

**Clinical trial results:**

**Safety and Efficacy of 120 mg and 240 mg BI 201335 once daily in combination with pegylated interferon alpha 2a and ribavirin for treatment of chronic Hepatitis C (HCV) genotype 1 infection in HIV/HCV-co-infected patients. A multinational, randomised, parallel group, open-label trial**

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

**Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-021734-59 |
| Trial protocol           | GB ES DE IT    |
| Global end of trial date | 19 June 2014   |

**Results information**

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 23 July 2016   |
| First version publication date | 26 July 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Data correction due to a system error in EudraCT - Results |

**Trial information****Trial identification**

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | 1220.19 |
|-----------------------|---------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01399619 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Boehringer Ingelheim   |
| Sponsor organisation address | Binger Strasse 173, 55216 Ingelheim am Rhein, Germany,   |
| Public contact               | QRPE Processes and Systems Coordination<br>Clinical Trial Information Disclosure , Boehringer Ingelheim,<br>+1 800 243 0127 , clintrriage.rdg@boehringer-ingelheim.com |
| Scientific contact           | QRPE Processes and Systems Coordination<br>Clinical Trial Information Disclosure , Boehringer Ingelheim,<br>+1 800 243 0127 , clintrriage.rdg@boehringer-ingelheim.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                                | No |

|                                |
|--------------------------------|
| 1901/2006 apply to this trial? |
|--------------------------------|

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 31 July 2014      |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 23 September 2013 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 19 June 2014      |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The objective of this trial is to evaluate the safety and efficacy of an open-label treatment with BI 201335 240 mg once daily given for 12 or 24 weeks (wk) or BI 201335 120 mg once daily for 24 wk, each in combination with pegylated interferon-alpha2a and ribavirin given for 24 or 48 wk in hepatitis C virus (HCV)/human immunodeficiency virus (HIV) coinfecting patients, who are HCV-treatment naive or HCV-treatment relapsers and HIV treatment-naïve- or, who are being treated with Highly active antiretroviral therapy (HAART) containing an acceptable combination of the following antiretrovirals: raltegravir, darunavir/ritonavir, efavirenz, atazanavir/ ritonavir (limited to 20 patients), maraviroc, tenofovir, abacavir, emtricitabine, and lamivudine. Results of this trial will be compared with historical efficacy and safety data of randomized trials of 48 wk of treatment with pegylated interferon-alpha2a and ribavirin for HCV genotype 1 (GT-1) infection in HIV/HCV co-infected patients.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy:

All treatment groups included a background therapy of pegylated interferon alpha 2a and ribavirin (pegIFN and RBV)

Evidence for comparator: -

|   |                     |
|---|---------------------|
| Actual start date of recruitment                          | 04 October 2011     |
| Long term follow-up planned                               | Yes                 |
| Long term follow-up rationale                             | Scientific research |
| Long term follow-up duration                              | 30 Months           |
| Independent data monitoring committee (IDMC) involvement? | Yes                 |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 119         |
| Country: Number of subjects enrolled | United Kingdom: 72 |
| Country: Number of subjects enrolled | France: 21         |
| Country: Number of subjects enrolled | Germany: 51        |
| Country: Number of subjects enrolled | Italy: 26          |
| Country: Number of subjects enrolled | Brazil: 28         |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 119 |
| Country: Number of subjects enrolled | Switzerland: 17    |
| Worldwide total number of subjects   | 453                |
| EEA total number of subjects         | 289                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                      | 441 |
| From 65 to 84 years                       | 12  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subject) met all strictly implemented inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated.

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | Faldaprevir 120 mg-24 Wk |
|------------------|--------------------------|

Arm description:

Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Faldaprevir   |
| Investigational medicinal product code | BI 201335     |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, soft |
| Routes of administration               | Oral use      |

Dosage and administration details:

one soft gelatine capsule of BI 201335 (Faldaprevir) once a day 120 mg

|  |                  |
|--|------------------|
| Investigational medicinal product name | pegIFN           |
| Investigational medicinal product code |                  |
| Other name                             | Pegasys®         |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Dose: 180 µg once weekly,

Mode of Admin.: Subcutaneous (SC) injection.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.

Mode of Admin.: Oral.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Faldaprevir 240 mg-12Wk |
|------------------|-------------------------|

**Arm description:**

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Faldaprevir   |
| Investigational medicinal product code | BI 201335     |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, soft |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

patient to receive two capsules of BI 201335 once a day (total daily dose 240 mg).

|  |                  |
|--|------------------|
| Investigational medicinal product name | pegIFN           |
| Investigational medicinal product code |                  |
| Other name                             | Pegasys®         |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Dose: 180 µg once weekly;

Mode of Admin.: Subcutaneous (SC) injection.

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

**Dosage and administration details:**

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.

Mode of Admin.: Oral.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Faldaprevir 240 mg-24Wk |
|------------------|-------------------------|

**Arm description:**

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Faldaprevir   |
| Investigational medicinal product code | BI 201335     |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, soft |
| Routes of administration               | Oral use      |

**Dosage and administration details:**

patient to receive two capsules of BI 201335 once a day for 24 weeks (total daily dose 240 mg).

|  |                  |
|--|------------------|
| Investigational medicinal product name | pegIFN           |
| Investigational medicinal product code |                  |
| Other name                             | Pegasys®         |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Dose: 180 µg once weekly,

Mode of Admin.: Subcutaneous (SC) injection.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.

Mode of Admin.: Oral.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR) |
|------------------|---|

Arm description:

Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Faldaprevir   |
| Investigational medicinal product code | BI 201335     |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, soft |
| Routes of administration               | Oral use      |

Dosage and administration details:

dose: 240 mg.

mode of admin.: Oral use.

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

Dosage and administration details:

Dose: 1000 mg (<75 kg body weight) or 1200 mg (≥75 kg body weight) total daily dose, divided in 2 doses for twice daily administration.

Mode of Admin.: Oral.

|  |                  |
|--|------------------|
| Investigational medicinal product name | pegIFN           |
| Investigational medicinal product code |                  |
| Other name                             | Pegasys®         |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Dose: 180 µg once weekly,

Mode of Admin.: Subcutaneous (SC) injection.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk |
|---|--------------------------|-------------------------|-------------------------|
| Started   | 123                      | 84                      | 86                      |
| Completed   | 98                       | 84                      | 74                      |
| Not completed                                       | 25                       | 0                       | 12                      |
| Consent withdrawn by subject                        | 6                        | -                       | 3                       |
| not treated   | -                        | -                       | -                       |

|                          |    |   |   |
|--------------------------|----|---|---|
| Adverse event, non-fatal | 10 | - | 4 |
| Lack of efficacy         | 9  | - | 5 |
| Protocol deviation       | -  | - | - |

|   |  |
|---|--|
| <b>Number of subjects in period 1<sup>[1]</sup></b> | Faldaprevir 240 mg<br>-Prior to Re-randomization at Week 12 (NR) |
| Started   | 17   |
| Completed   | 0  |
| Not completed                                       | 17   |
| Consent withdrawn by subject                        | 4  |
| not treated   | 2  |
| Adverse event, non-fatal                            | 10   |
| Lack of efficacy                                    | -  |
| Protocol deviation                                  | 1  |

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Notes:

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

Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Faldaprevir 120 mg-24 Wk                                      |
| Reporting group description:<br>Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.   |   |
| Reporting group title  | Faldaprevir 240 mg-12Wk                                       |
| Reporting group description:<br>Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48. |   |
| Reporting group title  | Faldaprevir 240 mg-24Wk                                       |
| Reporting group description:<br>Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.                              |   |
| Reporting group title  | Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR) |
| Reporting group description:<br>Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.   |   |

| Reporting group values             | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk |
|------------------------------------|--------------------------|-------------------------|-------------------------|
| Number of subjects                 | 123                      | 84                      | 86                      |
| Age categorical<br>Units: Subjects |                          |                         |                         |

|  |        |        |        |
|--|--------|--------|--------|
| Age continuous   |        |        |        |
| Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy. |        |        |        |
| Units: years   |        |        |        |
| arithmetic mean  | 47.6   | 46.1   | 46     |
| standard deviation   | ± 7.63 | ± 8.64 | ± 7.97 |
| Gender categorical   |        |        |        |
| based on FAS population.   |        |        |        |
| Units: Subjects  |        |        |        |
| Female   | 20     | 18     | 18     |
| Male   | 103    | 66     | 68     |

| Reporting group values             | Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR) | Total |  |
|------------------------------------|---|-------|--|
| Number of subjects                 | 17  | 310   |  |
| Age categorical<br>Units: Subjects |   |       |  |



|  |        |     |  |
|--|--------|-----|--|
| Age continuous   |        |     |  |
| Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy. |        |     |  |
| Units: years   |        |     |  |
| arithmetic mean  | 51.8   |     |  |
| standard deviation   | ± 9.09 | -   |  |
| Gender categorical   |        |     |  |
| based on FAS population.   |        |     |  |
| Units: Subjects  |        |     |  |
| Female   | 4      | 60  |  |
| Male   | 13     | 250 |  |

### Subject analysis sets

|  |                                |
|--|--------------------------------|
| Subject analysis set title   | Faldaprevir 240 mg - Total (T) |
| Subject analysis set type  | Full analysis                  |
| Subject analysis set description:  |                                |
| Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12. |                                |
| Subject analysis set title   | Faldaprevir - Total            |
| Subject analysis set type  | Full analysis                  |
| Subject analysis set description:  |                                |
| Total subjects who were treated with faldaprevir.  |                                |

| Reporting group values | Faldaprevir 240 mg - Total (T) | Faldaprevir - Total |  |
|------------------------|--------------------------------|---------------------|--|
| Number of subjects     | 185                            | 308                 |  |
| Age categorical        |                                |                     |  |
| Units: Subjects        |                                |                     |  |

|  |        |        |  |
|--|--------|--------|--|
| Age continuous   |        |        |  |
| Full analysis Set (FAS) population: All patients who were randomized and received at least one dose of assigned therapy. |        |        |  |
| Units: years   |        |        |  |
| arithmetic mean  | 46.5   | 46.9   |  |
| standard deviation   | ± 8.36 | ± 8.08 |  |
| Gender categorical   |        |        |  |
| based on FAS population.   |        |        |  |
| Units: Subjects  |        |        |  |
| Female   | 40     | 60     |  |
| Male   | 145    | 248    |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Faldaprevir 120 mg-24 Wk                                      |
| Reporting group description:<br>Faldaprevir (BI 201335) 120 mg once a day (QD) combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.   |   |
| Reporting group title  | Faldaprevir 240 mg-12Wk                                       |
| Reporting group description:<br>Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48. |   |
| Reporting group title  | Faldaprevir 240 mg-24Wk                                       |
| Reporting group description:<br>Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.                              |   |
| Reporting group title  | Faldaprevir 240 mg -Prior to Re-randomization at Week 12 (NR) |
| Reporting group description:<br>Patients initially assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at WK 12.   |   |
| Subject analysis set title   | Faldaprevir 240 mg - Total (T)                                |
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12.  |   |
| Subject analysis set title   | Faldaprevir - Total   |
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>Total subjects who were treated with faldaprevir.   |   |

### Primary: Sustained Virological Response (SVR12)

|  |  |
|--|--|
| End point title  | Sustained Virological Response (SVR12) <sup>[1][2]</sup> |
| End point description:<br>Percentage of participants with sustained Virological Response (SVR12): Plasma Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Level <25 IU/mL, Undetected 12 Weeks After the Planned End of Treatment.<br><br>The 95% confidence interval (CI) based on the normal approximation to the binomial distribution was calculated for SVR12 rates |  |
| End point type   | Primary  |
| End point timeframe:<br>60 weeks   |  |

#### 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                             | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|--|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                           | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed                  | 123 <sup>[3]</sup>       | 84 <sup>[4]</sup>       | 86 <sup>[5]</sup>       | 185 <sup>[6]</sup>             |
| Units: percentage of participants with SVR12 |                          |                         |                         |                                |
| number (confidence interval 95%)             | 70.7 (62.7 to 78.8)      | 78.6 (69.8 to 87.3)     | 76.7 (67.8 to 85.7)     | 72.4 (66 to 78.9)              |

Notes:

[3] - FAS

[4] - FAS

[5] - FAS

[6] - FAS

| End point values                             | Faldaprevir - Total  |  |  |  |
|--|----------------------|--|--|--|
| Subject group type                           | Subject analysis set |  |  |  |
| Number of subjects analysed                  | 308 <sup>[7]</sup>   |  |  |  |
| Units: percentage of participants with SVR12 |                      |  |  |  |
| number (confidence interval 95%)             | 71.8 (66.7 to 76.8)  |  |  |  |

Notes:

[7] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Virological Response 24 Weeks Post Treatment (SVR24)

|  |   |
|--|---|
| End point title  | Virological Response 24 Weeks Post Treatment (SVR24) <sup>[8]</sup> |
| End point description:<br>Percentage of participants with virological response 24 weeks post treatment (SVR24): Plasma HCV RNA Level<25IU/mL undetected 24 Weeks After the Planned End of Treatment. |   |
| End point type   | Secondary   |
| End point timeframe:<br>72 weeks   |   |

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                  | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|-----------------------------------|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed       | 123 <sup>[9]</sup>       | 84 <sup>[10]</sup>      | 86 <sup>[11]</sup>      | 185 <sup>[12]</sup>            |
| Units: percentage of participants |                          |                         |                         |                                |
| number (confidence interval 95%)  | 69.9 (61.8 to 78)        | 78.6 (69.8 to 87.3)     | 74.4 (65.2 to 83.6)     | 71.4 (64.8 to 77.9)            |

Notes:

[9] - FAS

[10] - FAS

[11] - FAS

| End point values                  | Faldaprevir - Total  |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 308 <sup>[13]</sup>  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (confidence interval 95%)  | 70.8 (65.7 to 75.9)  |  |  |  |

Notes:

[13] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Early Treatment Success (ETS)

|                        |   |
|------------------------|---|
| End point title        | Early Treatment Success (ETS) <sup>[14]</sup>   |
| End point description: | Early Treatment Success (ETS): Plasma HCV RNA Level<25 IU/mL (Detected or Undetected) at Week 4 and HCV RNA< 25 IU/mL, Undetected at Week 8 |
| End point type         | Secondary   |
| End point timeframe:   | Week 4, Week 8 and Week 60.   |

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                                  | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|---|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                                | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed                       | 123 <sup>[15]</sup>      | 84 <sup>[16]</sup>      | 86 <sup>[17]</sup>      | 185 <sup>[18]</sup>            |
| Units: participant(s)                             |                          |                         |                         |                                |
| number (not applicable)                           |                          |                         |                         |                                |
| number of subjects with ETS =yes                  | 95                       | 70                      | 73                      | 150                            |
| number of subjects with SVR12 among ETS=yes group | 83                       | 62                      | 63                      | 127                            |

Notes:

[15] - FAS

[16] - FAS

[17] - FAS

[18] - FAS

| End point values                 | Faldaprevir - Total  |  |  |  |
|----------------------------------|----------------------|--|--|--|
| Subject group type               | Subject analysis set |  |  |  |
| Number of subjects analysed      | 308 <sup>[19]</sup>  |  |  |  |
| Units: participant(s)            |                      |  |  |  |
| number (not applicable)          |                      |  |  |  |
| number of subjects with ETS =yes | 245                  |  |  |  |

|   |     |  |  |  |
|---|-----|--|--|--|
| number of subjects with SVR12 among ETS=yes group | 210 |  |  |  |
|---|-----|--|--|--|

Notes:

[19] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: The number of participants with Alanine Aminotransferase (ALT) Normalisation at post treatment

|                 |  |
|-----------------|--|
| End point title | The number of participants with Alanine Aminotransferase (ALT) Normalisation at post treatment <sup>[20]</sup> |
|-----------------|--|

End point description:

The number of participants with Alanine Aminotransferase (ALT) Normalisation: ALT in Normal Range at Post Treatment (SVR12 Visit) based on SVR12=yes or SVR12=no.  
BL=baseline.

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

End point timeframe:

60 weeks

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                                | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|---|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                              | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed                     | 123 <sup>[21]</sup>      | 84 <sup>[22]</sup>      | 86 <sup>[23]</sup>      | 185 <sup>[24]</sup>            |
| Units: participant(s)                           |                          |                         |                         |                                |
| SVR12=yes                                       | 87                       | 66                      | 66                      | 134                            |
| SVR12=yes, BL normal to SVR12 normal            | 28                       | 17                      | 26                      | 45                             |
| SVR12=yes, BL elevated to SVR12 normal          | 52                       | 46                      | 35                      | 81                             |
| SVR12=yes, no ALT data available at SVR12 visit | 4                        | 0                       | 1                       | 1                              |
| SVR12=no  | 36                       | 18                      | 20                      | 51                             |
| SVR12=no, BL normal to SVR12 normal             | 8                        | 1                       | 3                       | 6                              |
| SVR12=no, BL elevated to SVR12 normal           | 1                        | 6                       | 3                       | 9                              |
| SVR12=no, no ALT data available at SVR12 visit  | 16                       | 4                       | 6                       | 20                             |

Notes:

[21] - FAS

[22] - FAS

[23] - FAS

[24] - FAS

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| End point values            | Faldaprevir - Total  |  |  |  |
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 308 <sup>[25]</sup>  |  |  |  |

|   |     |  |  |  |
|---|-----|--|--|--|
| Units: participant(s)                           |     |  |  |  |
| SVR12=yes                                       | 221 |  |  |  |
| SVR12=yes, BL normal to SVR12 normal            | 73  |  |  |  |
| SVR12=yes, BL elevated to SVR12 normal          | 133 |  |  |  |
| SVR12=yes, no ALT data available at SVR12 visit | 5   |  |  |  |
| SVR12=no  | 87  |  |  |  |
| SVR12=no, BL normal to SVR12 normal             | 14  |  |  |  |
| SVR12=no, BL elevated to SVR12 normal           | 10  |  |  |  |
| SVR12=no, no ALT data available at SVR12 visit  | 36  |  |  |  |

Notes:

[25] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: The number of participants with Alanine Aminotransferase (ALT) Normalisation at end of treatment

|                 |  |
|-----------------|--|
| End point title | The number of participants with Alanine Aminotransferase (ALT) Normalisation at end of treatment <sup>[26]</sup> |
|-----------------|--|

End point description:

Alanine Aminotransferase (ALT) normalisation at End of Treatment (EoT) based on SVR12=yes or SVR12=no.

BL = baseline.

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

End point timeframe:

48 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                     | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|--------------------------------------|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                   | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed          | 123 <sup>[27]</sup>      | 84 <sup>[28]</sup>      | 86 <sup>[29]</sup>      | 185 <sup>[30]</sup>            |
| Units: participant(s)                |                          |                         |                         |                                |
| SVR12=yes                            | 87                       | 66                      | 66                      | 134                            |
| SVR12=yes, BL normal to EoT normal   | 29                       | 16                      | 26                      | 43                             |
| SVR12=yes, BL elevated to EoT normal | 45                       | 34                      | 32                      | 66                             |
| SVR12=yes, no BL or EoT data         | 0                        | 0                       | 0                       | 1                              |
| SVR12=no                             | 36                       | 18                      | 20                      | 51                             |
| SVR12=no, BL normal to EoT normal    | 18                       | 5                       | 5                       | 18                             |
| SVR12=no, BL elevated to EoT normal  | 12                       | 8                       | 9                       | 21                             |
| SVR12=no, no BL or EoT data          | 2                        | 0                       | 0                       | 0                              |

Notes:

[27] - FAS

[28] - FAS

[29] - FAS

[30] - FAS

| End point values                     | Faldaprevir - Total  |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 308 <sup>[31]</sup>  |  |  |  |
| Units: participant(s)                |                      |  |  |  |
| SVR12=yes                            | 221                  |  |  |  |
| SVR12=yes, BL normal to EoT normal   | 72                   |  |  |  |
| SVR12=yes, BL elevated to EoT normal | 111                  |  |  |  |
| SVR12=yes, no BL or EoT data         | 1                    |  |  |  |
| SVR12=no                             | 87                   |  |  |  |
| SVR12=no, BL normal to EoT normal    | 36                   |  |  |  |
| SVR12=no, BL elevated to EoT normal  | 33                   |  |  |  |
| SVR12=no, no BL or EoT data          | 2                    |  |  |  |

Notes:

[31] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: The number of participants with Aspartate Aminotransferase (AST) Normalisation at end of treatment

|                 |  |
|-----------------|--|
| End point title | The number of participants with Aspartate Aminotransferase (AST) Normalisation at end of treatment <sup>[32]</sup> |
|-----------------|--|

End point description:

Aspartate Aminotransferase (AST) normalisation at End of Treatment (EoT) based on SVR12=yes or SVR12 =no.

BL = baseline.

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

End point timeframe:

48 weeks

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                     | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|--------------------------------------|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                   | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed          | 123 <sup>[33]</sup>      | 84 <sup>[34]</sup>      | 86 <sup>[35]</sup>      | 185 <sup>[36]</sup>            |
| Units: participant(s)                |                          |                         |                         |                                |
| SVR12=yes                            | 87                       | 66                      | 66                      | 134                            |
| SVR12=yes, BL normal to EoT normal   | 41                       | 25                      | 28                      | 54                             |
| SVR12=yes, BL elevated to EoT normal | 32                       | 25                      | 27                      | 52                             |
| SVR12=yes, no BL or EoT data         | 0                        | 0                       | 0                       | 1                              |
| SVR12=no                             | 36                       | 18                      | 20                      | 51                             |
| SVR12=no, BL normal to EoT normal    | 14                       | 6                       | 7                       | 19                             |
| SVR12=no, BL elevated to EoT normal  | 12                       | 6                       | 8                       | 19                             |

|                             |   |   |   |   |
|-----------------------------|---|---|---|---|
| SVR12=no, no BL or EoT data | 2 | 0 | 0 | 0 |
|-----------------------------|---|---|---|---|

Notes:

[33] - FAS

[34] - FAS

[35] - FAS

[36] - FAS

| End point values                     | Faldaprevir - Total  |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 308 <sup>[37]</sup>  |  |  |  |
| Units: participant(s)                |                      |  |  |  |
| SVR12=yes                            | 221                  |  |  |  |
| SVR12=yes, BL normal to EoT normal   | 95                   |  |  |  |
| SVR12=yes, BL elevated to EoT normal | 84                   |  |  |  |
| SVR12=yes, no BL or EoT data         | 1                    |  |  |  |
| SVR12=no                             | 87                   |  |  |  |
| SVR12=no, BL normal to EoT normal    | 33                   |  |  |  |
| SVR12=no, BL elevated to EoT normal  | 31                   |  |  |  |
| SVR12=no, no BL or EoT data          | 2                    |  |  |  |

Notes:

[37] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: The number of participants with Aspartate Aminotransferase (AST) Normalisation at post treatment

|                        |  |
|------------------------|--|
| End point title        | The number of participants with Aspartate Aminotransferase (AST) Normalisation at post treatment <sup>[38]</sup> |
| End point description: | AST in normal range at Post Treatment (SVR12 Visit) based on SVR12=yes or SVR12=no.<br>BL = baseline.            |
| End point type         | Secondary  |
| End point timeframe:   | 60 weeks   |

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those arms for which the statistics are presented in the clinical trial report thus, those that would yield meaningful results were reported.

| End point values                       | Faldaprevir 120 mg-24 Wk | Faldaprevir 240 mg-12Wk | Faldaprevir 240 mg-24Wk | Faldaprevir 240 mg - Total (T) |
|--|--------------------------|-------------------------|-------------------------|--------------------------------|
| Subject group type                     | Reporting group          | Reporting group         | Reporting group         | Subject analysis set           |
| Number of subjects analysed            | 123 <sup>[39]</sup>      | 84 <sup>[40]</sup>      | 86 <sup>[41]</sup>      | 185 <sup>[42]</sup>            |
| Units: participant(s)                  |                          |                         |                         |                                |
| SVR12=yes                              | 87                       | 66                      | 66                      | 134                            |
| SVR12=yes, BL normal to SVR12 normal   | 41                       | 27                      | 28                      | 57                             |
| SVR12=yes, BL elevated to SVR12 normal | 36                       | 36                      | 33                      | 69                             |



|   |    |    |    |    |
|---|----|----|----|----|
| SVR12=yes, no AST data available at SVR12 visit | 4  | 0  | 1  | 1  |
| SVR12=no  | 36 | 18 | 20 | 51 |
| SVR12=no, BL normal to SVR12 normal             | 6  | 4  | 6  | 13 |
| SVR12=no, BL elevated to SVR12 normal           | 2  | 3  | 0  | 3  |
| SVR12=no, no AST data available at SVR12 visit  | 16 | 4  | 6  | 20 |

Notes:

[39] - FAS

[40] - FAS

[41] - FAS

[42] - FAS

| End point values                                | Faldaprevir - Total  |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                              | Subject analysis set |  |  |  |
| Number of subjects analysed                     | 308 <sup>[43]</sup>  |  |  |  |
| Units: participant(s)                           |                      |  |  |  |
| SVR12=yes                                       | 221                  |  |  |  |
| SVR12=yes, BL normal to SVR12 normal            | 98                   |  |  |  |
| SVR12=yes, BL elevated to SVR12 normal          | 105                  |  |  |  |
| SVR12=yes, no AST data available at SVR12 visit | 5                    |  |  |  |
| SVR12=no  | 87                   |  |  |  |
| SVR12=no, BL normal to SVR12 normal             | 19                   |  |  |  |
| SVR12=no, BL elevated to SVR12 normal           | 5                    |  |  |  |
| SVR12=no, no AST data available at SVR12 visit  | 36                   |  |  |  |

Notes:

[43] - FAS

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from the start date of trial medication up to 52 weeks ( AEs occurred from the start date of trial medication up to four weeks after all treatment discontinuation).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | Faldaprevir 120 mg -24 Wk |
|-----------------------|---------------------------|

Reporting group description:

Faldaprevir 120 mg QD combined with pegIFN/RBV for 24 weeks, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Faldaprevir 240 mg-12Wk |
|-----------------------|-------------------------|

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to stop Faldaprevir and continue pegIFN/RBV alone until Week 24; at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Faldaprevir 240 mg-24Wk |
|-----------------------|-------------------------|

Reporting group description:

Faldaprevir 240 mg QD plus pegIFN/RBV for 12 weeks followed by re-randomisation at Week 12 to continue Faldaprevir to Week 24, at Week 24, randomisation of patients who achieved early treatment success (ETS) to an additional 24 weeks of pegIFN/RBV or to stop treatment; patients who did not achieve ETS received pegIFN/RBV until Week 48.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Faldaprevir 240 mg - T |
|-----------------------|------------------------|

Reporting group description:

Faldaprevir 240mg-12w + Faldaprevir 240mg-24w + patients initially randomized or assigned to Faldaprevir 240 mg who discontinued prior to re-randomization at Week 12.

| Serious adverse events  | Faldaprevir 120 mg<br>-24 Wk | Faldaprevir 240 mg-<br>12Wk | Faldaprevir 240 mg-<br>24Wk |
|---|------------------------------|-----------------------------|-----------------------------|
| Total subjects affected by serious adverse events                   |                              |                             |                             |
| subjects affected / exposed   | 17 / 123 (13.82%)            | 5 / 84 (5.95%)              | 5 / 86 (5.81%)              |
| number of deaths (all causes)                                       | 0                            | 1                           | 1                           |
| number of deaths resulting from adverse events                      | 0                            | 0                           | 0                           |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                              |                             |                             |
| Lymphoma  |                              |                             |                             |
| subjects affected / exposed   | 0 / 123 (0.00%)              | 0 / 84 (0.00%)              | 0 / 86 (0.00%)              |
| occurrences causally related to treatment / all                     | 0 / 0                        | 0 / 0                       | 0 / 0                       |
| deaths causally related to treatment / all                          | 0 / 0                        | 0 / 0                       | 0 / 0                       |
| Vascular disorders  |                              |                             |                             |
| Haematoma   |                              |                             |                             |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| General disorders and administration site conditions |                 |                |                |
| Asthenia   |                 |                |                |
| subjects affected / exposed                          | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Pyrexia  |                 |                |                |
| subjects affected / exposed                          | 3 / 123 (2.44%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 3           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Immune system disorders                              |                 |                |                |
| Sarcoidosis  |                 |                |                |
| subjects affected / exposed                          | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Social circumstances                                 |                 |                |                |
| Substance use  |                 |                |                |
| subjects affected / exposed                          | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders             |                 |                |                |
| Benign prostatic hyperplasia                         |                 |                |                |
| subjects affected / exposed                          | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Injury, poisoning and procedural complications       |                 |                |                |
| Accidental overdose                                  |                 |                |                |
| subjects affected / exposed                          | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Cardiac disorders                                    |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Acute coronary syndrome                         |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Acute myocardial infarction                     |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Nervous system disorders                        |                 |                |                |
| Epilepsy  |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                 |                |                |
| Anaemia   |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                 |                |                |
| Abdominal pain                                  |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 1 / 84 (1.19%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Enterovesical fistula                           |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                           | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Nausea  |                 |                |                |
| subjects affected / exposed                           | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Vomiting  |                 |                |                |
| subjects affected / exposed                           | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                               |                 |                |                |
| Cholecystitis   |                 |                |                |
| subjects affected / exposed                           | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders                |                 |                |                |
| Drug reaction with eosinophilia and systemic symptoms |                 |                |                |
| subjects affected / exposed                           | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Rash  |                 |                |                |
| subjects affected / exposed                           | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Rash erythematous                                     |                 |                |                |
| subjects affected / exposed                           | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |
| Rash maculo-papular                                   |                 |                |                |
| subjects affected / exposed                           | 2 / 123 (1.63%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all       | 2 / 2           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0          | 0 / 0          |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Toxic skin eruption                             |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                 |                |                |
| Nephrolithiasis                                 |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Endocrine disorders                             |                 |                |                |
| Hyperthyroidism                                 |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (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          |
| Infections and infestations                     |                 |                |                |
| Appendicitis                                    |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Diverticulitis                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Escherichia urinary tract infection             |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Gastroenteritis viral                           |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 123 (0.00%) | 1 / 84 (1.19%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Infected cyst                                   |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Leishmaniasis                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Neurosyphilis                                   |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Pneumonia                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia bacterial                             |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pulmonary tuberculosis                          |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Sepsis  |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (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          |
| Urosepsis                                       |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                 |                |                |
| Decreased appetite                              |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Dehydration                                     |                 |                |                |
| subjects affected / exposed                     | 1 / 123 (0.81%) | 0 / 84 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hypokalaemia                                    |                 |                |                |
| subjects affected / exposed                     | 0 / 123 (0.00%) | 0 / 84 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |

|   |                           |  |  |
|---|---------------------------|--|--|
| <b>Serious adverse events</b>                                       | Faldaprevir 240 mg<br>- T |  |  |
| Total subjects affected by serious adverse events                   |                           |  |  |
| subjects affected / exposed   | 15 / 185 (8.11%)          |  |  |
| number of deaths (all causes)                                       | 3                         |  |  |
| number of deaths resulting from adverse events                      | 1                         |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                           |  |  |
| Lymphoma  |                           |  |  |
| subjects affected / exposed   | 1 / 185 (0.54%)           |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                     |  |  |
| deaths causally related to treatment / all                          | 0 / 0                     |  |  |
| Vascular disorders  |                           |  |  |
| Haematoma   |                           |  |  |
| subjects affected / exposed   | 0 / 185 (0.00%)           |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                     |  |  |
| deaths causally related to treatment / all                          | 0 / 0                     |  |  |
| General disorders and administration site conditions                |                           |  |  |
| Asthenia  |                           |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pyrexia   |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| Sarcoidosis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Social circumstances                            |                 |  |  |
| Substance use                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Benign prostatic hyperplasia                    |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Accidental overdose                             |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Acute coronary syndrome                         |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute myocardial infarction                     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Epilepsy  |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 2 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |
| Anaemia   |                 |  |  |
| subjects affected / exposed                     | 2 / 185 (1.08%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Thrombocytopenia                                |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Abdominal pain                                  |                 |  |  |
| subjects affected / exposed                     | 2 / 185 (1.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diarrhoea                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Enterovesical fistula                           |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nausea  |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Vomiting  |                 |  |  |
| subjects affected / exposed                           | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all       | 1 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Hepatobiliary disorders                               |                 |  |  |
| Cholecystitis   |                 |  |  |
| subjects affected / exposed                           | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all       | 0 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders                |                 |  |  |
| Drug reaction with eosinophilia and systemic symptoms |                 |  |  |
| subjects affected / exposed                           | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all       | 1 / 1           |  |  |
| deaths causally related to treatment / all            | 1 / 1           |  |  |
| Rash  |                 |  |  |
| subjects affected / exposed                           | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all       | 1 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Rash erythematous                                     |                 |  |  |
| subjects affected / exposed                           | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all       | 0 / 0           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Rash maculo-papular                                   |                 |  |  |
| subjects affected / exposed                           | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all       | 0 / 0           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Toxic skin eruption                                   |                 |  |  |
| subjects affected / exposed                           | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all       | 1 / 1           |  |  |
| deaths causally related to treatment / all            | 0 / 0           |  |  |
| Renal and urinary disorders                           |                 |  |  |
| Nephrolithiasis                                       |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endocrine disorders                             |                 |  |  |
| Hyperthyroidism                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Appendicitis                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diverticulitis                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Escherichia urinary tract infection             |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastroenteritis                                 |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastroenteritis viral                           |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infected cyst                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Leishmaniasis                                   |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neurosyphilis                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia bacterial                             |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary tuberculosis                          |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Sepsis  |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urosepsis                                       |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Decreased appetite                              |                 |  |  |
| subjects affected / exposed                     | 0 / 185 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dehydration                                     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypokalaemia                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Faldaprevir 120 mg<br>-24 Wk | Faldaprevir 240 mg-<br>12Wk | Faldaprevir 240 mg-<br>24Wk |
|---|------------------------------|-----------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                              |                             |                             |
| subjects affected / exposed                           | 116 / 123 (94.31%)           | 80 / 84 (95.24%)            | 84 / 86 (97.67%)            |
| General disorders and administration site conditions  |                              |                             |                             |
| Asthenia  |                              |                             |                             |
| subjects affected / exposed                           | 31 / 123 (25.20%)            | 21 / 84 (25.00%)            | 17 / 86 (19.77%)            |
| occurrences (all)                                     | 34                           | 23                          | 17                          |
| Chills  |                              |                             |                             |
| subjects affected / exposed                           | 5 / 123 (4.07%)              | 2 / 84 (2.38%)              | 7 / 86 (8.14%)              |
| occurrences (all)                                     | 6                            | 2                           | 8                           |
| Fatigue   |                              |                             |                             |
| subjects affected / exposed                           | 39 / 123 (31.71%)            | 29 / 84 (34.52%)            | 30 / 86 (34.88%)            |
| occurrences (all)                                     | 40                           | 31                          | 32                          |
| Influenza like illness                                |                              |                             |                             |
| subjects affected / exposed                           | 14 / 123 (11.38%)            | 17 / 84 (20.24%)            | 12 / 86 (13.95%)            |
| occurrences (all)                                     | 14                           | 18                          | 14                          |
| Injection site reaction                               |                              |                             |                             |
| subjects affected / exposed                           | 3 / 123 (2.44%)              | 2 / 84 (2.38%)              | 6 / 86 (6.98%)              |
| occurrences (all)                                     | 3                            | 2                           | 6                           |
| Pyrexia   |                              |                             |                             |
| subjects affected / exposed                           | 29 / 123 (23.58%)            | 11 / 84 (13.10%)            | 10 / 86 (11.63%)            |
| occurrences (all)                                     | 37                           | 12                          | 12                          |
| Irritability  |                              |                             |                             |

|  |                         |                     |                     |
|--|-------------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 19 / 123 (15.45%)<br>19 | 8 / 84 (9.52%)<br>8 | 5 / 86 (5.81%)<br>5 |
| Respiratory, thoracic and mediastinal disorders  |                         |                     |                     |
| Cough  |                         |                     |                     |
| subjects affected / exposed                      | 13 / 123 (10.57%)       | 8 / 84 (9.52%)      | 10 / 86 (11.63%)    |
| occurrences (all)                                | 13                      | 8                   | 11                  |
| Dyspnoea   |                         |                     |                     |
| subjects affected / exposed                      | 12 / 123 (9.76%)        | 8 / 84 (9.52%)      | 3 / 86 (3.49%)      |
| occurrences (all)                                | 12                      | 8                   | 3                   |
| Oropharyngeal pain                               |                         |                     |                     |
| subjects affected / exposed                      | 3 / 123 (2.44%)         | 6 / 84 (7.14%)      | 2 / 86 (2.33%)      |
| occurrences (all)                                | 3                       | 7                   | 2                   |
| Psychiatric disorders                            |                         |                     |                     |
| Anxiety  |                         |                     |                     |
| subjects affected / exposed                      | 9 / 123 (7.32%)         | 5 / 84 (5.95%)      | 2 / 86 (2.33%)      |
| occurrences (all)                                | 9                       | 5                   | 2                   |
| Depressed mood                                   |                         |                     |                     |
| subjects affected / exposed                      | 6 / 123 (4.88%)         | 4 / 84 (4.76%)      | 7 / 86 (8.14%)      |
| occurrences (all)                                | 6                       | 4                   | 7                   |
| Depression                                       |                         |                     |                     |
| subjects affected / exposed                      | 11 / 123 (8.94%)        | 9 / 84 (10.71%)     | 13 / 86 (15.12%)    |
| occurrences (all)                                | 11                      | 10                  | 13                  |
| Insomnia   |                         |                     |                     |
| subjects affected / exposed                      | 29 / 123 (23.58%)       | 11 / 84 (13.10%)    | 14 / 86 (16.28%)    |
| occurrences (all)                                | 29                      | 11                  | 14                  |
| Sleep disorder                                   |                         |                     |                     |
| subjects affected / exposed                      | 4 / 123 (3.25%)         | 3 / 84 (3.57%)      | 5 / 86 (5.81%)      |
| occurrences (all)                                | 4                       | 3                   | 5                   |
| Investigations                                   |                         |                     |                     |
| Weight decreased                                 |                         |                     |                     |
| subjects affected / exposed                      | 16 / 123 (13.01%)       | 10 / 84 (11.90%)    | 13 / 86 (15.12%)    |
| occurrences (all)                                | 16                      | 10                  | 13                  |
| Nervous system disorders                         |                         |                     |                     |
| Dizziness  |                         |                     |                     |
| subjects affected / exposed                      | 9 / 123 (7.32%)         | 10 / 84 (11.90%)    | 6 / 86 (6.98%)      |
| occurrences (all)                                | 9                       | 10                  | 6                   |

|  |                         |                        |                        |
|--|-------------------------|------------------------|------------------------|
| Headache<br>subjects affected / exposed<br>occurrences (all)             | 29 / 123 (23.58%)<br>31 | 21 / 84 (25.00%)<br>22 | 22 / 86 (25.58%)<br>24 |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)             | 1 / 123 (0.81%)<br>1    | 3 / 84 (3.57%)<br>3    | 5 / 86 (5.81%)<br>5    |
| Blood and lymphatic system disorders                                     |                         |                        |                        |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)              | 27 / 123 (21.95%)<br>27 | 13 / 84 (15.48%)<br>14 | 15 / 86 (17.44%)<br>15 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)          | 27 / 123 (21.95%)<br>32 | 6 / 84 (7.14%)<br>6    | 15 / 86 (17.44%)<br>16 |
| Eye disorders  |                         |                        |                        |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)              | 3 / 123 (2.44%)<br>3    | 5 / 84 (5.95%)<br>5    | 0 / 86 (0.00%)<br>0    |
| Gastrointestinal disorders   |                         |                        |                        |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)       | 7 / 123 (5.69%)<br>7    | 11 / 84 (13.10%)<br>11 | 4 / 86 (4.65%)<br>4    |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 7 / 123 (5.69%)<br>7    | 7 / 84 (8.33%)<br>8    | 3 / 86 (3.49%)<br>3    |
| Cheilitis<br>subjects affected / exposed<br>occurrences (all)            | 8 / 123 (6.50%)<br>8    | 4 / 84 (4.76%)<br>4    | 3 / 86 (3.49%)<br>4    |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 32 / 123 (26.02%)<br>34 | 24 / 84 (28.57%)<br>31 | 23 / 86 (26.74%)<br>27 |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)            | 6 / 123 (4.88%)<br>6    | 5 / 84 (5.95%)<br>5    | 2 / 86 (2.33%)<br>2    |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)            | 6 / 123 (4.88%)<br>7    | 4 / 84 (4.76%)<br>4    | 7 / 86 (8.14%)<br>8    |
| Nausea   |                         |                        |                        |



|   |                         |                        |                        |
|---|-------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)  | 34 / 123 (27.64%)<br>36 | 38 / 84 (45.24%)<br>44 | 36 / 86 (41.86%)<br>39 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 12 / 123 (9.76%)<br>16  | 14 / 84 (16.67%)<br>19 | 23 / 86 (26.74%)<br>28 |
| Hepatobiliary disorders<br>Jaundice<br>subjects affected / exposed<br>occurrences (all)                           | 7 / 123 (5.69%)<br>8    | 8 / 84 (9.52%)<br>8    | 10 / 86 (11.63%)<br>10 |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all)            | 7 / 123 (5.69%)<br>7    | 4 / 84 (4.76%)<br>4    | 6 / 86 (6.98%)<br>6    |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)  | 17 / 123 (13.82%)<br>17 | 9 / 84 (10.71%)<br>9   | 18 / 86 (20.93%)<br>19 |
| Erythema<br>subjects affected / exposed<br>occurrences (all)  | 8 / 123 (6.50%)<br>9    | 5 / 84 (5.95%)<br>5    | 5 / 86 (5.81%)<br>6    |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)  | 7 / 123 (5.69%)<br>7    | 6 / 84 (7.14%)<br>6    | 3 / 86 (3.49%)<br>3    |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 19 / 123 (15.45%)<br>21 | 16 / 84 (19.05%)<br>16 | 17 / 86 (19.77%)<br>17 |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 22 / 123 (17.89%)<br>24 | 16 / 84 (19.05%)<br>17 | 13 / 86 (15.12%)<br>14 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 11 / 123 (8.94%)<br>13  | 6 / 84 (7.14%)<br>6    | 6 / 86 (6.98%)<br>6    |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 3 / 123 (2.44%)<br>3    | 3 / 84 (3.57%)<br>3    | 6 / 86 (6.98%)<br>6    |
| Myalgia   |                         |                        |                        |

|  |                         |                        |                        |
|--|-------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 17 / 123 (13.82%)<br>20 | 9 / 84 (10.71%)<br>12  | 15 / 86 (17.44%)<br>16 |
| Infections and infestations<br>Oral herpes<br>subjects affected / exposed<br>occurrences (all)               | 8 / 123 (6.50%)<br>9    | 0 / 84 (0.00%)<br>0    | 2 / 86 (2.33%)<br>2    |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 29 / 123 (23.58%)<br>29 | 14 / 84 (16.67%)<br>14 | 18 / 86 (20.93%)<br>19 |

|   |                           |  |  |
|---|---------------------------|--|--|
| <b>Non-serious adverse events</b>   | Faldaprevir 240 mg<br>- T |  |  |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                 | 178 / 185 (96.22%)        |  |  |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all) | 39 / 185 (21.08%)<br>41   |  |  |
| Chills<br>subjects affected / exposed<br>occurrences (all)  | 11 / 185 (5.95%)<br>12    |  |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 65 / 185 (35.14%)<br>69   |  |  |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)  | 31 / 185 (16.76%)<br>34   |  |  |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)   | 8 / 185 (4.32%)<br>8      |  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 24 / 185 (12.97%)<br>27   |  |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)  | 13 / 185 (7.03%)<br>13    |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| Respiratory, thoracic and mediastinal disorders |                   |  |  |
| Cough   |                   |  |  |
| subjects affected / exposed                     | 18 / 185 (9.73%)  |  |  |
| occurrences (all)                               | 19                |  |  |
| Dyspnoea  |                   |  |  |
| subjects affected / exposed                     | 12 / 185 (6.49%)  |  |  |
| occurrences (all)                               | 12                |  |  |
| Oropharyngeal pain                              |                   |  |  |
| subjects affected / exposed                     | 9 / 185 (4.86%)   |  |  |
| occurrences (all)                               | 10                |  |  |
| Psychiatric disorders                           |                   |  |  |
| Anxiety   |                   |  |  |
| subjects affected / exposed                     | 8 / 185 (4.32%)   |  |  |
| occurrences (all)                               | 8                 |  |  |
| Depressed mood                                  |                   |  |  |
| subjects affected / exposed                     | 12 / 185 (6.49%)  |  |  |
| occurrences (all)                               | 12                |  |  |
| Depression                                      |                   |  |  |
| subjects affected / exposed                     | 24 / 185 (12.97%) |  |  |
| occurrences (all)                               | 25                |  |  |
| Insomnia  |                   |  |  |
| subjects affected / exposed                     | 28 / 185 (15.14%) |  |  |
| occurrences (all)                               | 28                |  |  |
| Sleep disorder                                  |                   |  |  |
| subjects affected / exposed                     | 8 / 185 (4.32%)   |  |  |
| occurrences (all)                               | 8                 |  |  |
| Investigations                                  |                   |  |  |
| Weight decreased                                |                   |  |  |
| subjects affected / exposed                     | 25 / 185 (13.51%) |  |  |
| occurrences (all)                               | 25                |  |  |
| Nervous system disorders                        |                   |  |  |
| Dizziness                                       |                   |  |  |
| subjects affected / exposed                     | 20 / 185 (10.81%) |  |  |
| occurrences (all)                               | 21                |  |  |
| Headache  |                   |  |  |

|                                      |                   |  |  |
|--------------------------------------|-------------------|--|--|
| subjects affected / exposed          | 47 / 185 (25.41%) |  |  |
| occurrences (all)                    | 50                |  |  |
| Lethargy                             |                   |  |  |
| subjects affected / exposed          | 8 / 185 (4.32%)   |  |  |
| occurrences (all)                    | 8                 |  |  |
| Blood and lymphatic system disorders |                   |  |  |
| Anaemia                              |                   |  |  |
| subjects affected / exposed          | 30 / 185 (16.22%) |  |  |
| occurrences (all)                    | 31                |  |  |
| Neutropenia                          |                   |  |  |
| subjects affected / exposed          | 22 / 185 (11.89%) |  |  |
| occurrences (all)                    | 23                |  |  |
| Eye disorders                        |                   |  |  |
| Dry eye                              |                   |  |  |
| subjects affected / exposed          | 6 / 185 (3.24%)   |  |  |
| occurrences (all)                    | 6                 |  |  |
| Gastrointestinal disorders           |                   |  |  |
| Abdominal pain                       |                   |  |  |
| subjects affected / exposed          | 17 / 185 (9.19%)  |  |  |
| occurrences (all)                    | 17                |  |  |
| Abdominal pain upper                 |                   |  |  |
| subjects affected / exposed          | 10 / 185 (5.41%)  |  |  |
| occurrences (all)                    | 11                |  |  |
| Cheilitis                            |                   |  |  |
| subjects affected / exposed          | 7 / 185 (3.78%)   |  |  |
| occurrences (all)                    | 8                 |  |  |
| Diarrhoea                            |                   |  |  |
| subjects affected / exposed          | 51 / 185 (27.57%) |  |  |
| occurrences (all)                    | 62                |  |  |
| Dry mouth                            |                   |  |  |
| subjects affected / exposed          | 7 / 185 (3.78%)   |  |  |
| occurrences (all)                    | 7                 |  |  |
| Dyspepsia                            |                   |  |  |
| subjects affected / exposed          | 11 / 185 (5.95%)  |  |  |
| occurrences (all)                    | 12                |  |  |
| Nausea                               |                   |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| subjects affected / exposed                     | 81 / 185 (43.78%) |  |  |
| occurrences (all)                               | 91                |  |  |
| Vomiting  |                   |  |  |
| subjects affected / exposed                     | 43 / 185 (23.24%) |  |  |
| occurrences (all)                               | 54                |  |  |
| Hepatobiliary disorders                         |                   |  |  |
| Jaundice  |                   |  |  |
| subjects affected / exposed                     | 19 / 185 (10.27%) |  |  |
| occurrences (all)                               | 19                |  |  |
| Skin and subcutaneous tissue disorders          |                   |  |  |
| Alopecia  |                   |  |  |
| subjects affected / exposed                     | 10 / 185 (5.41%)  |  |  |
| occurrences (all)                               | 10                |  |  |
| Dry skin  |                   |  |  |
| subjects affected / exposed                     | 27 / 185 (14.59%) |  |  |
| occurrences (all)                               | 28                |  |  |
| Erythema  |                   |  |  |
| subjects affected / exposed                     | 10 / 185 (5.41%)  |  |  |
| occurrences (all)                               | 11                |  |  |
| Night sweats                                    |                   |  |  |
| subjects affected / exposed                     | 9 / 185 (4.86%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Pruritus  |                   |  |  |
| subjects affected / exposed                     | 34 / 185 (18.38%) |  |  |
| occurrences (all)                               | 34                |  |  |
| Rash  |                   |  |  |
| subjects affected / exposed                     | 31 / 185 (16.76%) |  |  |
| occurrences (all)                               | 33                |  |  |
| Musculoskeletal and connective tissue disorders |                   |  |  |
| Arthralgia                                      |                   |  |  |
| subjects affected / exposed                     | 13 / 185 (7.03%)  |  |  |
| occurrences (all)                               | 13                |  |  |
| Muscle spasms                                   |                   |  |  |
| subjects affected / exposed                     | 9 / 185 (4.86%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Myalgia   |                   |  |  |

|  |                         |  |  |
|--|-------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 27 / 185 (14.59%)<br>31 |  |  |
| Infections and infestations<br>Oral herpes<br>subjects affected / exposed<br>occurrences (all)               | 2 / 185 (1.08%)<br>2    |  |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 36 / 185 (19.46%)<br>37 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 03 October 2011 | main amendments:<br>1. Description and rationale of the new trial design (inclusion of the FDV 120 mg group).<br>2. Explanation of loading dose.<br>3. Added information about the results of drug interaction trials with ARVs.  |
| 11 October 2011 | Main amendments:<br>1. Clarification of ATZ/RTV intensive PK sampling: medication administration; parameters to be determined; sampling timepoints; assay for ARV concentration determination; and sample handling.   |
| 01 May 2012     | Main amendments:<br>1. Clarification and guidance on when and how to conduct the progression of liver disease assessment.<br>2. Change of the primary efficacy endpoint from SVR24 to SVR12 based on regulatory presentations and retrospective analysis of phase II data indicating a 98% positive predictive value (PPV) of SVR12 predicting SVR24.<br>3. Clarification of inclusion criteria: definition of stable HAART.<br>4. Clarification of exclusion criteria: allowed enrolment of patients with Child-Turcotte-Pugh classification (CTP) score above threshold due to comedication effect, but not liver decompensation, consistent with update of RBV label; which patients with chronic obstructive pulmonary disease (COPD) should be excluded; limited exception for the white blood cell (WBC) and absolute neutrophil count (ANC) thresholds.<br>5. Clarification of the stopping rule implementation.<br>6. Clarification of the criteria for virologic failure.<br>7. Clarification in wording for AEs and SAEs to comply with BI SOP.<br>8. Clarification of use of the eCRF skin form page to capture rashes and photosensitivity reactions (protocol-defined AEs of special interest).<br>9. Clarification of procedures to be done when a patient prematurely discontinued.<br>10. Clarification of analyses for the SVR12 timepoint; primary and secondary analyses; and safety analyses for HIV disease characteristics. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported