Clinical trial results:
A Phase 1, Open-Label, Randomized, 2-Panel, 3-Way Crossover Study in Healthy Adult Subjects to Assess the Relative Bioavailability of Simeprevir Following Single Dose Administration of Age-Appropriate Oral Formulation Candidates, Compared to the 150-mg Oral Capsule, and to Assess the Effect of Food on the Bioavailability of Simeprevir Following Single Dose Administration of a Selected Age-Appropriate Oral Formulation Candidate

Summary

EudraCT number	2014-005448-17
Trial protocol	GB
Global end of trial date	09 September 2015

Results information

Result version number	v1 (current)
This version publication date	04 August 2016
First version publication date	04 August 2016

Trial information

Trial identification

Sponsor protocol code	TMC435HPC1010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02385071
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development
Sponsor organisation address	Archimedsweg 29-2333CM, Leiden, Netherlands, B235-0
Public contact	Clinical Registry Group, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research and Development, 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	09 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were: 1. To compare the rate and extent of absorption of simeprevir (SMV) following administration of a single dose of 2 different oral formulation candidates and following administration of a single dose of the 150 milligram (mg) oral capsule, after a standardized breakfast in healthy adult subjects; 2. To compare the rate and extent of absorption of simeprevir following administration of a single dose of a selected oral formulation candidate in the fed (standardized breakfast) and fasted state in healthy adult subjects; and, 3. To compare the rate and extent of absorption of simeprevir following administration of a single dose of a selected oral formulation candidate after intake with water and after intake with yogurt or apple juice, after a standardized breakfast in healthy adult subjects.

Protection of trial subjects:

The safety assessments included specific toxicities, clinical laboratory tests (hematology, chemistry and urinalysis), electrocardiogram, vital signs and physical examination. Adverse events were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	48
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 108 subjects were Screened, of whom 60 were not randomized and not treated mainly due to not fulfilling all inclusion or exclusion criteria. In total, 48 subjects were enrolled in Panels 1 and 2 of the study, each containing 24 subjects.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Sequence ABC

Arm description:

Subjects received treatment A (Simeprevir 150 mg [1 * 150 mg] capsule orally once on Day 1) under fed (standardized breakfast) condition followed by treatment B (Simeprevir 150 mg [3 * 50 mg] capsule with minitablets orally once on Day 1) under fed (standardized breakfast) condition followed by treatment C (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence BCA

Arm description:

Subjects received treatment B under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence CAB

Arm description:

Subjects received treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence CBA

Arm description:

Subjects received treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence BAC

Arm description:

Subjects received treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence ACB

Arm description:

Subjects received treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
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 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

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 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Arm title	Sequence DEF

Arm description:

Subjects received treatment D (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fasted condition followed by treatment F (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Arm title	Sequence EFD

Arm description:

Subjects received treatment E under fasted condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed

(standardized breakfast: tablets dispersed in apple juice) condition.

Arm title	Sequence FDE

Arm description:

Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Arm title	Sequence FED

Arm description:

Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Arm title	Sequence EDF

Arm description:

Subjects received treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Arm title	Sequence DFE

Arm description:

Subjects received treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.

Arm type	Experimental

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

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

Dosage and administration details:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Number of subjects in period 1	Sequence ABC	Sequence BCA	Sequence CAB
Started	4	4	4
Completed	4	4	4

Number of subjects in period 1	Sequence CBA	Sequence BAC	Sequence ACB
Started	4	4	4
Completed	4	4	4

Number of subjects in period 1	Sequence DEF	Sequence EFD	Sequence FDE
Started	4	4	4
Completed	4	4	4

Number of subjects in period 1	Sequence FED	Sequence EDF	Sequence DFE
Started	4	4	4
Completed	4	4	4

Reporting groups	
Reporting group title	Sequence ABC
Reporting group description:	
Subjects received treatment A (Simeprevir 150 mg [1 * 150 mg] capsule orally once on Day 1) under fed (standardized breakfast) condition followed by treatment B (Simeprevir 150 mg [3 * 50 mg] capsule with minitablets orally once on Day 1) under fed (standardized breakfast) condition followed by treatment C (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence BCA
Reporting group description:	
Subjects received treatment B under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence CAB
Reporting group description:	
Subjects received treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence CBA
Reporting group description:	
Subjects received treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence BAC
Reporting group description:	
Subjects received treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence ACB
Reporting group description:	
Subjects received treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence DEF
Reporting group description:	
Subjects received treatment D (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fasted condition followed by treatment F (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence EFD
Reporting group description:	
Subjects received treatment E under fasted condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence FDE
Reporting group description:	
Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.	
Reporting group title	Sequence FED

Reporting group description:

Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence EDF

Reporting group description:

Subjects received treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence DFE

Reporting group description:

Subjects received treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group values	Sequence ABC	Sequence BCA	Sequence CAB
Number of subjects	4	4	4
Title for AgeCategorical Units: subjects			
Title for AgeContinuous Units: years			
arithmetic mean	38.5	29.8	29.8
standard deviation	± 16.18	± 8.66	± 4.11
Title for Gender Units: subjects			
Female	1	1	2
Male	3	3	2

Reporting group values	Sequence CBA	Sequence BAC	Sequence ACB
Number of subjects	4	4	4
Title for AgeCategorical Units: subjects			
Title for AgeContinuous Units: years			
arithmetic mean	36.5	28.8	25.3
standard deviation	± 12.87	± 2.06	± 5.97
Title for Gender Units: subjects			
Female	1	2	1
Male	3	2	3

Reporting group values	Sequence DEF	Sequence EFD	Sequence FDE
Number of subjects	4	4	4
Title for AgeCategorical Units: subjects			

Title for AgeContinuous Units: years			
arithmetic mean	30.5	42	33.8
standard deviation	± 5.92	± 7.87	± 12.95
Title for Gender Units: subjects			
Female	3	0	1
Male	1	4	3

Reporting group values	Sequence FED	Sequence EDF	Sequence DFE
Number of subjects	4	4	4
Title for AgeCategorical Units: subjects			

Title for AgeContinuous Units: years			
arithmetic mean	44.8	49.3	25.8
standard deviation	± 6.18	± 7.8	± 2.99
Title for Gender Units: subjects			
Female	3	2	2
Male	1	2	2

Reporting group values	Total		
Number of subjects	48		
Title for AgeCategorical Units: subjects			

Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender Units: subjects			
Female	19		
Male	29		

End points

End points reporting groups

Reporting group title	Sequence ABC

Reporting group description:

Subjects received treatment A (Simeprevir 150 mg [1 * 150 mg] capsule orally once on Day 1) under fed (standardized breakfast) condition followed by treatment B (Simeprevir 150 mg [3 * 50 mg] capsule with minitablets orally once on Day 1) under fed (standardized breakfast) condition followed by treatment C (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence BCA

Reporting group description:

Subjects received treatment B under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence CAB

Reporting group description:

Subjects received treatment C under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence CBA

Reporting group description:

Subjects received treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence BAC

Reporting group description:

Subjects received treatment B under fed (standardized breakfast) condition followed by treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence ACB

Reporting group description:

Subjects received treatment A under fed (standardized breakfast) condition followed by treatment C under fed (standardized breakfast) condition followed by treatment B under fed (standardized breakfast) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence DEF

Reporting group description:

Subjects received treatment D (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fasted condition followed by treatment F (Simeprevir 150 mg [3 * 50 mg] dispersible tablets orally once on Day 1) under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence EFD

Reporting group description:

Subjects received treatment E under fasted condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence FDE

Reporting group description:

Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence FED

Reporting group description:

Subjects received treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence EDF

Reporting group description:

Subjects received treatment E under fasted condition followed by treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition. The treatment sessions were separated by a washout period of at least 7 days.

Reporting group title	Sequence DFE

Reporting group description:

Subjects received treatment D under fed (standardized breakfast: tablets dispersed in water) condition followed by treatment F under fed (standardized breakfast: tablets dispersed in apple juice) condition followed by treatment E under fasted condition. The treatment sessions were separated by a washout period of at least 7 days.

Subject analysis set title	Treatment A
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.

Subject analysis set title	Treatment B
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.

Subject analysis set title	Treatment C
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.

Subject analysis set title	Treatment D
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in water) condition.

Subject analysis set title	Treatment E
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.

Subject analysis set title	Treatment F
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: tablets dispersed in apple juice) condition.

Primary: Maximum Observed Plasma Concentration (Cmax) of Simeprevir

End point title	Maximum Observed Plasma Concentration (Cmax) of Simeprevir

End point description:

The Cmax is the maximum observed plasma concentration of Simeprevir. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Primary

End point timeframe:
Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)	1425 (± 599)	1271 (± 499)	1190 (± 476)	1241 (± 556)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)	1143 (± 888)	1083 (± 517)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment A v Treatment B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.038
Method	ANOVA
Parameter estimate	Least Square Mean ratio
Point estimate	89.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	83.94
upper limit	96.42

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment A v Treatment C

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.038
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	83.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	78.16
upper limit	89.79

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment C v Treatment B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.038
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	107.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	100.2
upper limit	115.1

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3182
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	73.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	58.72
upper limit	91.21

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment F
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3182
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	86.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	69.5
upper limit	107.96

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment F v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3182
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	84.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	67.78
upper limit	105.3

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Simeprevir

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of Simeprevir[1]
End point description: The Tmax is defined as actual sampling time to reach maximum observed simeprevir concentration. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.	
End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

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 statistics were done, no inferential statistical analyses were performed.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hour				
median (full range (min-max))	5.05 (3.97 to 10.07)	5.02 (4.95 to 8.03)	6.02 (4.88 to 10.05)	5.51 (4.97 to 10.03)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: hour				
median (full range (min-max))	5 (2.98 to 10.02)	5.49 (2.98 to 10.05)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Time (AUC[0-last])

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Time (AUC[0-last])

End point description:

The AUC(0-last) is the area under the plasma concentration-time curve from time zero to last quantifiable time. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: nanogram * hour per milliliter (ng.h/ml)				
arithmetic mean (standard deviation)	15762 (± 6271)	14597 (± 6076)	13614 (± 5398)	15477 (± 7736)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: nanogram * hour per milliliter (ng.h/ml)				
arithmetic mean (standard deviation)	12436 (± 8880)	13414 (± 6654)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment B v Treatment A
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6727
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	92.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	86.63
upper limit	98.37

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment A v Treatment C
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6727
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	86.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	81.1
upper limit	92.09

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment C v Treatment B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6727
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	106.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	100.24
upper limit	113.83

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8528
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	69.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	56.09
upper limit	85.33

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment F

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8528
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	87.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	70.87
upper limit	107.82

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment F v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8528
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	79.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	64.17
upper limit	97.61

Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity])

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity])

End point description:

The AUC (0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: ng.h/ml				
arithmetic mean (standard deviation)	15889 (± 6362)	14691 (± 6117)	13709 (± 5454)	15693 (± 7974)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: ng.h/ml				
arithmetic mean (standard deviation)	12547 (± 8938)	13599 (± 6810)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment A v Treatment B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6386
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	92.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	86.55
upper limit	98.26

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment A v Treatment C
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6386
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	86.42

Confidence interval	
level	90 %
sides	2-sided
lower limit	81.11
upper limit	92.09

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment C v Treatment B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6386
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	106.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	100.14
upper limit	113.7

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8651
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	69.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	56.28
upper limit	85.34

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment D v Treatment F

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8651
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	87.53
Confidence interval	
level	90 %
sides	2-sided
lower limit	71.08
upper limit	107.79

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Number of subjects included in analysis was 24 instead of 48.	
Comparison groups	Treatment F v Treatment E
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8651
Method	ANOVA
Parameter estimate	Least Square Means ratio
Point estimate	79.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	64.3
upper limit	97.5

Primary: Elimination Rate Constant (Lambda[z])

End point title	Elimination Rate Constant (Lambda[z])[2]

End point description:

Lambda(z) is first-order elimination rate constant associated with the terminal portion of the curve, determined as the negative slope of the terminal log-linear phase of the drug concentration-time curve. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: 1 per hour				
arithmetic mean (standard deviation)	0.0792 (± 0.014)	0.079 (± 0.0118)	0.0824 (± 0.0195)	0.0773 (± 0.019)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: 1 per hour				
arithmetic mean (standard deviation)	0.0757 (± 0.0168)	0.0761 (± 0.0171)		

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Elimination Half-Life (t1/2 term)

End point title	Terminal Elimination Half-Life (t1/2 term)[3]

End point description:

The terminal elimination half-life (t1/2 term) is the time measured for the plasma concentration to decrease by 1 half to its original concentration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z). Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hour				
arithmetic mean (standard deviation)	9.1 (± 1.9)	9 (± 1.4)	8.7 (± 1.6)	9.6 (± 2.9)

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: hour				
arithmetic mean (standard deviation)	9.6 (± 2.3)	9.6 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants within Each Category of Taste Questionnaire

End point title	Number of Participants within Each Category of Taste Questionnaire

End point description:

Participants were assessed the palatability of the simeprevir formulations by Taste Questionnaire, Question 1 assessed sweetness, bitterness, flavor and overall taste of the formulation; and Question 2 consists of visual analog scale wherein participants were to place a cross in the box beneath the scores, corresponding to the 5-point hedonic scale (dislike it very much; dislike it a little; not sure, like it a little, like it very much). Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Secondary

End point timeframe:

5 to 15 Minutes Postdose on Day 1 of Each Treatment Period

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: participants				
Sweetness: None	22	18	20	21
Sweetness: Weak	1	5	3	3
Sweetness: Moderate	1	1	1	0
Sweetness: Strong	0	0	0	0
Bitterness: None	22	10	12	12
Bitterness: Weak	1	10	8	8
Bitterness: Moderate	1	2	2	4
Bitterness: Strong	0	2	2	0
Flavour: None	23	11	10	17
Flavour: Weak	1	7	8	5
Flavour: Moderate	0	4	4	2
Flavour: Strong	0	2	2	0
Overall acceptability: Bad	1	4	3	1
Overall acceptability: Almost Acceptable	1	5	6	7
Overall acceptability: Acceptable	11	14	13	15
Overall acceptability: Good	11	1	2	1
Hedonic scale: Dislike it Very Much	0	4	3	1
Hedonic scale: Dislike it a Little	1	4	8	9
Hedonic scale: Not Sure	12	8	7	8
Hedonic scale: Like it a Little	4	7	6	6
Hedonic scale: Like it Very Much	7	1	0	0

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: participants				
Sweetness: None	21	6		
Sweetness: Weak	2	1		
Sweetness: Moderate	0	14		
Sweetness: Strong	1	3		
Bitterness: None	13	14		
Bitterness: Weak	6	10		
Bitterness: Moderate	5	0		
Bitterness: Strong	0	0		
Flavour: None	20	7		
Flavour: Weak	4	2		
Flavour: Moderate	0	12		
Flavour: Strong	0	3		
Overall acceptability: Bad	3	0		
Overall acceptability: Almost Acceptable	8	0		
Overall acceptability: Acceptable	9	14		
Overall acceptability: Good	4	10		
Hedonic scale: Dislike it Very Much	3	0		
Hedonic scale: Dislike it a Little	7	1		
Hedonic scale: Not Sure	9	6		
Hedonic scale: Like it a Little	3	15		
Hedonic scale: Like it Very Much	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) and Serious AEs

End point title	Number of Participants with Adverse Events (AEs) and Serious AEs

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (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. Intent-to-Treat population included all subjects who received at least 1 dose of any study drug and were summarized separately for Panels 1 and 2 of the study.

End point type	Secondary

End point timeframe:

Screening up to follow-up (7 days after last dose administration)

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: participants				
AEs	9	6	6	5
SAEs	0	0	0	0

End point values	Treatment E	Treatment F		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: participants				
AEs	3	6		
SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Screening up to 5-7 Days After Last Study Drug Intake or After Dropout	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Treatment A
Reporting group description:	
Subjects received Simeprevir 150 mg (1 * 150 mg) capsule orally once on Day 1 under fed (standardized breakfast) condition.	
Reporting group title	Treatment B
Reporting group description:	
Subjects received Simeprevir 150 mg (3 * 50 mg) capsule with minitablets orally once on Day 1 under fed (standardized breakfast) condition.	
Reporting group title	Treatment C
Reporting group description:	
Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast) condition.	
Reporting group title	Treatment D
Reporting group description:	
Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: Tablets dispersed in water) condition.	
Reporting group title	Treatment E
Reporting group description:	
Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fasted condition.	
Reporting group title	Treatment F
Reporting group description:	
Subjects received Simeprevir 150 mg (3 * 50 mg) dispersible tablets orally once on Day 1 under fed (standardized breakfast: Tablets dispersed in apple juice) condition.	

Serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Treatment D	Treatment E	Treatment F
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (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: 0 %

Non-serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 24 (37.50%)	6 / 24 (25.00%)	6 / 24 (25.00%)
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Dizziness Postural			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 24 (20.83%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	7	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0

Fatigue			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Feeling Hot			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Peripheral Swelling			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Abdominal Distension			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Haematochezia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin Irritation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0

Limb Discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Neck Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	1 / 24 (4.17%)
occurrences (all)	0	2	1

Non-serious adverse events	Treatment D	Treatment E	Treatment F
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 24 (20.83%)	3 / 24 (12.50%)	6 / 24 (25.00%)
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Dizziness Postural			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Hypoaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Feeling Hot			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Peripheral Swelling			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Abdominal Distension			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nasal Congestion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Skin Irritation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Insomnia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Limb Discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Neck Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported