



## Clinical trial results:

### A Phase 2, Open-Label Study of Daclatasvir (BMS-790052) and TMC435 in Combination With or Without Ribavirin (RBV) For Treatment-Naive Subjects or Null Responders to Prior Peginterferon Alfa (PegIFN)/RBV Therapy with Genotype 1 Chronic Hepatitis C

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2012-000070-28   |
| Trial protocol           | HU DE ES         |
| Global end of trial date | 21 November 2013 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 16 February 2017 |
| First version publication date | 16 February 2017 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | AI444-062 |
|-----------------------|-----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01628692 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                              |
|------------------------------|--------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Bristol-Myers Squibb                                                                                         |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170                                                            |
| Public contact               | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com |
| Scientific contact           | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb International Corporation, clinical.trials@bms.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                       | 21 November 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 21 November 2013 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To assess efficacy of daclatasvir and TMC435 with and without ribavirin, as determined by the proportion of subjects with sustained virologic response at post-treatment follow-up Week 12 (SVR12), defined as hepatitis C virus (HCV) ribonucleic acid (RNA) < lower limit of quantitation (LLOQ) at post-treatment Week 12.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 29 June 2012 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Argentina: 18     |
| Country: Number of subjects enrolled | United States: 48 |
| Country: Number of subjects enrolled | Spain: 29         |
| Country: Number of subjects enrolled | France: 75        |
| Country: Number of subjects enrolled | Germany: 35       |
| Country: Number of subjects enrolled | Hungary: 25       |
| Worldwide total number of subjects   | 230               |
| EEA total number of subjects         | 164               |

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)      | 185 |
| From 65 to 84 years       | 45  |
| 85 years and over         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 25 sites in 6 countries.

### Pre-assignment

Screening details:

A total of 230 subjects were enrolled and 168 were treated. 62 subjects were enrolled, but did not enter the treatment period. Reasons for non-treatment include 54 subjects no longer met the study entry criteria, 6 subjects withdrew consent, and 2 subjects were lost to follow-up.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Treatment Period        |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |                                               |
|------------------------------|-----------------------------------------------|
| Are arms mutually exclusive? | Yes                                           |
| <b>Arm title</b>             | Genotype 1b: Daclatasvir + Simeprevir (Naive) |

Arm description:

Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                  |                                              |
|------------------|----------------------------------------------|
| <b>Arm title</b> | Genotype 1b: Daclatasvir + Simeprevir (Null) |
|------------------|----------------------------------------------|

Arm description:

Subjects with hepatitis C virus genotype 1b, and who never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal QD, for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                  |                                                           |
|------------------|-----------------------------------------------------------|
| <b>Arm title</b> | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
|------------------|-----------------------------------------------------------|

**Arm description:**

Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>= 75 kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Ribavirin          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Ribavirin administered at a daily weight stratified dose of 1,000 to 1,200 mg orally in 2 divided doses. Subjects received either 400 mg (2 tablets for subjects < 75 kg) or 600 mg (3 tablets for subjects ≥ 75 kg) of Ribavirin in the morning with food and 600 mg (3 tablets) of RBV in the evening with food. mg=milligram; kg=kilogram

|                  |                                                          |
|------------------|----------------------------------------------------------|
| <b>Arm title</b> | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) |
|------------------|----------------------------------------------------------|

**Arm description:**

Subjects with hepatitis C virus genotype 1b, who never attained ≥2 log10 decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30

mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID were continued to receive treatment for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up period.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Ribavirin          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Subjects received Ribavirin administered at a daily weight stratified dose of 1,000 to 1,200 mg orally in 2 divided doses. Subjects received either 400 mg (2 tablets for subjects < 75 kg) or 600 mg (3 tablets for subjects ≥ 75 kg) of Ribavirin in the morning with food and 600 mg (3 tablets) of RBV in the evening with food. mg=milligram; kg=kilogram

|                  |                                                           |
|------------------|-----------------------------------------------------------|
| <b>Arm title</b> | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) |
|------------------|-----------------------------------------------------------|

Arm description:

Subjects with no prior treatment of hepatitis C virus genotype 1a. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Ribavirin          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Ribavirin administered at a daily weight stratified dose of 1,000 to 1,200 mg orally in 2 divided doses. Subjects received either 400 mg (2 tablets for subjects < 75 kg) or 600 mg (3 tablets for subjects ≥ 75 kg) of Ribavirin in the morning with food and 600 mg (3 tablets) of RBV in the evening with food. mg=milligram; kg=kilogram

|                  |                                                          |
|------------------|----------------------------------------------------------|
| <b>Arm title</b> | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |
|------------------|----------------------------------------------------------|

**Arm description:**

Subjects with hepatitis C virus genotype 1a, who never attained ≥2 log10 decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Daclatasvir        |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Daclatasvir orally 30-mg tablets once daily (QD). Daclatasvir was administered as 1 tablet with or without food for the duration of assigned treatment. mg=milligram

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Simeprevir    |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

Subjects received Simeprevir orally 150-mg gelatin capsule once daily (QD). Simeprevir was administered as 1 gelatin capsule with a light to standard meal for the duration of assigned treatment. mg=milligram

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Ribavirin          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Subjects received Ribavirin administered at a daily weight stratified dose of 1,000 to 1,200 mg orally in 2 divided doses. Subjects received either 400 mg (2 tablets for subjects < 75 kg) or 600 mg (3 tablets for subjects ≥ 75 kg) of Ribavirin in the morning with food and 600 mg (3 tablets) of RBV in the evening with food. mg=milligram; kg=kilogram

| Number of subjects in period 1 <sup>[1]</sup> | Genotype 1b: Daclatasvir + Simeprevir (Naive) | Genotype 1b: Daclatasvir + Simeprevir (Null) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
|-----------------------------------------------|-----------------------------------------------|----------------------------------------------|-----------------------------------------------------------|
|                                               |                                               |                                              |                                                           |
| Started                                       | 53                                            | 23                                           | 51                                                        |
| Completed                                     | 46                                            | 17                                           | 43                                                        |
| Not completed                                 | 7                                             | 6                                            | 8                                                         |
| Withdrawal by Subject                         | -                                             | 1                                            | 1                                                         |
| Adverse Event                                 | 2                                             | -                                            | 2                                                         |
| Poor compliance/noncompliance                 | 1                                             | -                                            | -                                                         |
| Death                                         | -                                             | 1                                            | -                                                         |
| Administrative Reason by Sponsor              | -                                             | -                                            | -                                                         |
| Completed 12 Week only                        | -                                             | -                                            | -                                                         |
| Lack of efficacy                              | 4                                             | 4                                            | 5                                                         |

| Number of subjects in period 1 <sup>[1]</sup> | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |
|-----------------------------------------------|----------------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|
|                                               |                                                          |                                                           |                                                          |
| Started                                       | 20                                                       | 12                                                        | 9                                                        |
| Completed                                     | 19                                                       | 8                                                         | 0                                                        |
| Not completed                                 | 1                                                        | 4                                                         | 9                                                        |
| Withdrawal by Subject                         | -                                                        | -                                                         | -                                                        |
| Adverse Event                                 | -                                                        | -                                                         | -                                                        |
| Poor compliance/noncompliance                 | -                                                        | -                                                         | -                                                        |
| Death                                         | -                                                        | -                                                         | -                                                        |
| Administrative Reason by Sponsor              | -                                                        | -                                                         | 1                                                        |
| Completed 12 Week only                        | -                                                        | -                                                         | 1                                                        |
| Lack of efficacy                              | 1                                                        | 4                                                         | 7                                                        |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 230 subjects who were enrolled, 168 subjects received at least 1 dose of study therapy.

**Period 2**

|                              |                  |
|------------------------------|------------------|
| Period 2 title               | Follow-up Period |
| Is this the baseline period? | No               |
| Allocation method            | Not applicable   |
| Blinding used                | Not blinded      |

**Arms**

|                              |    |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1b: Daclatasvir + Simeprevir (Naive)             |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.                                                                                                                                                                                                                                                            |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1b: Daclatasvir + Simeprevir (Null)              |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with hepatitis C virus genotype 1b, and who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal QD, for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                             |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                                                    |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with hepatitis C virus genotype 1b, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID were continued to receive treatment for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up period. |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for 24 weeks for subjects with no prior treatment of hepatitis C virus genotype 1a. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                                                                                                                                                                                            |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
| Post-treatment follow-up for 24 weeks for subjects with hepatitis C virus genotype 1a, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                                                                                   |                                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | No intervention                                           |
| No investigational medicinal product assigned in this arm                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |

| Number of subjects in period 2                      | Genotype 1b:<br>Daclatasvir +<br>Simeprevir (Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir (Null) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Naive) |
|-----------------------------------------------------|-----------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------|
|                                                     |                                                     |                                                    |                                                                    |
| Started                                             | 46                                                  | 17                                                 | 43                                                                 |
| Completed                                           | 51                                                  | 21                                                 | 44                                                                 |
| Not completed                                       | 0                                                   | 0                                                  | 3                                                                  |
| Consent withdrawn by subject                        | -                                                   | -                                                  | 1                                                                  |
| Death                                               | -                                                   | -                                                  | 1                                                                  |
| Lost to follow-up                                   | -                                                   | -                                                  | 1                                                                  |
| Joined                                              | 5                                                   | 4                                                  | 4                                                                  |
| Did not complete treatment, but<br>joined follow up | 5                                                   | 4                                                  | 4                                                                  |

| Number of subjects in period 2                      | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Naive) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |
|-----------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------|-------------------------------------------------------------------|
|                                                     |                                                                   |                                                                    |                                                                   |
| Started                                             | 19                                                                | 8                                                                  | 2                                                                 |
| Completed                                           | 20                                                                | 10                                                                 | 2                                                                 |
| Not completed                                       | 0                                                                 | 0                                                                  | 0                                                                 |
| Consent withdrawn by subject                        | -                                                                 | -                                                                  | -                                                                 |
| Death                                               | -                                                                 | -                                                                  | -                                                                 |
| Lost to follow-up                                   | -                                                                 | -                                                                  | -                                                                 |
| Joined                                              | 1                                                                 | 2                                                                  | 0                                                                 |
| Did not complete treatment, but<br>joined follow up | 1                                                                 | 2                                                                  | -                                                                 |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Naive)             |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.                                                                                                                                                                                                                                                            |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Null)              |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with hepatitis C virus genotype 1b, and who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal QD, for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                             |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                                                    |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with hepatitis C virus genotype 1b, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID were continued to receive treatment for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up period. |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with no prior treatment of hepatitis C virus genotype 1a. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                                                                                                                               |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                           |
| Subjects with hepatitis C virus genotype 1a, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                      |                                                           |

| Reporting group values  | Genotype 1b: Daclatasvir + Simeprevir (Naive) | Genotype 1b: Daclatasvir + Simeprevir (Null) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
|-------------------------|-----------------------------------------------|----------------------------------------------|-----------------------------------------------------------|
| Number of subjects      | 53                                            | 23                                           | 51                                                        |
| Age categorical         |                                               |                                              |                                                           |
| Units: Subjects         |                                               |                                              |                                                           |
| < 21 years              | 0                                             | 0                                            | 0                                                         |
| Between 21 and 64 years | 41                                            | 19                                           | 42                                                        |
| $\geq 65$ years         | 12                                            | 4                                            | 9                                                         |
| Age continuous          |                                               |                                              |                                                           |
| Units: years            |                                               |                                              |                                                           |
| arithmetic mean         | 53.6                                          | 53.8                                         | 53                                                        |
| standard deviation      | $\pm 12.98$                                   | $\pm 11.26$                                  | $\pm 11.29$                                               |

|                                                       |    |    |    |
|-------------------------------------------------------|----|----|----|
| Gender categorical<br>Units: Subjects                 |    |    |    |
| Female                                                | 31 | 11 | 26 |
| Male                                                  | 22 | 12 | 25 |
| Hepatitis C Virus RNA Distribution<br>Units: Subjects |    |    |    |
| <800,000 IU/mL                                        | 12 | 3  | 11 |
| ≥800,000 IU/mL                                        | 41 | 20 | 40 |
| Randomization Stratum<br>Units: Subjects              |    |    |    |
| Hepatitis C Virus Genotype 1b                         | 53 | 23 | 51 |
| Hepatitis C Virus Genotype 1a                         | 0  | 0  | 0  |

| <b>Reporting group values</b>                         | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Naive) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |
|-------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------|-------------------------------------------------------------------|
| Number of subjects                                    | 20                                                                | 12                                                                 | 9                                                                 |
| Age categorical<br>Units: Subjects                    |                                                                   |                                                                    |                                                                   |
| < 21 years                                            | 1                                                                 | 1                                                                  | 0                                                                 |
| Between 21 and 64 years                               | 11                                                                | 11                                                                 | 9                                                                 |
| ≥65 years                                             | 8                                                                 | 0                                                                  | 0                                                                 |
| Age continuous<br>Units: years                        |                                                                   |                                                                    |                                                                   |
| arithmetic mean                                       | 57.2                                                              | 50                                                                 | 48.1                                                              |
| standard deviation                                    | ± 14.94                                                           | ± 11.15                                                            | ± 6.09                                                            |
| Gender categorical<br>Units: Subjects                 |                                                                   |                                                                    |                                                                   |
| Female                                                | 11                                                                | 5                                                                  | 2                                                                 |
| Male                                                  | 9                                                                 | 7                                                                  | 7                                                                 |
| Hepatitis C Virus RNA Distribution<br>Units: Subjects |                                                                   |                                                                    |                                                                   |
| <800,000 IU/mL                                        | 4                                                                 | 5                                                                  | 0                                                                 |
| ≥800,000 IU/mL                                        | 16                                                                | 7                                                                  | 9                                                                 |
| Randomization Stratum<br>Units: Subjects              |                                                                   |                                                                    |                                                                   |
| Hepatitis C Virus Genotype 1b                         | 20                                                                | 0                                                                  | 0                                                                 |
| Hepatitis C Virus Genotype 1a                         | 0                                                                 | 12                                                                 | 9                                                                 |

| <b>Reporting group values</b>      | Total |  |  |
|------------------------------------|-------|--|--|
| Number of subjects                 | 168   |  |  |
| Age categorical<br>Units: Subjects |       |  |  |
| < 21 years                         | 2     |  |  |
| Between 21 and 64 years            | 133   |  |  |
| ≥65 years                          | 33    |  |  |
| Age continuous<br>Units: years     |       |  |  |
| arithmetic mean                    |       |  |  |
| standard deviation                 | -     |  |  |

|                                    |     |  |  |
|------------------------------------|-----|--|--|
| Gender categorical                 |     |  |  |
| Units: Subjects                    |     |  |  |
| Female                             | 86  |  |  |
| Male                               | 82  |  |  |
| Hepatitis C Virus RNA Distribution |     |  |  |
| Units: Subjects                    |     |  |  |
| <800,000 IU/mL                     | 35  |  |  |
| ≥800,000 IU/mL                     | 133 |  |  |
| Randomization Stratum              |     |  |  |
| Units: Subjects                    |     |  |  |
| Hepatitis C Virus Genotype 1b      | 147 |  |  |
| Hepatitis C Virus Genotype 1a      | 21  |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Naive)             |
| Reporting group description:<br>Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.                                                                                                                                                                                                                                                            |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Null)              |
| Reporting group description:<br>Subjects with hepatitis C virus genotype 1b, and who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal QD, for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                             |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Reporting group description:<br>Subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                                                                                                                                                    |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Reporting group description:<br>Subjects with hepatitis C virus genotype 1b, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID were continued to receive treatment for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up period. |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Reporting group description:<br>Subjects with no prior treatment of hepatitis C virus genotype 1a. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                                                                                                                               |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null)  |
| Reporting group description:<br>Subjects with hepatitis C virus genotype 1a, who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing $<75/>=75$ kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.                                                                                      |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Naive)             |
| Reporting group description:<br>Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.                                                                                                                                                     |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir (Null)              |
| Reporting group description:<br>Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with hepatitis C virus genotype 1b, and who never attained $\geq 2$ log <sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal QD, for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.                                      |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) |
| Reporting group description:<br>Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with no prior treatment of hepatitis C virus genotype 1b. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg                                                                                                                                                                                                                                                      |                                                           |

for participants weighing <75/>= 75 kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) |
|-----------------------|----------------------------------------------------------|

Reporting group description:

Post-treatment follow-up for either 24 or 36 weeks depending on the duration of treatment assigned for subjects with hepatitis C virus genotype 1b, who never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID were continued to receive treatment for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up period.

|                       |                                                           |
|-----------------------|-----------------------------------------------------------|
| Reporting group title | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) |
|-----------------------|-----------------------------------------------------------|

Reporting group description:

Post-treatment follow-up for 24 weeks for subjects with no prior treatment of hepatitis C virus genotype 1a. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |
|-----------------------|----------------------------------------------------------|

Reporting group description:

Post-treatment follow-up for 24 weeks for subjects with hepatitis C virus genotype 1a, who never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA level after at least 12 weeks of prior therapy. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for participants weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

|                            |                                                      |
|----------------------------|------------------------------------------------------|
| Subject analysis set title | Genotype 1b: Daclatasvir + Simeprevir (Naive + Null) |
|----------------------------|------------------------------------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects with hepatitis C virus genotype 1b and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.

|                            |                                                                |
|----------------------------|----------------------------------------------------------------|
| Subject analysis set title | Genotype1b: Daclatasvir +Simeprevir + Ribavirin (Naive + Null) |
|----------------------------|----------------------------------------------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects with hepatitis C virus genotype 1b and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for subjects weighing <75/>= 75 kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.

|                            |                                                               |
|----------------------------|---------------------------------------------------------------|
| Subject analysis set title | Genotype1a: Daclatasvir +Simeprevir + Ribavirin(Naive + Null) |
|----------------------------|---------------------------------------------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects with hepatitis C virus genotype 1a and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for subjects weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

## Primary: Percentage of Subjects With Sustained Virologic Response Rate at Post-treatment Week 12 (SVR12)

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With Sustained Virologic Response Rate at Post-treatment Week 12 (SVR12) <sup>[1]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

SVR12 rate was defined as hepatitis C virus (HCV) RNA levels to be <lower limit of quantitation, target detected or target not detected, at post-treatment Week 12. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All participants who were randomized and received at least 1 dose of active study therapy (daclatasvir, simeprevir, ribavirin).

|                                                                                                                                                                     |                                               |                                              |                                                           |                                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|
| End point type                                                                                                                                                      | Primary                                       |                                              |                                                           |                                                          |
| End point timeframe:                                                                                                                                                |                                               |                                              |                                                           |                                                          |
| Post Treatment Week 12 (Follow-up 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: Only descriptive summary statistics were planned for this outcome measure.                                                                           |                                               |                                              |                                                           |                                                          |
| End point values                                                                                                                                                    | Genotype 1b: Daclatasvir + Simeprevir (Naive) | Genotype 1b: Daclatasvir + Simeprevir (Null) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) |
|                                                                                                                                                                     | Subject group type                            | Reporting group                              | Reporting group                                           | Reporting group                                          |
|                                                                                                                                                                     | Number of subjects analysed                   | 53                                           | 23                                                        | 51                                                       |
|                                                                                                                                                                     | Units: Percentage of subjects                 |                                              |                                                           |                                                          |
|                                                                                                                                                                     | number (confidence interval 80%)              | 84.9 (78.6 to 91.2)                          | 69.6 (57.3 to 81.9)                                       | 74.5 (66.7 to 82.3)                                      |

|                                  |                                                           |                                                          |  |  |
|----------------------------------|-----------------------------------------------------------|----------------------------------------------------------|--|--|
| <b>End point values</b>          | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |  |  |
| Subject group type               | Reporting group                                           | Reporting group                                          |  |  |
| Number of subjects analysed      | 12                                                        | 9 <sup>[2]</sup>                                         |  |  |
| Units: Percentage of subjects    |                                                           |                                                          |  |  |
| number (confidence interval 80%) | 66.7 (49.2 to 84.1)                                       | 0 (-99999 to 99999)                                      |  |  |

Notes:

[2] - As no subjects achieved SVR12, 80% confidence interval value is not available.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Rapid Virologic Response (RVR)

|                                                                                                                                                                                                                                                           |                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                           | Percentage of Subjects With Rapid Virologic Response (RVR) |
| End point description:                                                                                                                                                                                                                                    |                                                            |
| RVR was defined as hepatitis C virus (HCV) RNA levels to be <lower limit of quantitation, target not detected at Week 4. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All treated subjects. |                                                            |
| End point type                                                                                                                                                                                                                                            | Secondary                                                  |
| End point timeframe:                                                                                                                                                                                                                                      |                                                            |
| Week 4                                                                                                                                                                                                                                                    |                                                            |

| End point values                 | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Null) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |
|----------------------------------|--------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|
| Subject group type               | Reporting group                                        | Reporting group                                       | Reporting group                                                       | Reporting group                                                   |
| Number of subjects analysed      | 53                                                     | 23                                                    | 51                                                                    | 20                                                                |
| Units: Percentage of Subjects    |                                                        |                                                       |                                                                       |                                                                   |
| number (confidence interval 80%) | 79.2 (72.1 to 86.4)                                    | 69.6 (57.3 to 81.9)                                   | 68.6 (60.3 to 77)                                                     | 85 (74.8 to 95.2)                                                 |

| End point values                 | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |  |  |
|----------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|--|--|
| Subject group type               | Reporting group                                                       | Reporting group                                                   |  |  |
| Number of subjects analysed      | 12                                                                    | 9                                                                 |  |  |
| Units: Percentage of Subjects    |                                                                       |                                                                   |  |  |
| number (confidence interval 80%) | 75 (59 to 91)                                                         | 33.3 (13.2 to 53.5)                                               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Complete Early Virologic Response (cEVR)

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | Percentage of Subjects With Complete Early Virologic Response (cEVR) |
|-----------------|----------------------------------------------------------------------|

End point description:

cEVR was defined as hepatitis C virus (HCV) RNA levels to be <lower limit of quantitation, target not detected at Week 12. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All treated subejcts.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

| End point values                 | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Null) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |
|----------------------------------|--------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|
| Subject group type               | Reporting group                                        | Reporting group                                       | Reporting group                                                       | Reporting group                                                   |
| Number of subjects analysed      | 53                                                     | 23                                                    | 51                                                                    | 20                                                                |
| Units: Percentage of Subjects    |                                                        |                                                       |                                                                       |                                                                   |
| number (confidence interval 80%) | 84.9 (78.6 to 91.2)                                    | 73.9 (62.2 to 85.6)                                   | 82.4 (75.5 to 89.2)                                                   | 90 (81.4 to 98.6)                                                 |

| End point values                 | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |  |  |
|----------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|--|--|
| Subject group type               | Reporting group                                                       | Reporting group                                                   |  |  |
| Number of subjects analysed      | 12                                                                    | 9                                                                 |  |  |
| Units: Percentage of Subjects    |                                                                       |                                                                   |  |  |
| number (confidence interval 80%) | 66.7 (49.2 to 84.1)                                                   | 11.1 (0 to 24.5)                                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Extended Rapid Virologic Response (eRVR)

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | Percentage of Subjects With Extended Rapid Virologic Response (eRVR) |
|-----------------|----------------------------------------------------------------------|

End point description:

eRVR were defined as hepatitis C virus (HCV) RNA levels to be <lower limit of quantitation, target not detected at both Week 4 and Week 12. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All treated subjects.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 4 and Week 12

| End point values                 | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Null) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1b:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |
|----------------------------------|--------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|
| Subject group type               | Reporting group                                        | Reporting group                                       | Reporting group                                                       | Reporting group                                                   |
| Number of subjects analysed      | 53                                                     | 23                                                    | 51                                                                    | 20                                                                |
| Units: Percentage of Subject     |                                                        |                                                       |                                                                       |                                                                   |
| number (confidence interval 80%) | 71.7 (63.8 to 79.6)                                    | 60.9 (47.8 to 73.9)                                   | 62.7 (54.1 to 71.4)                                                   | 75 (62.6 to 87.4)                                                 |

| End point values             | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin<br>(Naive) | Genotype 1a:<br>Daclatasvir +<br>Simeprevir +<br>Ribavirin (Null) |  |  |
|------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|--|--|
| Subject group type           | Reporting group                                                       | Reporting group                                                   |  |  |
| Number of subjects analysed  | 12                                                                    | 9                                                                 |  |  |
| Units: Percentage of Subject |                                                                       |                                                                   |  |  |

|                                  |                     |                  |  |  |
|----------------------------------|---------------------|------------------|--|--|
| number (confidence interval 80%) | 58.3 (40.1 to 76.6) | 11.1 (0 to 24.5) |  |  |
|----------------------------------|---------------------|------------------|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With End of Treatment Response (EOTR)

|                                                                                                                                                                                                                                                                                           |                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                           | Percentage of Subjects With End of Treatment Response (EOTR) |
| End point description:<br>EOTR were defined as hepatitis C virus (HCV) RNA levels <lower limit of quantitation, target not detected at end of treatment. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All treated subjects. |                                                              |
| End point type                                                                                                                                                                                                                                                                            | Secondary                                                    |
| End point timeframe:<br>End of treatment (Week 24)                                                                                                                                                                                                                                        |                                                              |

| End point values                 | Genotype 1b: Daclatasvir + Simeprevir (Naive) | Genotype 1b: Daclatasvir + Simeprevir (Null) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) |
|----------------------------------|-----------------------------------------------|----------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|
| Subject group type               | Reporting group                               | Reporting group                              | Reporting group                                           | Reporting group                                          |
| Number of subjects analysed      | 53                                            | 23                                           | 51                                                        | 20                                                       |
| Units: Percentage of Subjects    |                                               |                                              |                                                           |                                                          |
| number (confidence interval 80%) | 88.7 (83.1 to 94.3)                           | 78.3 (67.2 to 89.3)                          | 78.4 (71.1 to 85.8)                                       | 95 (88.8 to 100)                                         |

| End point values                 | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |  |  |
|----------------------------------|-----------------------------------------------------------|----------------------------------------------------------|--|--|
| Subject group type               | Reporting group                                           | Reporting group                                          |  |  |
| Number of subjects analysed      | 12                                                        | 9                                                        |  |  |
| Units: Percentage of Subjects    |                                                           |                                                          |  |  |
| number (confidence interval 80%) | 66.7 (49.2 to 84.1)                                       | 0 (-99999 to 99999)                                      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) by rs12979860 Single Nucleotide Polymorphisms in the IL-28B Gene Categories

|                 |                                                                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With Sustained Virologic Response at Follow-up Week 12 (SVR12) by rs12979860 Single Nucleotide Polymorphisms in the IL-28B Gene Categories |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects were categorized into 3 genotypes based on single nucleotide polymorphisms in the IL28B gene. SVR12 was defined as hepatitis C virus (HCV) RNA levels below lower limit of quantitation, target detected or target not detected at follow-up Week 12. HCV RNA levels were measured by the Roche COBAS® TaqMan® HCV Test version 2.0 from the central laboratory. All treated subjects. Here 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Post-treatment Week 12 (Follow-up period)

| End point values                             | Genotype 1b: Daclatasvir + Simeprevir (Naive) | Genotype 1b: Daclatasvir + Simeprevir (Null) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1b: Daclatasvir + Simeprevir + Ribavirin (Null) |
|----------------------------------------------|-----------------------------------------------|----------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|
| Subject group type                           | Reporting group                               | Reporting group                              | Reporting group                                           | Reporting group                                          |
| Number of subjects analysed                  | 53                                            | 23                                           | 51                                                        | 20                                                       |
| Units: Percentage of Subjects                |                                               |                                              |                                                           |                                                          |
| number (not applicable)                      |                                               |                                              |                                                           |                                                          |
| IL28B Genotype CC type (n= 16,1,13,1,3,0)    | 87.5                                          | 100                                          | 84.6                                                      | 100                                                      |
| IL28B Genotype CT type (n= 22,15, 28,10,9,8) | 95.5                                          | 60                                           | 82.1                                                      | 90                                                       |
| IL28B Genotype TT type (n= 12,6,10,7,0,1)    | 66.7                                          | 83.3                                         | 40                                                        | 100                                                      |

| End point values                             | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Naive) | Genotype 1a: Daclatasvir + Simeprevir + Ribavirin (Null) |  |  |
|----------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------|--|--|
| Subject group type                           | Reporting group                                           | Reporting group                                          |  |  |
| Number of subjects analysed                  | 12                                                        | 9                                                        |  |  |
| Units: Percentage of Subjects                |                                                           |                                                          |  |  |
| number (not applicable)                      |                                                           |                                                          |  |  |
| IL28B Genotype CC type (n= 16,1,13,1,3,0)    | 66.7                                                      | 99999                                                    |  |  |
| IL28B Genotype CT type (n= 22,15, 28,10,9,8) | 66.7                                                      | 0                                                        |  |  |
| IL28B Genotype TT type (n= 12,6,10,7,0,1)    | 99999                                                     | 0                                                        |  |  |

## Statistical analyses

## Secondary: Number of Subjects With Serious Adverse Events (SAEs) and Discontinuations Due to Adverse Events (AEs) and Who Died

|                 |                                                                                                                     |
|-----------------|---------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Serious Adverse Events (SAEs) and Discontinuations Due to Adverse Events (AEs) and Who Died |
|-----------------|---------------------------------------------------------------------------------------------------------------------|

End point description:

AE was defined as any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that does not necessarily have a causal relationship with treatment. SAE was defined as a medical event that at any dose resulted in death, persistent or significant disability/incapacity, or drug dependency/abuse; was life-threatening, an important medical event, or a congenital anomaly/birth defect; or required or prolonged hospitalization. Based on the severity, AEs were categorized as Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling, Gr 5=Death. All treated subjects.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From start of treatment (Day 1) up to 7 days post last dose of study treatment (Week 24)

| End point values               | Genotype 1b:<br>Daclatasvir +<br>Simeprevir<br>(Naive + Null) | Genotype1b:<br>Daclatasvir<br>+Simeprevir +<br>Ribavirin<br>(Naive + Null) | Genotype1a:<br>Daclatasvir<br>+Simeprevir +<br>Ribavirin(Naive<br>+ Null) |  |
|--------------------------------|---------------------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------|--|
| Subject group type             | Subject analysis set                                          | Subject analysis set                                                       | Subject analysis set                                                      |  |
| Number of subjects analysed    | 76                                                            | 71                                                                         | 21                                                                        |  |
| Units: Subjects                |                                                               |                                                                            |                                                                           |  |
| SAEs                           | 7                                                             | 3                                                                          | 1                                                                         |  |
| AEs Leading to Discontinuation | 2                                                             | 2                                                                          | 0                                                                         |  |
| Death                          | 1                                                             | 0                                                                          | 0                                                                         |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Day 1) up to 7 days post last dose of study treatment (24 Weeks)

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |                                                      |
|-----------------------|------------------------------------------------------|
| Reporting group title | Genotype 1b: Daclatasvir + Simeprevir (Naive + Null) |
|-----------------------|------------------------------------------------------|

Reporting group description:

Subjects with hepatitis C virus genotype 1b and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food and simeprevir 150 mg with a light to standard meal once daily (QD), for a period of 12 weeks or 24 weeks based on re-randomization and continued into a post-treatment follow-up period.

|                       |                                                                |
|-----------------------|----------------------------------------------------------------|
| Reporting group title | Genotype1b: Daclatasvir +Simeprevir + Ribavirin (Naive + Null) |
|-----------------------|----------------------------------------------------------------|

Reporting group description:

Subjects with hepatitis C virus genotype 1b and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for subjects weighing <75/>= 75 kg, respectively) ribavirin twice daily (BID) for a period of 12 or 24 weeks based on re-randomization and continued into post-treatment follow-up.

|                       |                                                               |
|-----------------------|---------------------------------------------------------------|
| Reporting group title | Genotype1a: Daclatasvir +Simeprevir + Ribavirin(Naive + Null) |
|-----------------------|---------------------------------------------------------------|

Reporting group description:

Subjects with hepatitis C virus genotype 1a and who either had no prior treatment or had never attained  $\geq 2$  log<sub>10</sub> decline in hepatitis C virus RNA levels after at least 12 weeks of prior therapy with peginterferon/ribavirin. Received daclatasvir 30 mg with or without food, simeprevir 150 mg with a light to standard meal QD, and weight stratified (1000/1200 mg for subjects weighing <75/>=75 kg, respectively) ribavirin BID for a period of 24 weeks and continued into post-treatment follow-up period of 24 weeks.

| Serious adverse events                                              | Genotype 1b:<br>Daclatasvir +<br>Simeprevir (Naive +<br>Null) | Genotype1b:<br>Daclatasvir<br>+Simeprevir +<br>Ribavirin (Naive +<br>Null) | Genotype1a:<br>Daclatasvir<br>+Simeprevir +<br>Ribavirin(Naive +<br>Null) |
|---------------------------------------------------------------------|---------------------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                               |                                                                            |                                                                           |
| subjects affected / exposed                                         | 7 / 76 (9.21%)                                                | 3 / 71 (4.23%)                                                             | 1 / 21 (4.76%)                                                            |
| number of deaths (all causes)                                       | 1                                                             | 0                                                                          | 0                                                                         |
| number of deaths resulting from adverse events                      |                                                               |                                                                            |                                                                           |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                               |                                                                            |                                                                           |
| Hepatic cancer                                                      |                                                               |                                                                            |                                                                           |
| subjects affected / exposed                                         | 0 / 76 (0.00%)                                                | 0 / 71 (0.00%)                                                             | 1 / 21 (4.76%)                                                            |
| occurrences causally related to treatment / all                     | 0 / 0                                                         | 0 / 0                                                                      | 0 / 1                                                                     |
| deaths causally related to treatment / all                          | 0 / 0                                                         | 0 / 0                                                                      | 0 / 0                                                                     |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Injury, poisoning and procedural complications  |                |                |                |
| Post lumbar puncture syndrome                   |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                              |                |                |                |
| Hypertension                                    |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 1 / 71 (1.41%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombophlebitis superficial                    |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 1 / 71 (1.41%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Hypoaesthesia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intracranial haematoma                          |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Ischaemic stroke                                |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neurotoxicity                                   |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Constipation                                    |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hepatobiliary disorders</b>                  |                |                |                |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 0 / 71 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Liver disorder                                  |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 1 / 71 (1.41%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Psychiatric disorders</b>                    |                |                |                |
| Depression                                      |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 0 / 71 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Infections and infestations</b>              |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 76 (1.32%) | 1 / 71 (1.41%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metabolism and nutrition disorders</b>       |                |                |                |
| Diabetes mellitus                               |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 0 / 71 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Type 1 diabetes mellitus                        |                |                |                |
| subjects affected / exposed                     | 0 / 76 (0.00%) | 1 / 71 (1.41%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                                                    | <b>Genotype 1b:<br/>Daclatasvir +<br/>Simeprevir (Naive +<br/>Null)</b> | <b>Genotype1b:<br/>Daclatasvir<br/>+Simeprevir +<br/>Ribavirin (Naive +<br/>Null)</b> | <b>Genotype1a:<br/>Daclatasvir<br/>+Simeprevir +<br/>Ribavirin(Naive +<br/>Null)</b> |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 49 / 76 (64.47%)                                                        | 63 / 71 (88.73%)                                                                      | 21 / 21 (100.00%)                                                                    |
| <b>Vascular disorders</b>                                                            |                                                                         |                                                                                       |                                                                                      |
| Hot flush<br>subjects affected / exposed                                             | 0 / 76 (0.00%)                                                          | 1 / 71 (1.41%)                                                                        | 2 / 21 (9.52%)                                                                       |
| occurrences (all)                                                                    | 0                                                                       | 2                                                                                     | 2                                                                                    |
| Hypertension<br>subjects affected / exposed                                          | 5 / 76 (6.58%)                                                          | 2 / 71 (2.82%)                                                                        | 1 / 21 (4.76%)                                                                       |
| occurrences (all)                                                                    | 5                                                                       | 2                                                                                     | 1                                                                                    |
| <b>General disorders and administration site conditions</b>                          |                                                                         |                                                                                       |                                                                                      |
| Asthenia<br>subjects affected / exposed                                              | 15 / 76 (19.74%)                                                        | 16 / 71 (22.54%)                                                                      | 5 / 21 (23.81%)                                                                      |
| occurrences (all)                                                                    | 17                                                                      | 19                                                                                    | 9                                                                                    |
| Chills<br>subjects affected / exposed                                                | 1 / 76 (1.32%)                                                          | 2 / 71 (2.82%)                                                                        | 2 / 21 (9.52%)                                                                       |
| occurrences (all)                                                                    | 1                                                                       | 2                                                                                     | 3                                                                                    |
| Fatigue<br>subjects affected / exposed                                               | 6 / 76 (7.89%)                                                          | 11 / 71 (15.49%)                                                                      | 7 / 21 (33.33%)                                                                      |
| occurrences (all)                                                                    | 6                                                                       | 12                                                                                    | 10                                                                                   |
| Influenza like illness<br>subjects affected / exposed                                | 5 / 76 (6.58%)                                                          | 1 / 71 (1.41%)                                                                        | 3 / 21 (14.29%)                                                                      |
| occurrences (all)                                                                    | 5                                                                       | 1                                                                                     | 7                                                                                    |
| Irritability<br>subjects affected / exposed                                          | 3 / 76 (3.95%)                                                          | 1 / 71 (1.41%)                                                                        | 2 / 21 (9.52%)                                                                       |
| occurrences (all)                                                                    | 3                                                                       | 1                                                                                     | 3                                                                                    |
| Pain<br>subjects affected / exposed                                                  | 3 / 76 (3.95%)                                                          | 1 / 71 (1.41%)                                                                        | 2 / 21 (9.52%)                                                                       |
| occurrences (all)                                                                    | 3                                                                       | 1                                                                                     | 2                                                                                    |
| <b>Respiratory, thoracic and mediastinal disorders</b>                               |                                                                         |                                                                                       |                                                                                      |
| Cough<br>subjects affected / exposed                                                 | 2 / 76 (2.63%)                                                          | 7 / 71 (9.86%)                                                                        | 4 / 21 (19.05%)                                                                      |
| occurrences (all)                                                                    | 3                                                                       | 9                                                                                     | 4                                                                                    |
| Dyspnoea                                                                             |                                                                         |                                                                                       |                                                                                      |

|                                                                                                          |                        |                        |                      |
|----------------------------------------------------------------------------------------------------------|------------------------|------------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                         | 4 / 76 (5.26%)<br>4    | 11 / 71 (15.49%)<br>11 | 2 / 21 (9.52%)<br>4  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 76 (0.00%)<br>0    | 2 / 71 (2.82%)<br>2    | 2 / 21 (9.52%)<br>2  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 76 (1.32%)<br>1    | 0 / 71 (0.00%)<br>0    | 2 / 21 (9.52%)<br>2  |
| Psychiatric disorders<br>Depressed mood<br>subjects affected / exposed<br>occurrences (all)              | 0 / 76 (0.00%)<br>0    | 0 / 71 (0.00%)<br>0    | 2 / 21 (9.52%)<br>5  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 76 (0.00%)<br>0    | 2 / 71 (2.82%)<br>2    | 2 / 21 (9.52%)<br>2  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                             | 4 / 76 (5.26%)<br>4    | 7 / 71 (9.86%)<br>7    | 1 / 21 (4.76%)<br>3  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                                       | 5 / 76 (6.58%)<br>7    | 5 / 71 (7.04%)<br>6    | 3 / 21 (14.29%)<br>5 |
| Nervous system disorders<br>Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 2 / 76 (2.63%)<br>2    | 0 / 71 (0.00%)<br>0    | 2 / 21 (9.52%)<br>2  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                             | 16 / 76 (21.05%)<br>22 | 10 / 71 (14.08%)<br>10 | 6 / 21 (28.57%)<br>7 |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)                                         | 2 / 76 (2.63%)<br>2    | 2 / 71 (2.82%)<br>2    | 3 / 21 (14.29%)<br>3 |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 76 (1.32%)<br>2    | 12 / 71 (16.90%)<br>13 | 5 / 21 (23.81%)<br>7 |
| Neutropenia                                                                                              |                        |                        |                      |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 0 / 76 (0.00%) | 0 / 71 (0.00%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 0              | 0              | 8               |
| Thrombocytopenia                 |                |                |                 |
| subjects affected / exposed      | 0 / 76 (0.00%) | 1 / 71 (1.41%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 0              | 1              | 4               |
| Eye disorders                    |                |                |                 |
| Dry eye                          |                |                |                 |
| subjects affected / exposed      | 1 / 76 (1.32%) | 1 / 71 (1.41%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 1              | 1              | 2               |
| Visual acuity reduced            |                |                |                 |
| subjects affected / exposed      | 0 / 76 (0.00%) | 0 / 71 (0.00%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 0              | 0              | 3               |
| Gastrointestinal disorders       |                |                |                 |
| Abdominal distension             |                |                |                 |
| subjects affected / exposed      | 4 / 76 (5.26%) | 0 / 71 (0.00%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 4              | 0              | 4               |
| Abdominal pain                   |                |                |                 |
| subjects affected / exposed      | 4 / 76 (5.26%) | 2 / 71 (2.82%) | 5 / 21 (23.81%) |
| occurrences (all)                | 4              | 2              | 6               |
| Abdominal pain upper             |                |                |                 |
| subjects affected / exposed      | 3 / 76 (3.95%) | 5 / 71 (7.04%) | 1 / 21 (4.76%)  |
| occurrences (all)                | 3              | 5              | 1               |
| Constipation                     |                |                |                 |
| subjects affected / exposed      | 6 / 76 (7.89%) | 5 / 71 (7.04%) | 4 / 21 (19.05%) |
| occurrences (all)                | 9              | 5              | 5               |
| Diarrhoea                        |                |                |                 |
| subjects affected / exposed      | 5 / 76 (6.58%) | 2 / 71 (2.82%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 5              | 2              | 3               |
| Dyspepsia                        |                |                |                 |
| subjects affected / exposed      | 2 / 76 (2.63%) | 5 / 71 (7.04%) | 0 / 21 (0.00%)  |
| occurrences (all)                | 2              | 5              | 0               |
| Gastric disorder                 |                |                |                 |
| subjects affected / exposed      | 0 / 76 (0.00%) | 0 / 71 (0.00%) | 2 / 21 (9.52%)  |
| occurrences (all)                | 0              | 0              | 3               |
| Gastrooesophageal reflux disease |                |                |                 |

|                                                                                                        |                        |                        |                      |
|--------------------------------------------------------------------------------------------------------|------------------------|------------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                       | 3 / 76 (3.95%)<br>4    | 4 / 71 (5.63%)<br>4    | 0 / 21 (0.00%)<br>0  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                             | 14 / 76 (18.42%)<br>18 | 11 / 71 (15.49%)<br>11 | 4 / 21 (19.05%)<br>5 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 76 (0.00%)<br>0    | 3 / 71 (4.23%)<br>3    | 2 / 21 (9.52%)<br>4  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)     | 1 / 76 (1.32%)<br>3    | 12 / 71 (16.90%)<br>19 | 3 / 21 (14.29%)<br>4 |
| Jaundice<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 76 (1.32%)<br>1    | 4 / 71 (5.63%)<br>4    | 0 / 21 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | 3 / 76 (3.95%)<br>3    | 4 / 71 (5.63%)<br>4    | 0 / 21 (0.00%)<br>0  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                           | 5 / 76 (6.58%)<br>5    | 5 / 71 (7.04%)<br>5    | 4 / 21 (19.05%)<br>5 |
| Eczema<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 76 (0.00%)<br>0    | 2 / 71 (2.82%)<br>2    | 2 / 21 (9.52%)<br>2  |
| Photosensitivity reaction<br>subjects affected / exposed<br>occurrences (all)                          | 6 / 76 (7.89%)<br>7    | 3 / 71 (4.23%)<br>5    | 1 / 21 (4.76%)<br>3  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                           | 5 / 76 (6.58%)<br>5    | 15 / 71 (21.13%)<br>16 | 5 / 21 (23.81%)<br>8 |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                               | 3 / 76 (3.95%)<br>3    | 9 / 71 (12.68%)<br>10  | 3 / 21 (14.29%)<br>6 |
| Musculoskeletal and connective tissue disorders                                                        |                        |                        |                      |

|                                                                        |                        |                       |                      |
|------------------------------------------------------------------------|------------------------|-----------------------|----------------------|
| Back pain<br>subjects affected / exposed<br>occurrences (all)          | 4 / 76 (5.26%)<br>5    | 0 / 71 (0.00%)<br>0   | 1 / 21 (4.76%)<br>2  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)            | 3 / 76 (3.95%)<br>3    | 1 / 71 (1.41%)<br>1   | 2 / 21 (9.52%)<br>3  |
| Infections and infestations                                            |                        |                       |                      |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)         | 2 / 76 (2.63%)<br>3    | 3 / 71 (4.23%)<br>3   | 2 / 21 (9.52%)<br>2  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)          | 0 / 76 (0.00%)<br>0    | 2 / 71 (2.82%)<br>2   | 2 / 21 (9.52%)<br>2  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)    | 10 / 76 (13.16%)<br>12 | 9 / 71 (12.68%)<br>11 | 2 / 21 (9.52%)<br>3  |
| Metabolism and nutrition disorders                                     |                        |                       |                      |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 3 / 76 (3.95%)<br>3    | 1 / 71 (1.41%)<br>2   | 4 / 21 (19.05%)<br>6 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 December 2012 | <p>The primary purpose of this amendment was to clarify certain inclusion and exclusion criteria and maintain consistency with other direct-acting antiviral program Phase 2 studies. In addition there were other minor administrative changes. A summary, but not the full list of changes included in this amendment are bulleted below.</p> <ul style="list-style-type: none"><li>• Changed the week for the interim analysis referring to treatment Week 12 to Week 16. Clarified that this would encompass subjects treated for at least 12 weeks of treatment and 4 weeks post treatment follow-up, (subtype 1b), or 16 weeks of treatment, (subtype 1a or 1b), or prematurely discontinued from the study</li><li>• Changed from a minimum of 10% black/African-American to Approximately 10% black/African American</li><li>• Additional information provided on how to define a Null responder</li><li>• Additional criteria provided defining F3 cirrhosis. Reference to support this addition also added.</li><li>• Further clarification on the types of psychiatric disorders and substance abuse that would be exclusionary in the study</li><li>• Removed "confirmed" reference under the Laboratory exclusion criteria</li><li>• Under prohibited and/or restricted treatments - included timeframe surrounding the stopping of such medications and starting study drug</li><li>• Under prohibited and/or restricted treatments - Additional restricted medications added under CYP3A4 inducers</li><li>• ECG added to Week 8 and End of Treatment study visits while in Treatment Phase and Week 8 and End of Treatment study visits if subject is in Rescue Treatment Phase</li><li>• Added a timeframe for how long the post treatment follow-up period should be for 1b subjects that discontinue prior to re-randomization</li><li>• Added the following sections; "Post Treatment Study Follow up", "Withdrawal of Consent", and "Lost to Follow up"</li><li>• Additional language added regarding study drug disposal and return</li><li>• Time window added for the Week 2 PK samples</li><li>• Added a note regarding the definition of HCV RNA results</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported