



## 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 minitables 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 minitables 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 minitables 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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 minitables 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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 minitables 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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 minitables 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.   |                    |
| <b>Arm title</b>   | 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 minitables 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.   |                    |
| <b>Arm title</b>   | 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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.  |                    |
| <b>Arm title</b>  | 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.  |                    |
| <b>Arm title</b>  | 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            |



## Baseline characteristics

### Reporting groups

|  |              |
|--|--------------|
| Reporting group title  | Sequence ABC |
| Reporting group description:<br>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 minitables 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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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<br>Units: subjects |              |              |              |

|   |         |        |        |
|---|---------|--------|--------|
| Title for AgeContinuous<br>Units: years |         |        |        |
| arithmetic mean                         | 38.5    | 29.8   | 29.8   |
| standard deviation                      | ± 16.18 | ± 8.66 | ± 4.11 |
| Title for Gender<br>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<br>Units: subjects |              |              |              |

|   |         |        |        |
|---|---------|--------|--------|
| Title for AgeContinuous<br>Units: years |         |        |        |
| arithmetic mean                         | 36.5    | 28.8   | 25.3   |
| standard deviation                      | ± 12.87 | ± 2.06 | ± 5.97 |
| Title for Gender<br>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<br>Units: subjects |              |              |              |

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

|   |              |              |              |
|---|--------------|--------------|--------------|
| <b>Reporting group values</b>               | Sequence FED | Sequence EDF | Sequence DFE |
| Number of subjects                          | 4            | 4            | 4            |
| Title for AgeCategorical<br>Units: subjects |              |              |              |

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

|   |       |  |  |
|---|-------|--|--|
| <b>Reporting group values</b>               | Total |  |  |
| Number of subjects                          | 48    |  |  |
| Title for AgeCategorical<br>Units: subjects |       |  |  |

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

## End points

### End points reporting groups

|  |              |
|--|--------------|
| Reporting group title  | Sequence ABC |
| Reporting group description:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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 minitables 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 (C<sub>max</sub>) of Simeprevir**

|                 |   |
|-----------------|---|
| End point title | Maximum Observed Plasma Concentration (C <sub>max</sub> ) of Simeprevir |
|-----------------|---|

End point description:

The C<sub>max</sub> 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:<br>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:<br>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                    |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | 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                     |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | 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                     |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                    |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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 <sup>[1]</sup> |
| 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)       |

| <b>End point values</b>                         | 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 ( $\pm$ 8880)  | 13414 ( $\pm$ 6654)  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>                             | 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                     |

| <b>Statistical analysis title</b>                             | 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                     |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                    |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                     |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                   |

|  |                           |
|--|---------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 6    |
| Statistical analysis description:<br>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                     |

|  |  |
|--|--|
| <b>Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity])</b>   |  |
| End point title  | Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity]) |
| End point description:<br>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:<br>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 ( $\pm$ 6362)  | 14691 ( $\pm$ 6117)  | 13709 ( $\pm$ 5454)  | 15693 ( $\pm$ 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 ( $\pm$ 8938)  | 13599 ( $\pm$ 6810)  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical Analysis 1    |
|--|---------------------------|
| Statistical analysis description:<br>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:<br>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   |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                     |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                     |

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>                             | 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                   |

|  |                           |
|--|---------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 6    |
| Statistical analysis description:<br>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                      |

|   |  |
|---|--|
| <b>Primary: Elimination Rate Constant (Lambda[z])</b>   |  |
| End point title   | Elimination Rate Constant (Lambda[z]) <sup>[2]</sup> |
| End point description:<br>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:<br>Predose, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, 48 and 72 hours Postdose After Each Treatment Period  |  |
| Notes:<br>[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.<br>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 ( $\pm$ 0.014) | 0.079 ( $\pm$ 0.0118) | 0.0824 ( $\pm$ 0.0195) | 0.0773 ( $\pm$ 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 ( $\pm$ 0.0168) | 0.0761 ( $\pm$ 0.0171) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Terminal Elimination Half-Life (t<sub>1/2</sub> term)

|                 |   |
|-----------------|---|
| End point title | Terminal Elimination Half-Life (t <sub>1/2</sub> term) <sup>[3]</sup> |
|-----------------|---|

End point description:

The terminal elimination half-life (t<sub>1/2</sub> 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 ( $\pm$ 1.9)     | 9 ( $\pm$ 1.4)       | 8.7 ( $\pm$ 1.6)     | 9.6 ( $\pm$ 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 ( $\pm$ 2.3)     | 9.6 ( $\pm$ 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)

| <b>End point values</b>     | 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                    |

| <b>End point values</b>     | 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 minitables 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                   |                |                |                |



Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | 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<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Neck Pain<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 2 / 24 (8.33%)<br>2 | 1 / 24 (4.17%)<br>1 |

| <b>Non-serious adverse events</b>  | Treatment D         | Treatment E         | Treatment F          |
|--|---------------------|---------------------|----------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                 | 5 / 24 (20.83%)     | 3 / 24 (12.50%)     | 6 / 24 (25.00%)      |
| Injury, poisoning and procedural complications<br>Arthropod Bite<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0  |
| Wound<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0  |
| Dizziness Postural<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 3 / 24 (12.50%)<br>3 |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>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<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Haematochezia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 |
| Nasal Congestion<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Oropharyngeal Pain<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Blister<br>subjects affected / exposed<br>occurrences (all)        | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 1 / 24 (4.17%)<br>1 | 0 / 24 (0.00%)<br>0 |
| Skin Irritation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 |
| Insomnia   |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 24 (0.00%)<br>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

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported