



## Clinical trial results:

### A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study of GS-5885, GS-9451, Tegobuvir and Ribavirin (RBV) Compared with GS-5885, GS-9451 with Tegobuvir or RBV in Treatment-Experienced Subjects with Chronic Genotype 1a or 1b Hepatitis C Virus (HCV) Infection

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-002748-28 |
| Trial protocol           | DE             |
| Global end of trial date | 29 July 2013   |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 22 March 2016  |
| First version publication date | 05 August 2015 |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-248-0131 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01435226 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Gilead Sciences                                                                                   |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404                                         |
| Public contact               | Clinical Trial Mailbox, Gilead Sciences International Ltd,<br>ClinicalTrialDisclosures@gilead.com |
| Scientific contact           | Clinical Trial Mailbox, Gilead Sciences International Ltd,<br>ClinicalTrialDisclosures@gilead.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                       | 29 July 2013 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 29 July 2013 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

This study was to evaluate the antiviral efficacy, safety, and tolerability of combination therapy with ledipasvir (LDV; formerly GS-5885), vedoprevir (VDV; formerly GS-9451), tegobuvir (TGV), and ribavirin (RBV) compared with LDV+VDV+TGV or LDV+VDV+RBV in treatment-experienced participants with chronic genotype 1a or 1b hepatitis C virus (HCV) infection. The treatment duration for all arms was 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had on-treatment virologic breakthrough, or relapse following completion of initial treatment were eligible for treatment with LDV+VDV+pegylated interferon (PEG)+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 12 September 2011 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 107 |
| Country: Number of subjects enrolled | Germany: 62        |
| Worldwide total number of subjects   | 169                |
| EEA total number of subjects         | 62                 |

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)                      | 153 |
| From 65 to 84 years                       | 16  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States and Germany. The first participant was screened on 21 September 2011. The last study visit occurred on 29 July 2013.

### Pre-assignment

Screening details:

266 participants were screened.

### Period 1

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 1 title               | Overall study (overall period)                                |
| Is this the baseline period? | Yes                                                           |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |                 |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes             |
| <b>Arm title</b>             | LDV+VDV+TGV+RBV |

Arm description:

Initial treatment: ledipasvir (LDV)+vedoprevir (VDV)+tegobuvir (TGV)+ribavirin (RBV) for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Ledipasvir   |
| Investigational medicinal product code |              |
| Other name                             | GS-5885      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Ledipasvir (LDV) 90 mg (3 x 30 mg tablets) administered orally once daily with food in the morning

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Vedoprevir |
| Investigational medicinal product code |            |
| Other name                             | GS-9451    |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Vedoprevir (VDV) 200 mg (2 x 100 mg tablets) administered orally once daily with food in the morning

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

Dosage and administration details:

Tegobuvir (TGV) 60 mg (2 x 30 mg capsules) administered orally with food once in the morning and once in the evening

|                                        |           |
|----------------------------------------|-----------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code |           |
| Other name                             | Copegus®  |
| Pharmaceutical forms                   | Tablet    |

|                                                                                                                                                                                                                                                                                                                                                                         |                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Oral use               |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Ribavirin (RBV) tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75 kg = 1000 mg and ≥ 75 kg = 1200 mg)                                                                                                                                                                                           |                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Pegylated interferon   |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              | PEG                    |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Solution for injection |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Intravenous use        |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Pegylated interferon alfa-2a (PEG) 180 µg was administered once weekly by subcutaneous injection for participants receiving treatment in the Rescue Therapy Substudy.                                                                                                                                                                                                   |                        |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                        | LDV+VDV+TGV            |
| Arm description:                                                                                                                                                                                                                                                                                                                                                        |                        |
| Initial treatment: LDV+VDV+TGV+RBV placebo for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy. |                        |
| Arm type                                                                                                                                                                                                                                                                                                                                                                | Experimental           |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Ledipasvir             |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              | GS-5885                |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Tablet                 |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Oral use               |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Ledipasvir (LDV) 90 mg (3 x 30 mg tablets) administered orally once daily with food in the morning                                                                                                                                                                                                                                                                      |                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Vedroprevir            |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              | GS-9451                |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Tablet                 |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Oral use               |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Vedroprevir (VDV) 200 mg (2 x 100 mg tablets) administered orally once daily with food in the morning                                                                                                                                                                                                                                                                   |                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Tegobuvir              |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              |                        |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Capsule                |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Oral use               |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Tegobuvir (TGV) 60 mg (2 x 30 mg capsules) administered orally with food once in the morning and once in the evening                                                                                                                                                                                                                                                    |                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Ribavirin placebo      |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              |                        |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Tablet                 |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                | Oral use               |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                      |                        |
| Placebo to match ribavirin tablets administered orally in a divided daily dose                                                                                                                                                                                                                                                                                          |                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                  | Pegylated interferon   |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                  |                        |
| Other name                                                                                                                                                                                                                                                                                                                                                              | PEG                    |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                    | Solution for injection |

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Pegylated interferon alfa-2a (PEG) 180 µg was administered once weekly by subcutaneous injection for participants receiving treatment in the Rescue Therapy Substudy.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | LDV+VDV+RBV |
|------------------|-------------|

Arm description:

Initial Treatment: LDV+VDV+TGV placebo+RBV for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had on-treatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Ledipasvir   |
| Investigational medicinal product code |              |
| Other name                             | GS-5885      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Ledipasvir (LDV) 90 mg (3 x 30 mg tablets) administered orally once daily with food in the morning

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Vedoprevir |
| Investigational medicinal product code |            |
| Other name                             | GS-9451    |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Vedoprevir (VDV) 200 mg (2 x 100 mg tablets) administered orally once daily with food in the morning

|                                        |                   |
|----------------------------------------|-------------------|
| Investigational medicinal product name | Tegobuvir placebo |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

Placebo to match tegobuvir capsules administered orally with food once in the morning and once in the evening

|                                        |           |
|----------------------------------------|-----------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code |           |
| Other name                             | Copegus®  |
| Pharmaceutical forms                   | Tablet    |
| Routes of administration               | Oral use  |

Dosage and administration details:

Ribavirin (RBV) tablets administered orally in a divided daily dose according to package insert weight-based dosing recommendations (< 75 kg = 1000 mg and ≥ 75 kg = 1200 mg)

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Pegylated interferon   |
| Investigational medicinal product code |                        |
| Other name                             | PEG                    |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Pegylated interferon alfa-2a (PEG) 180 µg was administered once weekly by subcutaneous injection for participants receiving treatment in the Rescue Therapy Substudy.

| <b>Number of subjects in period 1</b> | <b>LDV+VDV+TGV+RB<br/>V</b> | <b>LDV+VDV+TGV</b> | <b>LDV+VDV+RBV</b> |
|---------------------------------------|-----------------------------|--------------------|--------------------|
| Started                               | 57                          | 56                 | 56                 |
| Entered Rescue Therapy Substudy       | 30 <sup>[1]</sup>           | 36                 | 42                 |
| Completed                             | 31                          | 25                 | 19                 |
| Not completed                         | 26                          | 31                 | 37                 |
| Physician decision                    | 2                           | -                  | 3                  |
| Adverse event, non-fatal              | 2                           | 5                  | 5                  |
| Protocol violation                    | 1                           | -                  | 1                  |
| Study terminated by sponsor           | -                           | -                  | 2                  |
| Lost to follow-up                     | 1                           | 1                  | 1                  |
| Lack of efficacy                      | 19                          | 22                 | 19                 |
| Withdrawal by subject                 | 1                           | 3                  | 6                  |

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Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The overall number completed includes participants who completed the initial treatment and did not continue in the Rescue Therapy Substudy, and those who continued after initial treatment and completed the Rescue Therapy Substudy.

## Baseline characteristics

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | LDV+VDV+TGV+RBV |
|-----------------------|-----------------|

Reporting group description:

Initial treatment: ledipasvir (LDV)+vedoprevir (VDV)+tegobuvir (TGV)+ribavirin (RBV) for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+TGV |
|-----------------------|-------------|

Reporting group description:

Initial treatment: LDV+VDV+TGV+RBV placebo for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+RBV |
|-----------------------|-------------|

Reporting group description:

Initial Treatment: LDV+VDV+TGV placebo+RBV for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

| Reporting group values                             | LDV+VDV+TGV+RBV | LDV+VDV+TGV | LDV+VDV+RBV |
|----------------------------------------------------|-----------------|-------------|-------------|
| Number of subjects                                 | 57              | 56          | 56          |
| Age categorical<br>Units: Subjects                 |                 |             |             |
| In utero                                           |                 |             |             |
| Preterm newborn infants (gestational age < 37 wks) |                 |             |             |
| Newborns (0-27 days)                               |                 |             |             |
| Infants and toddlers (28 days-23 months)           |                 |             |             |
| Children (2-11 years)                              |                 |             |             |
| Adolescents (12-17 years)                          |                 |             |             |
| Adults (18-64 years)                               |                 |             |             |
| From 65-84 years                                   |                 |             |             |
| 85 years and over                                  |                 |             |             |
| Age continuous<br>Units: years                     |                 |             |             |
| arithmetic mean                                    | 53              | 54          | 56          |
| standard deviation                                 | ± 8.8           | ± 7.6       | ± 8.5       |
| Gender categorical<br>Units: Subjects              |                 |             |             |
| Female                                             | 16              | 19          | 24          |
| Male                                               | 41              | 37          | 32          |
| Race<br>Units: Subjects                            |                 |             |             |
| White                                              | 46              | 45          | 51          |
| Black or African American                          | 9               | 9           | 4           |
| Asian                                              | 0               | 1           | 1           |

|                                                               |        |        |        |
|---------------------------------------------------------------|--------|--------|--------|
| American Indian or Alaska Native                              | 0      | 1      | 0      |
| Not Permitted                                                 | 1      | 0      | 0      |
| Other                                                         | 1      | 0      | 0      |
| Ethnicity<br>Units: Subjects                                  |        |        |        |
| Hispanic or Latino                                            | 4      | 5      | 5      |
| Not Hispanic or Latino                                        | 53     | 51     | 51     |
| HCV Genotype<br>Units: Subjects                               |        |        |        |
| 1a                                                            | 35     | 34     | 35     |
| 1b                                                            | 22     | 22     | 21     |
| IL28B Status                                                  |        |        |        |
| CC, CT, and TT alleles are different forms of the IL28b gene. |        |        |        |
| Units: Subjects                                               |        |        |        |
| CC                                                            | 5      | 1      | 6      |
| CT                                                            | 38     | 40     | 39     |
| TT                                                            | 14     | 15     | 11     |
| HCV RNA<br>Units: log10 IU/mL                                 |        |        |        |
| arithmetic mean                                               | 6.7    | 6.5    | 6.5    |
| standard deviation                                            | ± 0.45 | ± 0.57 | ± 0.51 |

|                                                       |       |  |  |
|-------------------------------------------------------|-------|--|--|
| <b>Reporting group values</b>                         | Total |  |  |
| Number of subjects                                    | 169   |  |  |
| Age categorical<br>Units: Subjects                    |       |  |  |
| In utero                                              | 0     |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 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)                                  | 0     |  |  |
| From 65-84 years                                      | 0     |  |  |
| 85 years and over                                     | 0     |  |  |
| Age continuous<br>Units: years                        |       |  |  |
| arithmetic mean                                       |       |  |  |
| standard deviation                                    | -     |  |  |
| Gender categorical<br>Units: Subjects                 |       |  |  |
| Female                                                | 59    |  |  |
| Male                                                  | 110   |  |  |
| Race<br>Units: Subjects                               |       |  |  |
| White                                                 | 142   |  |  |
| Black or African American                             | 22    |  |  |
| Asian                                                 | 2     |  |  |
| American Indian or Alaska Native                      | 1     |  |  |
| Not Permitted                                         | 1     |  |  |

|                                                               |     |  |  |
|---------------------------------------------------------------|-----|--|--|
| Other                                                         | 1   |  |  |
| Ethnicity                                                     |     |  |  |
| Units: Subjects                                               |     |  |  |
| Hispanic or Latino                                            | 14  |  |  |
| Not Hispanic or Latino                                        | 155 |  |  |
| HCV Genotype                                                  |     |  |  |
| Units: Subjects                                               |     |  |  |
| 1a                                                            | 104 |  |  |
| 1b                                                            | 65  |  |  |
| IL28B Status                                                  |     |  |  |
| CC, CT, and TT alleles are different forms of the IL28b gene. |     |  |  |
| Units: Subjects                                               |     |  |  |
| CC                                                            | 12  |  |  |
| CT                                                            | 117 |  |  |
| TT                                                            | 40  |  |  |
| HCV RNA                                                       |     |  |  |
| Units: log10 IU/mL                                            |     |  |  |
| arithmetic mean                                               |     |  |  |
| standard deviation                                            | -   |  |  |

## End points

### End points reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | LDV+VDV+TGV+RBV |
|-----------------------|-----------------|

Reporting group description:

Initial treatment: ledipasvir (LDV)+vedoprevir (VDV)+tegobuvir (TGV)+ribavirin (RBV) for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+TGV |
|-----------------------|-------------|

Reporting group description:

Initial treatment: LDV+VDV+TGV+RBV placebo for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+RBV |
|-----------------------|-------------|

Reporting group description:

Initial Treatment: LDV+VDV+TGV placebo+RBV for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | LDV+VDV+TGV+RBV - Main Study |
|----------------------------|------------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

LDV+VDV+TGV+RBV for 24 weeks

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | LDV+VDV+TGV - Main Study |
|----------------------------|--------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

LDV+VDV+TGV+RBV placebo for 24 weeks

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | LDV+VDV+RBV - Main Study |
|----------------------------|--------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

LDV+VDV+TGV placebo+RBV for 24 weeks

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | LDV+VDV+TGV+RBV - Rescue Therapy Substudy |
|----------------------------|-------------------------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Initial treatment: LDV+VDV+TGV+RBV for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                            |                                       |
|----------------------------|---------------------------------------|
| Subject analysis set title | LDV+VDV+TGV - Rescue Therapy Substudy |
|----------------------------|---------------------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Initial treatment: LDV+VDV+TGV+RBV placebo for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with LDV+VDV+PEG+RBV for an additional 24 to 48 weeks in the Rescue Therapy Substudy.

|                            |                                       |
|----------------------------|---------------------------------------|
| Subject analysis set title | LDV+VDV+RBV - Rescue Therapy Substudy |
|----------------------------|---------------------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Initial treatment: LDV+VDV+TGV placebo+RBV for 24 weeks. Participants who did not achieve a very rapid virologic response (vRVR, defined as HCV RNA < LLOQ at Week 2), had ontreatment virologic breakthrough, or relapse following initial treatment were eligible for treatment with

**Primary: Percentage of participants with sustained virologic response (SVR) 24 weeks after discontinuation of therapy (SVR24)**

|                 |                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of participants with sustained virologic response (SVR) 24 weeks after discontinuation of therapy (SVR24) <sup>[1]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|

End point description:

SVR24 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 25 IU/mL) 24 weeks following the last dose of study drug.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Posttreatment Week 24

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: No statistical hypothesis testing was planned or performed.

| End point values                  | LDV+VDV+TGV<br>+RBV - Main<br>Study | LDV+VDV+TGV<br>- Main Study | LDV+VDV+RBV<br>- Main Study |  |
|-----------------------------------|-------------------------------------|-----------------------------|-----------------------------|--|
| Subject group type                | Subject analysis set                | Subject analysis set        | Subject analysis set        |  |
| Number of subjects analysed       | 57                                  | 54                          | 55                          |  |
| Units: percentage of participants |                                     |                             |                             |  |
| number (not applicable)           | 33.3                                | 22.2                        | 9.1                         |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Percentage of participants who experienced an adverse event leading to permanent discontinuation from any study drug**

|                 |                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of participants who experienced an adverse event leading to permanent discontinuation from any study drug <sup>[2]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 24 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical hypothesis testing was planned or performed.

| End point values                  | LDV+VDV+TGV<br>+RBV - Main<br>Study | LDV+VDV+TGV<br>- Main Study | LDV+VDV+RBV<br>- Main Study |  |
|-----------------------------------|-------------------------------------|-----------------------------|-----------------------------|--|
| Subject group type                | Subject analysis set                | Subject analysis set        | Subject analysis set        |  |
| Number of subjects analysed       | 57                                  | 56                          | 56                          |  |
| Units: percentage of participants |                                     |                             |                             |  |
| number (not applicable)           | 0                                   | 7.1                         | 3.6                         |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with SVR4 and SVR12

|                                                                                                                                                |                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                                                                                                | Percentage of participants with SVR4 and SVR12 |
| End point description:<br>SVR4 and SVR12 were defined as HCV RNA < LLOQ at 4 and 12 weeks following the last dose of study drug, respectively. |                                                |
| End point type                                                                                                                                 | Secondary                                      |
| End point timeframe:<br>Posttreatment Weeks 4 and 12                                                                                           |                                                |

| End point values                  | LDV+VDV+TGV<br>+RBV - Main<br>Study | LDV+VDV+TGV<br>- Main Study | LDV+VDV+RBV<br>- Main Study |  |
|-----------------------------------|-------------------------------------|-----------------------------|-----------------------------|--|
| Subject group type                | Subject analysis set                | Subject analysis set        | Subject analysis set        |  |
| Number of subjects analysed       | 57                                  | 54                          | 55                          |  |
| Units: percentage of participants |                                     |                             |                             |  |
| number (not applicable)           |                                     |                             |                             |  |
| SVR4                              | 35.1                                | 24.1                        | 10.9                        |  |
| SVR12                             | 33.3                                | 22.2                        | 9.1                         |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: In the rescue therapy substudy, percentage of participants with SVR4, SVR12, and SVR24

|                                                                                                                                                                                                                                                                                |                                                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                | In the rescue therapy substudy, percentage of participants with SVR4, SVR12, and SVR24 |
| End point description:<br>SVR4, SVR12, and SVR24 were defined as HCV RNA < LLOQ at 4, 12, and 24 weeks following the last dose of study drug during the rescue therapy substudy, respectively. This endpoint only includes data from the Rescue Therapy Substudy Analysis Set. |                                                                                        |
| End point type                                                                                                                                                                                                                                                                 | Secondary                                                                              |

---

End point timeframe:

Posttreatment Weeks 4, 12, and 24

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| <b>End point values</b>           | LDV+VDV+TGV<br>+RBV - Rescue<br>Therapy<br>Substudy | LDV+VDV+TGV<br>- Rescue<br>Therapy<br>Substudy | LDV+VDV+RBV<br>- Rescue<br>Therapy<br>Substudy |  |
|-----------------------------------|-----------------------------------------------------|------------------------------------------------|------------------------------------------------|--|
| Subject group type                | Subject analysis set                                | Subject analysis set                           | Subject analysis set                           |  |
| Number of subjects analysed       | 30                                                  | 36                                             | 42                                             |  |
| Units: percentage of participants |                                                     |                                                |                                                |  |
| number (not applicable)           |                                                     |                                                |                                                |  |
| SVR4                              | 40                                                  | 44.4                                           | 40.5                                           |  |
| SVR12                             | 30                                                  | 36.1                                           | 31                                             |  |
| SVR24                             | 30                                                  | 33.3                                           | 31                                             |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 24 weeks plus 30 days

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 16 |
|--------------------|----|

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | LDV+VDV+TGV+RBV |
|-----------------------|-----------------|

Reporting group description:

Ledipasvir (LDV) + vedroprevir (VDV) + tegobuvir (TGV) + ribavirin (RBV) for 24 weeks

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+TGV |
|-----------------------|-------------|

Reporting group description:

LDV+VDV+TGV+RBV placebo for 24 weeks

|                       |             |
|-----------------------|-------------|
| Reporting group title | LDV+VDV+RBV |
|-----------------------|-------------|

Reporting group description:

LDV+VDV+TGV placebo+RBV for 24 weeks

| Serious adverse events                            | LDV+VDV+TGV+RBV | LDV+VDV+TGV    | LDV+VDV+RBV    |
|---------------------------------------------------|-----------------|----------------|----------------|
| Total subjects affected by serious adverse events |                 |                |                |
| subjects affected / exposed                       | 1 / 57 (1.75%)  | 1 / 56 (1.79%) | 1 / 56 (1.79%) |
| number of deaths (all causes)                     | 0               | 0              | 0              |
| number of deaths resulting from adverse events    | 0               | 0              | 0              |
| Immune system disorders                           |                 |                |                |
| Hypersensitivity                                  |                 |                |                |
| subjects affected / exposed                       | 0 / 57 (0.00%)  | 1 / 56 (1.79%) | 0 / 56 (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          |
| Gastrointestinal disorders                        |                 |                |                |
| Duodenal ulcer                                    |                 |                |                |
| subjects affected / exposed                       | 1 / 57 (1.75%)  | 0 / 56 (0.00%) | 0 / 56 (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          |
| Duodenitis                                        |                 |                |                |
| subjects affected / exposed                       | 1 / 57 (1.75%)  | 0 / 56 (0.00%) | 0 / 56 (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          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic obstructive pulmonary disease           |                |                |                |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 0 / 56 (0.00%) | 1 / 56 (1.79%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| 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>                     | LDV+VDV+TGV+RBV  | LDV+VDV+TGV      | LDV+VDV+RBV      |
|-------------------------------------------------------|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                  |
| subjects affected / exposed                           | 43 / 57 (75.44%) | 38 / 56 (67.86%) | 41 / 56 (73.21%) |
| Vascular disorders                                    |                  |                  |                  |
| Hypertension                                          |                  |                  |                  |
| subjects affected / exposed                           | 3 / 57 (5.26%)   | 0 / 56 (0.00%)   | 0 / 56 (0.00%)   |
| occurrences (all)                                     | 3                | 0                | 0                |
| Nervous system disorders                              |                  |                  |                  |
| Headache                                              |                  |                  |                  |
| subjects affected / exposed                           | 15 / 57 (26.32%) | 12 / 56 (21.43%) | 13 / 56 (23.21%) |
| occurrences (all)                                     | 19               | 15               | 15               |
| Dizziness                                             |                  |                  |                  |
| subjects affected / exposed                           | 4 / 57 (7.02%)   | 7 / 56 (12.50%)  | 0 / 56 (0.00%)   |
| occurrences (all)                                     | 5                | 7                | 0                |
| Blood and lymphatic system disorders                  |                  |                  |                  |
| Anaemia                                               |                  |                  |                  |
| subjects affected / exposed                           | 2 / 57 (3.51%)   | 0 / 56 (0.00%)   | 4 / 56 (7.14%)   |
| occurrences (all)                                     | 2                | 0                | 4                |
| General disorders and administration site conditions  |                  |                  |                  |
| Fatigue                                               |                  |                  |                  |
| subjects affected / exposed                           | 20 / 57 (35.09%) | 13 / 56 (23.21%) | 15 / 56 (26.79%) |
| occurrences (all)                                     | 20               | 13               | 15               |
| Irritability                                          |                  |                  |                  |
| subjects affected / exposed                           | 2 / 57 (3.51%)   | 3 / 56 (5.36%)   | 4 / 56 (7.14%)   |
| occurrences (all)                                     | 2                | 3                | 4                |
| Asthenia                                              |                  |                  |                  |

|                                                                  |                        |                      |                        |
|------------------------------------------------------------------|------------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                 | 5 / 57 (8.77%)<br>5    | 1 / 56 (1.79%)<br>1  | 2 / 56 (3.57%)<br>2    |
| Chills<br>subjects affected / exposed<br>occurrences (all)       | 1 / 57 (1.75%)<br>1    | 0 / 56 (0.00%)<br>0  | 3 / 56 (5.36%)<br>3    |
| Gastrointestinal disorders                                       |                        |                      |                        |
| Nausea<br>subjects affected / exposed<br>occurrences (all)       | 9 / 57 (15.79%)<br>13  | 8 / 56 (14.29%)<br>8 | 9 / 56 (16.07%)<br>11  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)    | 8 / 57 (14.04%)<br>9   | 3 / 56 (5.36%)<br>3  | 3 / 56 (5.36%)<br>3    |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)    | 10 / 57 (17.54%)<br>16 | 2 / 56 (3.57%)<br>2  | 2 / 56 (3.57%)<br>2    |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)     | 4 / 57 (7.02%)<br>5    | 0 / 56 (0.00%)<br>0  | 3 / 56 (5.36%)<br>3    |
| Constipation<br>subjects affected / exposed<br>occurrences (all) | 1 / 57 (1.75%)<br>1    | 2 / 56 (3.57%)<br>2  | 3 / 56 (5.36%)<br>3    |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)    | 2 / 57 (3.51%)<br>2    | 0 / 56 (0.00%)<br>0  | 3 / 56 (5.36%)<br>3    |
| Flatulence<br>subjects affected / exposed<br>occurrences (all)   | 1 / 57 (1.75%)<br>2    | 3 / 56 (5.36%)<br>3  | 1 / 56 (1.79%)<br>1    |
| Respiratory, thoracic and mediastinal disorders                  |                        |                      |                        |
| Cough<br>subjects affected / exposed<br>occurrences (all)        | 7 / 57 (12.28%)<br>8   | 2 / 56 (3.57%)<br>2  | 11 / 56 (19.64%)<br>11 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)     | 3 / 57 (5.26%)<br>3    | 1 / 56 (1.79%)<br>1  | 5 / 56 (8.93%)<br>5    |
| Dyspnoea exertional                                              |                        |                      |                        |

|                                                                               |                        |                      |                      |
|-------------------------------------------------------------------------------|------------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                              | 0 / 57 (0.00%)<br>0    | 1 / 56 (1.79%)<br>1  | 7 / 56 (12.50%)<br>7 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)        | 3 / 57 (5.26%)<br>3    | 1 / 56 (1.79%)<br>1  | 1 / 56 (1.79%)<br>1  |
| Skin and subcutaneous tissue disorders                                        |                        |                      |                      |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                  | 10 / 57 (17.54%)<br>13 | 7 / 56 (12.50%)<br>7 | 7 / 56 (12.50%)<br>8 |
| Rash<br>subjects affected / exposed<br>occurrences (all)                      | 5 / 57 (8.77%)<br>6    | 3 / 56 (5.36%)<br>3  | 4 / 56 (7.14%)<br>4  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                  | 4 / 57 (7.02%)<br>4    | 0 / 56 (0.00%)<br>0  | 4 / 56 (7.14%)<br>4  |
| Photosensitivity reaction<br>subjects affected / exposed<br>occurrences (all) | 3 / 57 (5.26%)<br>3    | 2 / 56 (3.57%)<br>2  | 0 / 56 (0.00%)<br>0  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 57 (5.26%)<br>3    | 0 / 56 (0.00%)<br>0  | 0 / 56 (0.00%)<br>0  |
| Psychiatric disorders                                                         |                        |                      |                      |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                  | 4 / 57 (7.02%)<br>4    | 3 / 56 (5.36%)<br>3  | 2 / 56 (3.57%)<br>2  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                   | 5 / 57 (8.77%)<br>5    | 0 / 56 (0.00%)<br>0  | 1 / 56 (1.79%)<br>1  |
| Musculoskeletal and connective tissue disorders                               |                        |                      |                      |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 57 (3.51%)<br>2    | 4 / 56 (7.14%)<br>4  | 2 / 56 (3.57%)<br>2  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                | 4 / 57 (7.02%)<br>4    | 3 / 56 (5.36%)<br>3  | 0 / 56 (0.00%)<br>0  |
| Back pain                                                                     |                        |                      |                      |

|                                                                          |                      |                     |                     |
|--------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                         | 4 / 57 (7.02%)<br>5  | 0 / 56 (0.00%)<br>0 | 1 / 56 (1.79%)<br>1 |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 57 (0.00%)<br>0  | 4 / 56 (7.14%)<br>4 | 0 / 56 (0.00%)<br>0 |
| Infections and infestations                                              |                      |                     |                     |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)      | 7 / 57 (12.28%)<br>8 | 4 / 56 (7.14%)<br>5 | 0 / 56 (0.00%)<br>0 |
| Oral herpes<br>subjects affected / exposed<br>occurrences (all)          | 1 / 57 (1.75%)<br>2  | 0 / 56 (0.00%)<br>0 | 3 / 56 (5.36%)<br>3 |
| Metabolism and nutrition disorders                                       |                      |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)   | 2 / 57 (3.51%)<br>2  | 2 / 56 (3.57%)<br>2 | 4 / 56 (7.14%)<br>5 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 29 July 2011      | The virologic breakthrough futility rule was revised based on FDA recommendation.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 15 September 2011 | Due to two cases of pancytopenia/aplastic anemia observed in subjects receiving tegobuvir plus a protease inhibitor plus PEG/RBV (in different studies), the decision was made to discontinue dosing of tegobuvir when given in combination with PEG/RBV and another oral antiviral. Therefore, tegobuvir was removed from the Rescue Therapy Substudy.                                                                                                                                                                                                                                                                                                                                                 |
| 11 April 2012     | On 26 March 2012, the Data Monitoring Committee (DMC) determined that the protocol-specified virologic breakthrough futility rule had been met for subjects with genotype 1a HCV infection in Arm 2 and Arm 3. Based on the DMC's recommendations, the following changes were made: <ul style="list-style-type: none"><li>- study was unblinded and the treatment assignment for every subject was provided to the treating investigator</li><li>- all genotype 1a subjects in Arms 2 and 3 was offered enrollment in the Rescue Therapy Substudy (GS-5885+GS-9451+PEG+RBV for 24-48 weeks). This instruction superseded any other references to eligibility for the Rescue Therapy Substudy.</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date          | Interruption                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Restart date  |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| 26 March 2012 | On 26 March 2012, the DMC determined that the protocol-specified virologic breakthrough futility rule had been met for subjects with genotype 1a HCV infection in Arm 2 and Arm 3. As the study completed enrollment in February 2012, the DMC's recommendations was implemented as follows: <ul style="list-style-type: none"><li>- the study was unblinded and the treatment assignment for every subject was provided to the treating investigator</li><li>- all genotype 1a subjects in Arms 2 and 3 was offered enrollment in the Rescue Therapy Substudy (LDV+VDV+PEG+RBV for 24-48 weeks). This instruction superseded any other references to eligibility for the Rescue Therapy Substudy.</li></ul> | 11 April 2012 |

Notes:

### Limitations and caveats

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

There were no limitations affecting the analysis or results.

Notes: