 to 80)	81.8 (0 to 100)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Proportion				
number (confidence interval 95%)	95.5 (0 to 100)	50 (22.5 to 77.5)	83.3 (52.3 to 95.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Adverse Events

End point title	Number of Subjects Reporting Adverse Events[3][4]

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to

possibility of causal relationship. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. ITT analysis set included all subjects who received at least one dose of TMC647055, Simeprevir (SMV), Ritonavir (RTV), or JNJ-56914845.

End point type	Primary

End point timeframe:

Up to Week 48 (36 weeks after end of treatment)

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: No statistical analysis was performed for this endpoint.

[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: No statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Subjects	7	6	6	20

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Subjects	22	10	12	

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Subjects With a Sustained Virological Response (SVR 4, SVR 12 and SVR 24)

End point title	Proportion of Subjects With a Sustained Virological Response (SVR 4, SVR 12 and SVR 24)[5][6]

End point description:

SVR is defined as hepatitis C virus (HCV) ribonucleic acid (RNA) undetectable at least 12 weeks after the actual end of all HCV treatment. ITT analysis set included all subjects who received at least one dose of TMC647055, SMV, RTV, or JNJ-56914845.

End point type	Primary

End point timeframe:

Week 4, 12 and 24

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: Descriptive statistical analysis was performed for this endpoint.

[6] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Percentage				
number (not applicable)				
SVR 4	44.4	85.7	50	81.8
SVR 12	44.4	85.7	50	81.8
SVR 24	44.4	85.7	37.5	81.8

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Percentage				
number (not applicable)				
SVR 4	95.5	50	83.3	
SVR 12	95.5	50	83.3	
SVR 24	95.5	40	83.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatitis C Virus (HCV) RNA levels Over Time

End point title	Hepatitis C Virus (HCV) RNA levels Over Time[7]

End point description:

ITT analysis set included all subjects who received at least one dose of TMC647055, SMV, RTV, or JNJ-56914845.

End point type	Secondary

End point timeframe:

Up to 36 weeks after end of treatment

Notes:

[7] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: International Unit per milliliter (IU/mL				
arithmetic mean (standard error)				
Baseline	6.23 (± 0.25)	6.504 (± 0.1782)	6.713 (± 0.1091)	6.606 (± 0.1129)
Day 3	2.49 (± 0.21)	2.575 (± 0.2068)	2.633 (± 0.1048)	2.848 (± 0.1093)
Week 1	1.55 (± 0.2)	1.83 (± 0.2001)	1.924 (± 0.1179)	2.186 (± 0.1256)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: International Unit per milliliter (IU/mL				
arithmetic mean (standard error)				
Baseline	6.437 (± 0.1209)	6.46 (± 0.14)	6.46 (± 0.14)	
Day 3	2.667 (± 0.1296)	2.34 (± 0.21)	2.82 (± 0.17)	
Week 1	1.987 (± 0.122)	1.56 (± 0.19)	1.96 (± 0.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Viral Breakthrough

End point title	Number of Subjects With Viral Breakthrough[8]

End point description:

On-treatment virologic failure is defined as an inadequate virologic response (HCV RNA >100 IU/mL confirmed, at Week 4 or afterwards until Week 11) OR with viral breakthrough, defined as a confirmed increase of >1 log10 IU/mL in HCV RNA level from the lowest level reached, OR a confirmed HCV RNA level of >100 IU/mL in subjects whose HCV RNA had previously been <25 IU/mL. ITT analysis set included all subjects who received at least one dose of TMC647055, SMV, RTV, or JNJ-56914845.

End point type	Secondary

End point timeframe:

End of study (Week 48)

Notes:

[8] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Subjects	1	0	1	0

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Subjects	1	5	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Viral Relapse

End point title	Number of Subjects With Viral Relapse[9]

End point description:

Viral relapse was defined as HCV RNA <25 IU/mL undetectable at the actual EOT and confirmed HCV RNA ≥25 IU/mL during posttreatment FU

End point type	Secondary

End point timeframe:

Up to 36 weeks after end of treatment

Notes:

[9] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Subjects	2	0	2	4

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Analyte Concentration of TMC435 (Cmin)

End point title	Minimum Observed Plasma Analyte Concentration of TMC435 (Cmin)[10]

End point description:

Cmin is defined as minimum observed plasma concentration of TMC435. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[10] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: Nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	1294 (± 1923)	2545 (± 2922)	3399 (± 5550)	1097 (± 1266)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	1962 (± 3170)	891 (± 1094)	1566 (± 2178)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Analyte Concentration of TMC435 (Cmax)

End point title	Maximum Observed Plasma Analyte Concentration of TMC435 (Cmax)[11]

End point description:

Cmax is defined as maximum observed plasma concentration of TMC435. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[11] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	4583 (± 3691)	5989 (± 4367)	8966 (± 6509)	4240 (± 2799)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	

Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	5419 (± 6166)	3043 (± 2509)	5280 (± 4157)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration of TMC435 (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration of TMC435 (Tmax)[12]

End point description:

Time to Reach Maximum Plasma Concentration (Tmax) is defined as actual sampling time to reach maximum observed analyte concentration Cmax. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[12] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: hour (h)				
median (full range (min-max))	5.97 (4.93 to 10)	5 (3.07 to 6.07)	5.05 (4.07 to 6.1)	5.64 (3.12 to 12)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: hour (h)				
median (full range (min-max))	5.09 (2.98 to 23.93)	5 (3 to 6.03)	5.95 (4 to 11.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of TMC435

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of TMC435[13]

End point description:

AUC (0-24) h is defined as area under the plasma concentration-time curve from time 0 up to 24 hours after giving doses. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[13] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: nanogram hour per milliliters (ng.h/mL)				
arithmetic mean (standard deviation)	67437 (± 76272)	91627 (± 82074)	127318 (± 148663)	59307 (± 48818)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram hour per milliliters (ng.h/mL)				
arithmetic mean (standard deviation)	80893 (± 103010)	40064 (± 38489)	67612 (± 67590)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration of TMC435 (Cavg)

End point title	Average Plasma Concentration of TMC435 (Cavg)[14]

End point description:

Cavg is defined as average plasma concentration at steady-state over the dose interval calculated by AUC at steady-state. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[14] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	2820 (± 3188)	3829 (± 3426)	5300 (± 6204)	2472 (± 2035)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	3368 (± 4298)	1674 (± 1609)	2825 (± 2825)	

Statistical analyses

No statistical analyses for this end point

Secondary: Fluctuation Index of TMC435 (FI)

End point title	Fluctuation Index of TMC435 (FI)[15]

End point description:

FI is defined as percentage fluctuation (variation) between maximum and minimum plasma concentration at steady-state, calculated as 100 ([Cmax - Cmin]/Cavg). PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Up to week 4

Notes:

[15] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: Percent				
arithmetic mean (standard deviation)	160 (± 71.1)	136 (± 67.4)	170 (± 86.5)	154 (± 58.2)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Percent				
arithmetic mean (standard deviation)	134 (± 46.9)	150 (± 39.6)	149 (± 48.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Analyte Concentration of TMC647055 (Cmin)

End point title	Minimum Observed Plasma Analyte Concentration of TMC647055 (Cmin)[16]

End point description:

Cmin is defined as minimum observed plasma concentration of TMC647055. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood

sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[16] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	798 (± 1464)	2710 (± 3825)	2591 (± 3594)	655 (± 826)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	1159 (± 2097)	670 (± 1071)	695 (± 1275)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Analyte Concentration of TMC647055 (Cmax)

End point title	Maximum Observed Plasma Analyte Concentration of TMC647055 (Cmax)[17]

End point description:

Cmax is defined as maximum observed plasma concentration of TMC647055. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[17] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	13936 (± 6228)	23714 (± 7255)	36288 (± 15229)	14189 (± 6686)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	13552 (± 10927)	14626 (± 6619)	15029 (± 9034)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration of TMC647055 (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration of TMC647055 (Tmax)[18]

End point description:

Time to Reach Maximum Plasma Concentration (Tmax) is defined as actual sampling time to reach maximum observed analyte concentration Cmax. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[18] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22

Units: hour (h)				
median (full range (min-max))	4.93 (3.93 to 5.07)	5 (4 to 6.05)	5 (4 to 6.08)	4.99 (2 to 8)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: hour (h)				
median (full range (min-max))	4.98 (2.98 to 8)	5 (3 to 6)	5 (4 to 9.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of TMC647055

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of TMC647055[19]

End point description:

AUC (0-24) h is defined as area under the plasma concentration-time curve from time 0 up to 24 hours after giving doses. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[19] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: nanogram hour per milliliter (ng.h/mL)				
arithmetic mean (standard deviation)	112769 (± 84867)	237623 (± 162469)	273964 (± 165632)	115983 (± 76401)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram hour per milliliter (ng.h/mL)				
arithmetic mean (standard deviation)	119731 (± 112601)	103452 (± 61231)	109672 (± 77498)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration of TMC647055 (Cavg)

End point title	Average Plasma Concentration of TMC647055 (Cavg)[20]

End point description:

Cavg is defined as average plasma concentration at steady-state over the dose interval calculated by AUC at steady-state. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[20] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	4716 (± 3547)	9933 (± 6784)	11410 (± 6921)	4836 (± 3183)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				

arithmetic mean (standard deviation)	4984 (± 4695)	4322 (± 2561)	4582 (± 3236)	

Statistical analyses

No statistical analyses for this end point

Secondary: Fluctuation Index of TMC647055 (FI)

End point title	Fluctuation Index of TMC647055 (FI)[21]

End point description:

FI is defined as percentage fluctuation (variation) between maximum and minimum plasma concentration at steady-state, calculated as 100 ([Cmax - Cmin]/Cavg). PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Up to week 4

Notes:

[21] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: Percent				
arithmetic mean (standard deviation)	329 (± 110)	284 (± 134)	340 (± 126)	310 (± 95.3)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Percent				
arithmetic mean (standard deviation)	290 (± 76.6)	345 (± 78.6)	322 (± 102)	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Analyte Concentration of Ritonavir (Cmin)

End point title	Minimum Observed Plasma Analyte Concentration of Ritonavir (Cmin)[22]

End point description:

Cmin is defined as minimum observed plasma concentration of Ritonavir. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.
NOTE: The value 99999 indicates no data value or not applicable.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[22] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	99999 (± 99999)	19.9 (± 20.3)	13.5 (± 13.9)	4.39 (± 3.53)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	5.07 (± 6.26)	7.15 (± 13.7)	2.87 (± 1.96)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Analyte Concentration of Ritonavir (Cmax)

End point title	Maximum Observed Plasma Analyte Concentration of Ritonavir (Cmax)[23]

End point description:

Cmax is defined as maximum observed plasma concentration of Ritonavir. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood

sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[23] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	134 (± 66.8)	389 (± 268)	517 (± 184)	141 (± 75.4)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	146 (± 112)	148 (± 95.4)	170 (± 73.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration of Ritonavir (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration of Ritonavir (Tmax)[24]

End point description:

Time to Reach Maximum Plasma Concentration (Tmax) is defined as actual sampling time to reach maximum observed analyte concentration Cmax. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[24] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	22
Units: hour (h)				
median (full range (min-max))	4 (2.93 to 5.05)	5 (0 to 5.07)	4.54 (3 to 5.1)	4.08 (0 to 6)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: hour (h)				
median (full range (min-max))	4.05 (3 to 6)	4 (3 to 6)	4.99 (3 to 7.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of Ritonavir

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to 24 Hours (AUC24h) of Ritonavir[25]

End point description:

AUC (0-24) h is defined as area under the plasma concentration-time curve from time 0 up to 24 hours after giving doses. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[25] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21

Units: nanogram hour per milliliter (ng.h/mL				
arithmetic mean (standard deviation)	776 (± 555)	3054 (± 1951)	2958 (± 1024)	852 (± 498)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram hour per milliliter (ng.h/mL				
arithmetic mean (standard deviation)	902 (± 754)	1002 (± 919)	957 (± 392)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration of Ritonavir (Cavg)

End point title	Average Plasma Concentration of Ritonavir (Cavg)[26]

End point description:

Cavg is defined as average plasma concentration at steady-state over the dose interval calculated by AUC at steady-state. PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[26] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	32.5 (± 23.2)	128 (± 81.6)	123 (± 42.7)	35.5 (± 20.7)

End point values	Panel 4: TMC647055 /Simeprevir	Panel 1: TMC647055 /Simeprevir	Panel 1: TMC647055 /Simeprevir	

	/Ritonavir /JNJ-56914845 60 mg	/Ritonavir w Ribavirin (GT1a)	/Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: nanogram per Milliliters (ng/mL)				
arithmetic mean (standard deviation)	37.5 (± 31.4)	41.8 (± 38.4)	40 (± 16.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Fluctuation Index of Ritonavir (FI)

End point title	Fluctuation Index of Ritonavir (FI)[27]

End point description:

FI is defined as percentage fluctuation (variation) between maximum and minimum plasma concentration at steady-state, calculated as 100 ([Cmax - Cmin]/Cavg). PK population included all evaluable subjects who received at least 1 dose of study medication and with at least 1 PK blood sample.

End point type	Secondary

End point timeframe:

Up to week 4

Notes:

[27] - 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: Descriptive statistical analysis was performed for this endpoint.

End point values	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	8	21
Units: Percent				
arithmetic mean (standard deviation)	473 (± 230)	295 (± 71.3)	421 (± 107)	397 (± 110)

End point values	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1a)	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin (GT1b)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	10	12	
Units: Percent				
arithmetic mean (standard deviation)	399 (± 87.8)	397 (± 108)	409 (± 73.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 48 (24 weeks after end of treatment)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin

Reporting group description:

Subjects (chronic HCV genotype 1a (GT1a) or 1b (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq; 200 mg/tablet) per day, divided in 2 doses for 12 weeks)

Reporting group title	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Reporting group description:

Subjects (chronic HCV genotype (GT1b) infected treatment-naive patients/prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily without RBV for 12 weeks

Reporting group title	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin

Reporting group description:

Subjects (chronic HCV GT1a infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily with ribavirin (RBV) 5 or 6 tablets (depending on body weight) (eq. 200 mg/tablet) per day, divided in 2 doses for 12 weeks

Reporting group title	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin

Reporting group description:

Subjects (chronic HCV GT1b infected treatment naïve patients/prior relapsers) received TMC647055 600 milligram (mg) capsules (4 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, and ritonavir (RTV) 50 mg oral solution (0.625 mL oral solution (80 mg/mL) given once daily without ribavirin (RBV) for 12 weeks

Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg

Reporting group description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 30 mg tablet (1 x 30mg) once daily for 12 weeks

Reporting group title	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg

Reporting group description:

Subjects (chronic HCV GT1a or GT1b infected treatment-naive patients/ prior relapsers) received TMC647055 450 milligram (mg) capsules (3 X 150 mg) given orally once daily, simeprevir (TMC435) 75 mg capsule (1 x 75 mg) given once daily, ritonavir (RTV) 30 mg oral solution (0.375 mL) given once daily and JNJ-56914845 60 mg tablet (2 x 30mg) once daily for 12 weeks

Serious adverse events	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Panel 1: TMC647055 /Simeprevir /Ritonavir w Ribavirin	Panel 2: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 3: TMC647055 /Simeprevir / Ritonavir w Ribavirin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	7 / 9 (77.78%)	6 / 7 (85.71%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	9 / 22 (40.91%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	13	0	1
Influenza like illness			
subjects affected / exposed	5 / 22 (22.73%)	2 / 9 (22.22%)	0 / 7 (0.00%)
occurrences (all)	5	3	0
Local swelling			

subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Insomnia			

subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	9 / 22 (40.91%)	5 / 9 (55.56%)	2 / 7 (28.57%)
occurrences (all)	11	6	3
Somnolence			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 22 (9.09%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Abdominal distension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	3 / 22 (13.64%)	2 / 9 (22.22%)	0 / 7 (0.00%)
occurrences (all)	4	2	0
Abdominal pain upper			
subjects affected / exposed	3 / 22 (13.64%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	3	1	0
Abdominal rigidity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 22 (13.64%)	3 / 9 (33.33%)	1 / 7 (14.29%)
occurrences (all)	4	4	2
Diverticulum			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	3 / 22 (13.64%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Lip dry			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 22 (13.64%)	1 / 9 (11.11%)	4 / 7 (57.14%)
occurrences (all)	3	1	5
Regurgitation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 22 (0.00%)	2 / 9 (22.22%)	1 / 7 (14.29%)
occurrences (all)	0	3	1
Vomiting			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Dry skin			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Eczema			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Photosensitivity reaction			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	4 / 22 (18.18%)	0 / 9 (0.00%)	2 / 7 (28.57%)
occurrences (all)	4	0	2
Rash			
subjects affected / exposed	3 / 22 (13.64%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	4	0	1
Skin lesion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Back pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Bone pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nail bed infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 22 (18.18%)	2 / 9 (22.22%)	1 / 7 (14.29%)
occurrences (all)	4	2	1
Periodontitis			

subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 22 (9.09%)	1 / 9 (11.11%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Panel 3: TMC647055 /Simeprevir /Ritonavir w/o Ribavirin	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 30 mg	Panel 4: TMC647055 /Simeprevir /Ritonavir /JNJ-56914845 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	19 / 22 (86.36%)	21 / 22 (95.45%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	5 / 22 (22.73%)	8 / 22 (36.36%)
occurrences (all)	5	5	10
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Local swelling			

subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	2 / 8 (25.00%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	2	2	0
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	3 / 22 (13.64%)
occurrences (all)	0	1	3
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	5 / 8 (62.50%)	8 / 22 (36.36%)	7 / 22 (31.82%)
occurrences (all)	8	11	8
Somnolence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	4 / 22 (18.18%)
occurrences (all)	1	1	4
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	4 / 22 (18.18%)	3 / 22 (13.64%)
occurrences (all)	0	4	4
Abdominal rigidity			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Diarrhoea			
subjects affected / exposed	4 / 8 (50.00%)	4 / 22 (18.18%)	10 / 22 (45.45%)
occurrences (all)	4	9	18
Diverticulum			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	3 / 8 (37.50%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	3	3	2
Regurgitation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Toothache			

subjects affected / exposed	1 / 8 (12.50%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	6 / 22 (27.27%)
occurrences (all)	0	2	7
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Photosensitivity reaction			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	3 / 22 (13.64%)
occurrences (all)	0	4	3
Pruritus			
subjects affected / exposed	2 / 8 (25.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	3	0	2
Rash			
subjects affected / exposed	0 / 8 (0.00%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Skin lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nail bed infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	5 / 22 (22.73%)	1 / 22 (4.55%)
occurrences (all)	2	5	1
Periodontitis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2012	The sponsor decided to reduce the frequency and maximum duration of the follow up (FU) visits after EOT. This change was also applicable to follow up (FU) visits in case of premature study drug withdrawal. In addition, an SMV 75-mg capsule was added as possible formulation. The posttreatment FU visits were scheduled at Week 4, 8, 12, and 24 after the actual end of treatment (EOT). In case of premature study drug withdrawal, the visit 2 weeks after study drug withdrawal did not change. The posttreatment FU visits at Week 4, 12, and 24 were scheduled for the determination of SVR4, SVR12, and SVR24. The review meetings were updated accordingly. The HCV RNA confirmation test when HCV RNA was detected after previous undetectability was changed from 'within 3' to 'within 4' weeks. This allowed the retest visit to coincide with one of the next scheduled visits. A minor change was made to the virologic stopping rules: an inadequate virologic response needed to be confirmed.For consistency reasons, the primary endpoint safety was added to the primary endpoints. A time window was added to the blood sampling times. A minor change was made to the criteria of the 36 weeks of PegIFN/RBV FU treatment in Panel 3: the FU treatment was also applicable to subjects with HCV RNA detectable at Week 4. A note was added to the hematology panel and urinalysis, giving extra information about what could or was also reported by the laboratory. Flow cytometry was not done in case of an abnormal urinalysis dipstick test. An SMV 75-mg capsule was added as possible formulation. This allowed more flexibility in the choice of the optimal dose. The Cardiovascular Safety Abnormalities was added and the references regarding cardiovascular abnormalities were updated. Minor inconsistencies and errors was corrected. Some clarifications were added. At implementation of the first general protocol amendment, 29 subjects in Panel 1 and 2 had been screened of whom 17 had started treatment.
05 December 2012	The sponsor decided to make the discontinuation of treatment criteria more precise and to streamline the age criteria between 2 of its HCV compounds. The discontinuation of treatment criteria were made more precise to distinguish between treatment-emergent liver-related AEs/abnormalities and abnormal laboratory values that were the consequence of the liver disease. Any related data in other sections were updated for consistency reasons. The age limit was increased up to 70-years-old (in good physical condition) to streamline the age criteria between SMV and TMC647055. If the subject had a positive urine drug test at screening a retesting was allowed after a time interval of minimum 7 days instead of at the same day. This was to exclude one-time and short usage. Minor errors and inconsistencies were corrected and clarifications were made. At implementation of the second general protocol amendment, 45 subjects in Panel 1 and 2 had been screened of whom 31 had started treatment.

24 April 2013	This amendment was made to replace Panel 3. Ongoing review of safety, PK, and HCV RNA data obtained from Panel 1 and 2 indicated that the combination treatment TMC647055 + SMV + RTV with and without RBV was generally safe and well tolerated and that exploration of higher dose levels of TMC647055 and RTV could optimize the PK profile and efficacy of the combination treatment. Therefore, the original third panel of 10 null responders described in the original protocol was replaced by a new panel. In order to optimize the PK profile and efficacy of the combination treatment, the original Panel 3 of null responders was replaced by a panel with 2 treatment arms: Arm 1, 8 HCV GT1a and Arm 2, 8 HCV GT1b treatment-naïve subjects or prior relapsers to a previous IFN-based therapy. The subjects in Panel 3 received a 12-week treatment with TMC647055 600 mg qd, SMV 75 mg qd, and RTV 50 mg qd with (Arm 1) or without (Arm 2) RBV 1,000 to 1,200 mg bid. A 36-week IFN/RBV FU treatment was planned for subjects with HCV RNA ≥25 IU/mL at Week 4. The tentative doses of Panel 1 and 2 were updated to the actual doses. The inclusion criteria were updated to reflect the current practice of confirming the HCV GT and subtype at screening. The data analysis and review meeting time points were updated to allow frequent monitoring of safety, PK, and HCV RNA data instead of at predefined time points. The preliminary statistical analysis was made optional and only occurred if deemed necessary. A brief description of the preliminary safety results was added. Additional information was provided regarding the sample size determination. Plasma concentrations of RTV were not incorporated in an existing population model and Cmax was removed from the PK parameters of SMV that were derived in each subject using Bayesian feedback. The text was updated to reflect the completion of study TMC647055HPC1006.
18 September 2013	This amendment was created to enable Proof-of-Concept data of the addition of the NS5A inhibitor JNJ-56914845 (at 2 dose levels) onto the currently studied regimen of the PI SMV and the NNI TMC647055, boosted by RTV, against HCV GT1a and GT1b. An additional panel (Panel 4) with 2 arms was included to evaluate the safety, PK, and efficacy of the coadministration of SMV 75 mg qd, TMC647055 450 mg qd, RTV 30 mg qd, and JNJ-56914845 (30 and 60 mg qd) for 12 weeks without RBV, in a population of 40 subjects infected with HCV GT1a or GT1b, with a maximum of 16 subjects infected with GT1b, naive to all hepatitis C treatment or relapsers from previous IFN- and RBV-based treatment. The subjects in this panel did not receive FU treatment. A dose rationale for JNJ-56914845 was added (see Section 3.2). As this study involved SMV, the sun protection measures were updated as recommended by the Food and Drug Administration. At implementation of the forth general protocol amendment, a total of 101 subjects were screened (45 in Panel 1 and 2; 56 in Panel 3 and 4) and a total of 59 had started treatment (31 in Panel 1 and 2; 28 in Panel 3 and 4).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The small sample size only allowed for Proof-of-Concept. No formal hypothesis was made. Statistical analysis for primary endpoint was not performed given the low sample size.

Notes: