



## Clinical trial results:

### Open-Label, Phase 3b Study To Determine Efficacy and Safety of Telaprevir, Pegylated-Interferon-alfa-2a and Ribavirin in Hepatitis C Genotype 1 Infected, Stable Liver Transplant Subjects

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2011-004724-35    |
| Trial protocol           | DE ES GB IT AT BE |
| Global end of trial date | 15 July 2014      |

## Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 16 July 2016   |
| First version publication date | 31 July 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>Correction of full data set</li><li>Review of data</li></ul> |

## Trial information

### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | VX-950HPC3006 |
|-----------------------|---------------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01571583 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Janssen-Cilag International NV   |
| Sponsor organisation address | Turnhoutseweg 30, 2340 Beerse, Belgium,  |
| Public contact               | Clinical Registry Group, Janssen-Cilag International NV,<br>ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen-Cilag International NV,<br>ClinicalTrialsEU@its.jnj.com |

Notes:

## Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 15 July 2014 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 15 July 2014 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

To determine the efficacy of telaprevir administered as 750 milligram (mg) every 8 hours (q8h) in combination with pegylated interferon (Peg-IFN)-alfa-2a and ribavirin (RBV) in genotype 1 chronic HCV infected liver transplant patients as measured by sustained virologic response SVR12planned. SVR12planned is defined as having HCV RNA < 25 IU/mL 12 weeks after the last planned dose of study medication.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Known instances of nonconformance were documented and are not considered to have had an impact on the overall conclusions of this study. The study protocol and amendments were reviewed by an Independent Ethics Committee or Institutional Review Board.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 28 December 2011 |
| 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 | Austria: 5         |
| Country: Number of subjects enrolled | Belgium: 2         |
| Country: Number of subjects enrolled | Germany: 12        |
| Country: Number of subjects enrolled | Spain: 25          |
| Country: Number of subjects enrolled | France: 7          |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Italy: 13          |
| Worldwide total number of subjects   | 74                 |
| EEA total number of subjects         | 74                 |

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)                     | 71 |
| From 65 to 84 years                      | 3  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Approximately 72 participants were planned to be included in this study.

### Pre-assignment

Screening details:

74 participants received at least one dose of study drugs: 50 participants were on a stable regimen with tacrolimus (TAC) and 24 participants were on a stable regimen with cyclosporine A (CsA).

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus |

Arm description:

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and Tacrolimus. All subjects received Tacrolimus (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit.

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

Dosage and administration details:

750 milligram (mg), administered as two 375-mg tablets, every 8 hours (q8h) up to Week 12.

|  |  |
|--|--|
| Investigational medicinal product name | Pegylated interferon [Peg-IFN-alfa-2a] |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection                 |
| Routes of administration               | Subcutaneous use                       |

Dosage and administration details:

180 microgram per week [ $\mu$ g/week], up to 48 weeks.

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

Dosage and administration details:

600 milligram per day [mg/day] (twice daily regimen) as starting dose.

|  |                  |
|--|------------------|
| Investigational medicinal product name | Tacrolimus (TAC) |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Tablet           |
| Routes of administration               | Oral use         |

**Dosage and administration details:**

For subjects whose pre-telaprevir TAC dose was 5 mg or less daily, the starting dose was between 0.2 mg (pediatric formulation) and 0.5 mg of TAC with subsequent dosing every 3 to 5 days.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A |
|------------------|---|

**Arm description:**

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and cyclosporine A. All subjects received cyclosporine A (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit.

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

**Dosage and administration details:**

750 milligram (mg), administered as two 375-mg tablets, every 8 hours (q8h) up to Week 12.

|  |  |
|--|--|
| Investigational medicinal product name | Pegylated interferon [Peg-IFN-alfa-2a] |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection                 |
| Routes of administration               | Subcutaneous use                       |

**Dosage and administration details:**

180 microgram per week [ $\mu\text{g}/\text{week}$ ], up to 48 weeks.

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

**Dosage and administration details:**

600 milligram per day [ $\text{mg}/\text{day}$ ] (twice daily regimen) as starting dose.

|  |                |
|--|----------------|
| Investigational medicinal product name | Cyclosporine A |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Tablet         |
| Routes of administration               | Oral use       |

**Dosage and administration details:**

For subjects whose pre-telaprevir dose was 100 to 200 mg CsA daily, the starting dose of CsA was between 25 and 50 mg daily.

| <b>Number of subjects in period 1</b> | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A |
|---------------------------------------|---|---|
| Started                               | 50  | 24  |
| Completed                             | 43  | 21  |
| Not completed                         | 7   | 3   |
| Consent withdrawn by subject          | 4   | 3   |

|  |   |   |
|--|---|---|
| Lost to follow-up                        | 1 | - |
| Subject ineligible to continue the trial | 2 | - |

## Baseline characteristics

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus |
|-----------------------|---|

Reporting group description:

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and Tacrolimus. All subjects received Tacrolimus (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit.

|                       |   |
|-----------------------|---|
| Reporting group title | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A |
|-----------------------|---|

Reporting group description:

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and cyclosporine A. All subjects received cyclosporine A (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit.

| Reporting group values                      | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | Total |
|---|---|---|-------|
| Number of subjects                          | 50  | 24  | 74    |
| Title for AgeCategorical<br>Units: subjects |   |   |       |
| Children (2-11 years)                       | 0   | 0   | 0     |
| Adolescents (12-17 years)                   | 0   | 0   | 0     |
| Adults (18-65 years)                        | 48  | 23  | 71    |
| From 66 to 84 years                         | 2   | 1   | 3     |
| 85 years and over                           | 0   | 0   | 0     |
| Title for AgeContinuous<br>Units: years     |   |   |       |
| arithmetic mean                             | 57  | 54.9  |       |
| standard deviation                          | ± 5.25  | ± 6.33  | -     |
| Title for Gender<br>Units: subjects         |   |   |       |
| Female                                      | 3   | 3   | 6     |
| Male  | 47  | 21  | 68    |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus     |
| Reporting group description:<br>Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and Tacrolimus. All subjects received Tacrolimus (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit.         |   |
| Reporting group title  | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A |
| Reporting group description:<br>Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and cyclosporine A. All subjects received cyclosporine A (Immunosuppressive therapy) throughout the study. Prestudy, this immunosuppressant therapy had to be stable, defined as no change in immunosuppressive agents and dose for 1 month prior to the screening visit. |   |
| Subject analysis set title   | All Subjects (Full Analysis (FA) Set)             |
| Subject analysis set type  | Full analysis                                     |
| Subject analysis set description:<br>FAS included all subjects who received at least one dose of study drugs.  |   |

### Primary: Percentage of Participants Achieving Sustained Virologic Response (SVR12) (planned [snapshot])

|   |   |
|---|---|
| End point title   | Percentage of Participants Achieving Sustained Virologic Response (SVR12) (planned [snapshot]) <sup>[1]</sup> |
| End point description:<br>SVR12 (planned) is defined as having plasma hepatitis C virus (HCV) ribonucleic acid (RNA) levels less than (<) 25 international unit per milliliter (IU/mL), 12 weeks after the last planned dose of study drugs. Snapshot approach is where the SVR assessment was based on the last HCV RNA value using a lower limit of quantification (LLOQ) of 25 IU/mL in the Week 12 follow-up visit window. The primary analysis on the primary endpoint was conducted using descriptive statistics along with the 95% exact CI for the proportion. The lower bound of the 2-sided 95% CI of SVR12planned in this study (59.9%) excluded the prespecified historical control SVR rate with Peg-IFN/RBV only (31%). Consequently, the null hypothesis that SVR in this study is 31%, is rejected. |   |
| End point type  | Primary   |
| End point timeframe:<br>Week 60   |   |
| Notes:<br>[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.<br>Justification: Descriptive statistics were done, no inferential statistical analyses were performed  |   |

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[2]</sup>                             | 24 <sup>[3]</sup>                                 | 74 <sup>[4]</sup>                     |  |
| Units: percentage of participants |   |   |                                       |  |
| number (confidence interval 95%)  | 66 (51.2 to 78.8)                             | 83.3 (62.6 to 95.3)                               | 71.6 (59.9 to 81.5)                   |  |

Notes:

[2] - FAS

[3] - FAS

[4] - FAS



## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Achieving sustained virologic response (SVR) 24 planned

|   |  |
|---|--|
| End point title   | Percentage of Participants Achieving sustained virologic response (SVR) 24 planned |
| End point description:<br>SVR24 planned is defined as having plasma HCV RNA levels <25 IU/mL 24 weeks after the last planned dose of study drugs, based on the last plasma HCV RNA value using an LLOQ of 25 IU/mL in the Week 24 follow-up visit window. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Week 72   |  |

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[5]</sup>                             | 24 <sup>[6]</sup>                                 | 74 <sup>[7]</sup>                     |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 68  | 83.3  | 73                                    |  |

Notes:

[5] - FAS

[6] - FAS

[7] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Rapid Virologic Response (RVR)

|  |  |
|--|--|
| End point title  | Percentage of Participants with Rapid Virologic Response (RVR) |
| End point description:<br>RVR defined as having plasma HCV RNA levels '<25 IU/mL, target not detected' at Week 4 of treatment. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Week 4   |  |

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[8]</sup>                             | 24 <sup>[9]</sup>                                 | 74 <sup>[10]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 38  | 16.7  | 31.1                                  |  |

Notes:

[8] - FAS

[9] - FAS

[10] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Extended Rapid Virologic Response (eRVR)

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with Extended Rapid Virologic Response (eRVR) |
|-----------------|--|

End point description:

eRVR is defined as having plasma HCV RNA levels <25 IU/mL, 'target not detected' at Week 4 and Week 12 of treatment.

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

End point timeframe:

Week 4, Week 12

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[11]</sup>                            | 24 <sup>[12]</sup>                                | 74 <sup>[13]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 38  | 16.7  | 31.1                                  |  |

Notes:

[11] - FAS

[12] - FAS

[13] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Complete Early Virologic Response (cEVR)

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with Complete Early Virologic Response (cEVR) |
|-----------------|--|

End point description:

cEVR is defined as having plasma HCV RNA levels <25 IU/mL, target not detected at Week 12 of treatment.

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

End point timeframe:

Week 12

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[14]</sup>                            | 24 <sup>[15]</sup>                                | 74 <sup>[16]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 80  | 87.5  | 82.4                                  |  |

Notes:

[14] - FAS

[15] - FAS

[16] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Having Plasma HCV RNA levels <25 IU/mL, Target not Detected' at the Actual End of Treatment

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Having Plasma HCV RNA levels <25 IU/mL, Target not Detected' at the Actual End of Treatment |
|-----------------|--|

End point description:

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

End point timeframe:

Week 48 or early discontinuation

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[17]</sup>                            | 24 <sup>[18]</sup>                                | 74 <sup>[19]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 78  | 83.3  | 79.7                                  |  |

Notes:

[17] - FAS

[18] - FAS

[19] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Having Plasma HCV RNA levels <25 IU/mL, Target not Detected, at the Planned End of Treatment

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Having Plasma HCV RNA levels <25 IU/mL, Target not Detected, at the Planned End of Treatment |
|-----------------|---|

End point description:

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

End point timeframe:

Week 48

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 44 <sup>[20]</sup>                            | 21 <sup>[21]</sup>                                | 65 <sup>[22]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 79.5  | 90.5  | 83.1                                  |  |

Notes:

[20] - FAS

[21] - FAS

[22] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with On-treatment Virologic Failure

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with On-treatment Virologic Failure |
|-----------------|--|

End point description:

Virologic failure (ie, subjects who met a virologic stopping rule and/or met the definition of viral breakthrough)

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

End point timeframe:

Baseline (Week 1) up to Week 48

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[23]</sup>                            | 24 <sup>[24]</sup>                                | 74 <sup>[25]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 12  | 8.3   | 10.8                                  |  |

Notes:

[23] - FAS

[24] - FAS

[25] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Relapse (Snapshot)

|  |  |
|--|--|
| End point title  | Percentage of Participants with Relapse (Snapshot) |
| End point description:<br>Relapse (Snapshot), defined as having confirmed detectable plasma HCV RNA (greater than or equal to ( $\geq$ ) 25 IU/mL) from planned end of treatment (ie, Week 48) onwards after previous ' $<25$ IU/mL at planned end of treatment, and not achieving SVR12planned (Snapshot).<br>Number of subjects analyzed included subjects who had HCV RNA $<25$ IU/mL at planned end of treatment, or a missing HCV RNA assessment at planned end of treatment (EOT) and HCV RNA $<25$ IU/mL during follow-up from planned EOT onwards. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Week 48 up to Week 60  |  |

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 37 <sup>[26]</sup>                            | 19 <sup>[27]</sup>                                | 56 <sup>[28]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 10.8  | 0   | 7.1                                   |  |

Notes:

[26] - FAS

[27] - FAS

[28] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Viral Breakthrough

|   |  |
|---|--|
| End point title   | Percentage of Participants with Viral Breakthrough |
| End point description:<br>Viral breakthrough, defined as an increase $>1$ log <sub>10</sub> in plasma HCV RNA level from the lowest level reached, or a value of HCV RNA $>100$ IU/mL in subjects whose HCV RNA had previously become $<25$ IU/mL during treatment. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline (Week 1) up to Week 48   |  |

| End point values                  | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus | Telaprevir/Peg-IFN-alfa-2a/RBV and Cyclosporine A | All Subjects (Full Analysis (FA) Set) |  |
|-----------------------------------|---|---|---------------------------------------|--|
| Subject group type                | Reporting group                               | Reporting group                                   | Subject analysis set                  |  |
| Number of subjects analysed       | 50 <sup>[29]</sup>                            | 24 <sup>[30]</sup>                                | 74 <sup>[31]</sup>                    |  |
| Units: Percentage of Participants |   |   |                                       |  |
| number (not applicable)           | 10  | 8.3   | 9.5                                   |  |

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Notes:

[29] - FAS

[30] - FAS

[31] - FAS

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### **Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Telaprevir/Peg-IFN-alfa-2a/RBV and cyclosporine A |
|-----------------------|---|

Reporting group description:

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and cyclosporine A.

|                       |   |
|-----------------------|---|
| Reporting group title | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus |
|-----------------------|---|

Reporting group description:

Subjects received Telaprevir 750 mg q8h in combination with Peg-IFN-alfa-2a, RBV and tacrolimus.

| <b>Serious adverse events</b>                        | Telaprevir/Peg-IFN-alfa-2a/RBV and cyclosporine A | Telaprevir/Peg-IFN-alfa-2a/RBV and Tacrolimus |  |
|--|---|---|--|
| Total subjects affected by serious adverse events    |   |   |  |
| subjects affected / exposed                          | 2 / 24 (8.33%)                                    | 7 / 50 (14.00%)                               |  |
| number of deaths (all causes)                        | 0   | 0   |  |
| number of deaths resulting from adverse events       |   |   |  |
| Blood and lymphatic system disorders                 |   |   |  |
| Anaemia  |   |   |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)                                    | 1 / 50 (2.00%)                                |  |
| occurrences causally related to treatment / all      | 0 / 0   | 1 / 1   |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   |  |
| Thrombocytopenia                                     |   |   |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)                                    | 1 / 50 (2.00%)                                |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1   |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   |  |
| General disorders and administration site conditions |   |   |  |
| Asthenia   |   |   |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)                                    | 1 / 50 (2.00%)                                |  |
| occurrences causally related to treatment / all      | 0 / 0   | 1 / 1   |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   |  |
| General Physical Health Deterioration                |   |   |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Lens Dislocation                                |                |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Ascites   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Autoimmune Hepatitis                            |                |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholestasis                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Depression                                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Renal Failure Acute                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Urinary Tract Infection                         |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                                   | Telaprevir/Peg-IFN-<br>alfa-2a/RBV and<br>cyclosporine A | Telaprevir/Peg-IFN-<br>alfa-2a/RBV and<br>Tacrolimus |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 24 / 24 (100.00%)  | 50 / 50 (100.00%)                                    |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Cholesteatoma   |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)   | 1 / 50 (2.00%)                                       |  |
| occurrences (all)   | 0  | 1  |  |
| Vascular disorders  |  |  |  |
| Flushing  |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)   | 1 / 50 (2.00%)                                       |  |
| occurrences (all)   | 0  | 1  |  |
| Hot Flush   |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)   | 1 / 50 (2.00%)                                       |  |
| occurrences (all)   | 0  | 1  |  |
| Hypertension  |  |  |  |
| subjects affected / exposed   | 1 / 24 (4.17%)   | 1 / 50 (2.00%)                                       |  |
| occurrences (all)   | 1  | 1  |  |
| General disorders and administration site conditions                |  |  |  |
| Asthenia  |  |  |  |
| subjects affected / exposed   | 11 / 24 (45.83%)   | 15 / 50 (30.00%)                                     |  |
| occurrences (all)   | 19   | 19   |  |
| Fatigue   |  |  |  |
| subjects affected / exposed   | 5 / 24 (20.83%)  | 16 / 50 (32.00%)                                     |  |
| occurrences (all)   | 5  | 22   |  |
| Chills  |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)   | 1 / 50 (2.00%)                                       |  |
| occurrences (all)   | 0  | 1  |  |
| Feeling Cold  |  |  |  |

|  |                 |                  |  |
|--|-----------------|------------------|--|
| subjects affected / exposed              | 2 / 24 (8.33%)  | 0 / 50 (0.00%)   |  |
| occurrences (all)                        | 2               | 0                |  |
| Feeling Hot                              |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)                        | 0               | 1                |  |
| Influenza Like Illness                   |                 |                  |  |
| subjects affected / exposed              | 1 / 24 (4.17%)  | 2 / 50 (4.00%)   |  |
| occurrences (all)                        | 1               | 3                |  |
| Irritability                             |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)                        | 0               | 1                |  |
| Injection Site Erythema                  |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 2 / 50 (4.00%)   |  |
| occurrences (all)                        | 0               | 4                |  |
| Mucosal Dryness                          |                 |                  |  |
| subjects affected / exposed              | 1 / 24 (4.17%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)                        | 1               | 2                |  |
| Malaise                                  |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)                        | 0               | 1                |  |
| Mucosal Inflammation                     |                 |                  |  |
| subjects affected / exposed              | 1 / 24 (4.17%)  | 0 / 50 (0.00%)   |  |
| occurrences (all)                        | 1               | 0                |  |
| Oedema Peripheral                        |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 3 / 50 (6.00%)   |  |
| occurrences (all)                        | 0               | 3                |  |
| Pyrexia                                  |                 |                  |  |
| subjects affected / exposed              | 5 / 24 (20.83%) | 10 / 50 (20.00%) |  |
| occurrences (all)                        | 10              | 13               |  |
| Reproductive system and breast disorders |                 |                  |  |
| Erectile Dysfunction                     |                 |                  |  |
| subjects affected / exposed              | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)                        | 0               | 1                |  |
| Penile Blister                           |                 |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Prostatitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Cough   |                 |                 |  |
| subjects affected / exposed                     | 4 / 24 (16.67%) | 5 / 50 (10.00%) |  |
| occurrences (all)                               | 4               | 5               |  |
| Asthma  |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 4 / 24 (16.67%) | 8 / 50 (16.00%) |  |
| occurrences (all)                               | 4               | 8               |  |
| Dyspnoea Exertional                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 3 / 50 (6.00%)  |  |
| occurrences (all)                               | 0               | 3               |  |
| Nasal Congestion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Oropharyngeal Pain                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                               | 0               | 3               |  |
| Pleural Effusion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Psychiatric disorders                           |                 |                 |  |
| Affect Lability                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Anxiety   |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                               | 0               | 2               |  |
| Depressed Mood                                  |                 |                 |  |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                  | 0               | 2               |  |
| Depression                         |                 |                 |  |
| subjects affected / exposed        | 1 / 24 (4.17%)  | 3 / 50 (6.00%)  |  |
| occurrences (all)                  | 1               | 3               |  |
| Insomnia                           |                 |                 |  |
| subjects affected / exposed        | 4 / 24 (16.67%) | 6 / 50 (12.00%) |  |
| occurrences (all)                  | 4               | 6               |  |
| Mood Swings                        |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Nervousness                        |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Investigations                     |                 |                 |  |
| Alanine Aminotransferase Increased |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                  | 0               | 2               |  |
| Blood Bilirubin Increased          |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Blood Amylase Increased            |                 |                 |  |
| subjects affected / exposed        | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Blood Creatinine Increased         |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                  | 0               | 2               |  |
| Blood Glucose Increased            |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                  | 0               | 2               |  |
| Blood Magnesium Decreased          |                 |                 |  |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Blood Uric Acid Increased          |                 |                 |  |
| subjects affected / exposed        | 1 / 24 (4.17%)  | 7 / 50 (14.00%) |  |
| occurrences (all)                  | 2               | 15              |  |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| Blood Phosphorus Decreased<br>subjects affected / exposed<br>occurrences (all)          | 1 / 24 (4.17%)<br>1 | 0 / 50 (0.00%)<br>0 |  |
| Body Temperature Increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Blood Urine Present<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Electrocardiogram QT Prolonged<br>subjects affected / exposed<br>occurrences (all)      | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Electrocardiogram T Wave Inversion<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Haemoglobin Decreased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 24 (4.17%)<br>1 | 1 / 50 (2.00%)<br>1 |  |
| Gamma-Glutamyltransferase Increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | 1 / 50 (2.00%)<br>1 |  |
| Mean Cell Volume Increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Platelet Count Decreased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 24 (4.17%)<br>1 | 2 / 50 (4.00%)<br>3 |  |
| White Blood Cell Count Decreased<br>subjects affected / exposed<br>occurrences (all)    | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |  |
| Injury, poisoning and procedural complications  |                     |                     |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Excoriation                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Incisional Hernia           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Limb Injury                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Scratch                     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Skin Injury                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Sunburn                     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Cardiac disorders           |                |                |  |
| Sinus Tachycardia           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Rebound Tachycardia         |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 50 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Tachycardia                 |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 50 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Nervous system disorders    |                |                |  |
| Disturbance in Attention    |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Burning Sensation           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences (all)           | 0              | 1              |  |
| Dizziness                   |                |                |  |

|                                      |                  |                  |  |
|--------------------------------------|------------------|------------------|--|
| subjects affected / exposed          | 1 / 24 (4.17%)   | 4 / 50 (8.00%)   |  |
| occurrences (all)                    | 1                | 5                |  |
| Dysgeusia                            |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 3 / 50 (6.00%)   |  |
| occurrences (all)                    | 0                | 3                |  |
| Headache                             |                  |                  |  |
| subjects affected / exposed          | 8 / 24 (33.33%)  | 17 / 50 (34.00%) |  |
| occurrences (all)                    | 12               | 21               |  |
| Lethargy                             |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 2 / 50 (4.00%)   |  |
| occurrences (all)                    | 0                | 2                |  |
| Neuropathy Peripheral                |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 1 / 50 (2.00%)   |  |
| occurrences (all)                    | 0                | 1                |  |
| Migraine                             |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 1 / 50 (2.00%)   |  |
| occurrences (all)                    | 0                | 1                |  |
| Restless Legs Syndrome               |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 1 / 50 (2.00%)   |  |
| occurrences (all)                    | 0                | 1                |  |
| Syncope                              |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 1 / 50 (2.00%)   |  |
| occurrences (all)                    | 0                | 1                |  |
| Tremor                               |                  |                  |  |
| subjects affected / exposed          | 1 / 24 (4.17%)   | 1 / 50 (2.00%)   |  |
| occurrences (all)                    | 1                | 1                |  |
| Blood and lymphatic system disorders |                  |                  |  |
| Anaemia                              |                  |                  |  |
| subjects affected / exposed          | 13 / 24 (54.17%) | 24 / 50 (48.00%) |  |
| occurrences (all)                    | 27               | 38               |  |
| Lymphopenia                          |                  |                  |  |
| subjects affected / exposed          | 0 / 24 (0.00%)   | 2 / 50 (4.00%)   |  |
| occurrences (all)                    | 0                | 3                |  |
| Leukopenia                           |                  |                  |  |
| subjects affected / exposed          | 3 / 24 (12.50%)  | 7 / 50 (14.00%)  |  |
| occurrences (all)                    | 4                | 12               |  |

|  |                      |                        |  |
|--|----------------------|------------------------|--|
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 24 (0.00%)<br>0  | 1 / 50 (2.00%)<br>1    |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 4 / 24 (16.67%)<br>4 | 8 / 50 (16.00%)<br>11  |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 4 / 24 (16.67%)<br>6 | 14 / 50 (28.00%)<br>22 |  |
| Ear and labyrinth disorders<br>Ear Discomfort<br>subjects affected / exposed<br>occurrences (all)      | 0 / 24 (0.00%)<br>0  | 1 / 50 (2.00%)<br>2    |  |
| Ear Pruritus<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 24 (4.17%)<br>2  | 0 / 50 (0.00%)<br>0    |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 2 / 24 (8.33%)<br>2  | 0 / 50 (0.00%)<br>0    |  |
| Eye disorders<br>Blepharitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 24 (0.00%)<br>0  | 2 / 50 (4.00%)<br>2    |  |
| Vision Blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 24 (0.00%)<br>0  | 1 / 50 (2.00%)<br>1    |  |
| Dry Eye<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0  | 2 / 50 (4.00%)<br>2    |  |
| Gastrointestinal disorders<br>Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1  | 2 / 50 (4.00%)<br>2    |  |
| Abdominal Distension<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 24 (0.00%)<br>0  | 1 / 50 (2.00%)<br>1    |  |
| Abdominal Pain Upper   |                      |                        |  |



|                             |                 |                  |
|-----------------------------|-----------------|------------------|
| subjects affected / exposed | 0 / 24 (0.00%)  | 2 / 50 (4.00%)   |
| occurrences (all)           | 0               | 2                |
| Abdominal Pain              |                 |                  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 0               | 2                |
| Anal Pruritus               |                 |                  |
| subjects affected / exposed | 5 / 24 (20.83%) | 9 / 50 (18.00%)  |
| occurrences (all)           | 7               | 9                |
| Anorectal Discomfort        |                 |                  |
| subjects affected / exposed | 3 / 24 (12.50%) | 6 / 50 (12.00%)  |
| occurrences (all)           | 3               | 7                |
| Aphthous Stomatitis         |                 |                  |
| subjects affected / exposed | 2 / 24 (8.33%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 2               | 1                |
| Ascites                     |                 |                  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 0               | 1                |
| Breath Odour                |                 |                  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 0               | 1                |
| Chapped Lips                |                 |                  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 0               | 1                |
| Cheilitis                   |                 |                  |
| subjects affected / exposed | 2 / 24 (8.33%)  | 0 / 50 (0.00%)   |
| occurrences (all)           | 2               | 0                |
| Constipation                |                 |                  |
| subjects affected / exposed | 2 / 24 (8.33%)  | 1 / 50 (2.00%)   |
| occurrences (all)           | 2               | 1                |
| Diarrhoea                   |                 |                  |
| subjects affected / exposed | 2 / 24 (8.33%)  | 17 / 50 (34.00%) |
| occurrences (all)           | 2               | 19               |
| Dry Mouth                   |                 |                  |
| subjects affected / exposed | 1 / 24 (4.17%)  | 2 / 50 (4.00%)   |
| occurrences (all)           | 1               | 2                |
| Dyspepsia                   |                 |                  |

|                                  |                 |                  |
|----------------------------------|-----------------|------------------|
| subjects affected / exposed      | 4 / 24 (16.67%) | 2 / 50 (4.00%)   |
| occurrences (all)                | 4               | 2                |
| Gastrooesophageal Reflux Disease |                 |                  |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 1               | 1                |
| Gingival Pain                    |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Glossodynia                      |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Haemorrhoids                     |                 |                  |
| subjects affected / exposed      | 2 / 24 (8.33%)  | 8 / 50 (16.00%)  |
| occurrences (all)                | 2               | 8                |
| Haematochezia                    |                 |                  |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 0 / 50 (0.00%)   |
| occurrences (all)                | 1               | 0                |
| Hyperchlorhydria                 |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Nausea                           |                 |                  |
| subjects affected / exposed      | 6 / 24 (25.00%) | 11 / 50 (22.00%) |
| occurrences (all)                | 8               | 15               |
| Painful Defaecation              |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Proctalgia                       |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 5 / 50 (10.00%)  |
| occurrences (all)                | 0               | 5                |
| Rectal Haemorrhage               |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Swollen Tongue                   |                 |                  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |
| occurrences (all)                | 0               | 1                |
| Stomatitis                       |                 |                  |

|  |                     |                      |  |
|--|---------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 2 / 50 (4.00%)<br>2  |  |
| Tongue Ulceration<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 24 (4.17%)<br>1 | 0 / 50 (0.00%)<br>0  |  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)  | 1 / 24 (4.17%)<br>1 | 0 / 50 (0.00%)<br>0  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 2 / 24 (8.33%)<br>3 | 6 / 50 (12.00%)<br>7 |  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>2  |  |
| Jaundice<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1  |  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 2 / 50 (4.00%)<br>2  |  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 0 / 50 (0.00%)<br>0  |  |
| Dry Skin<br>subjects affected / exposed<br>occurrences (all)   | 2 / 24 (8.33%)<br>2 | 5 / 50 (10.00%)<br>6 |  |
| Eczema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 2 / 50 (4.00%)<br>2  |  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1 | 2 / 50 (4.00%)<br>4  |  |
| Lichenification  |                     |                      |  |

|                             |                 |                  |  |
|-----------------------------|-----------------|------------------|--|
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Night Sweats                |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Petechiae                   |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Pruritus                    |                 |                  |  |
| subjects affected / exposed | 6 / 24 (25.00%) | 27 / 50 (54.00%) |  |
| occurrences (all)           | 8               | 31               |  |
| Pruritus Generalised        |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 2 / 50 (4.00%)   |  |
| occurrences (all)           | 0               | 2                |  |
| Rash                        |                 |                  |  |
| subjects affected / exposed | 3 / 24 (12.50%) | 17 / 50 (34.00%) |  |
| occurrences (all)           | 3               | 21               |  |
| Rash Erythematous           |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Rash Maculo-Papular         |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 2                |  |
| Skin Ulcer                  |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Rash Papular                |                 |                  |  |
| subjects affected / exposed | 1 / 24 (4.17%)  | 0 / 50 (0.00%)   |  |
| occurrences (all)           | 1               | 0                |  |
| Swelling Face               |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |
| Renal and urinary disorders |                 |                  |  |
| Azotaemia                   |                 |                  |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)   |  |
| occurrences (all)           | 0               | 1                |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Incontinence                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Dysuria   |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Nocturia  |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Renal Failure                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 1               | 1               |  |
| Renal Impairment                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back Pain                                       |                 |                 |  |
| subjects affected / exposed                     | 2 / 24 (8.33%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                               | 2               | 1               |  |
| Arthralgia                                      |                 |                 |  |
| subjects affected / exposed                     | 3 / 24 (12.50%) | 6 / 50 (12.00%) |  |
| occurrences (all)                               | 3               | 7               |  |
| Muscle Spasms                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 5 / 50 (10.00%) |  |
| occurrences (all)                               | 1               | 5               |  |
| Pain in Extremity                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 3 / 50 (6.00%)  |  |
| occurrences (all)                               | 0               | 3               |  |
| Myalgia   |                 |                 |  |
| subjects affected / exposed                     | 2 / 24 (8.33%)  | 6 / 50 (12.00%) |  |
| occurrences (all)                               | 3               | 6               |  |
| Infections and infestations                     |                 |                 |  |
| Anal Abscess                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Bronchitis                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed               | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                         | 1               | 0               |  |
| <b>Dermatitis Infected</b>                |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                         | 0               | 1               |  |
| <b>Bronchopneumonia</b>                   |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                         | 0               | 1               |  |
| <b>Ear Infection</b>                      |                 |                 |  |
| subjects affected / exposed               | 1 / 24 (4.17%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                         | 1               | 1               |  |
| <b>Enterobiasis</b>                       |                 |                 |  |
| subjects affected / exposed               | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                         | 2               | 0               |  |
| <b>Escherichia Sepsis</b>                 |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                         | 0               | 1               |  |
| <b>Gastroenteritis</b>                    |                 |                 |  |
| subjects affected / exposed               | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |  |
| occurrences (all)                         | 1               | 0               |  |
| <b>Lower Respiratory Tract Infection</b>  |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                         | 0               | 2               |  |
| <b>Influenza</b>                          |                 |                 |  |
| subjects affected / exposed               | 3 / 24 (12.50%) | 6 / 50 (12.00%) |  |
| occurrences (all)                         | 3               | 6               |  |
| <b>Oral Candidiasis</b>                   |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 3 / 50 (6.00%)  |  |
| occurrences (all)                         | 0               | 3               |  |
| <b>Nasopharyngitis</b>                    |                 |                 |  |
| subjects affected / exposed               | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |  |
| occurrences (all)                         | 0               | 1               |  |
| <b>Urinary Tract Infection</b>            |                 |                 |  |
| subjects affected / exposed               | 1 / 24 (4.17%)  | 2 / 50 (4.00%)  |  |
| occurrences (all)                         | 1               | 2               |  |
| <b>Metabolism and nutrition disorders</b> |                 |                 |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| Cachexia                    |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |
| Decreased Appetite          |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 9 / 50 (18.00%) |
| occurrences (all)           | 1               | 9               |
| Hypercholesterolaemia       |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |
| occurrences (all)           | 1               | 0               |
| Hypercreatininaemia         |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |
| Hyperglycaemia              |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |
| Hyperkalaemia               |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 0 / 50 (0.00%)  |
| occurrences (all)           | 1               | 0               |
| Hypertriglyceridaemia       |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 2 / 50 (4.00%)  |
| occurrences (all)           | 1               | 3               |
| Hyperuricaemia              |                 |                 |
| subjects affected / exposed | 6 / 24 (25.00%) | 3 / 50 (6.00%)  |
| occurrences (all)           | 10              | 4               |
| Hypoglycaemia               |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |
| Hypomagnesaemia             |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 2 / 50 (4.00%)  |
| occurrences (all)           | 0               | 3               |
| Impaired Fasting Glucose    |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |
| Metabolic Disorder          |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               |





## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date        | Amendment  |
|-------------|--|
| 31 May 2012 | The primary analysis was changed to a snapshot analysis. SVR12 planned and SVR24 planned were analyzed using a snapshot approach, where the SVR assessment is based on the last HCV RNA value utilizing lower limit of quantification (LLOQ; 25 IU/mL) in the Week 12 and Week 24 follow-up visit window, respectively. The snapshot analysis has been accepted by the European Medicines Agency and Food and Drug Administration for previous telaprevir Phase 3 studies. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported