



Clinical trial results:

Long-Term Follow-Up of Subjects in a Phase 1, 2, or 3 Clinical Trial in Which Boceprevir or Narlaprevir was Administered for the Treatment of Chronic Hepatitis C

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2006-006529-25 |
| Trial protocol | FR DE ES IT NL PT |
| Global end of trial date | 13 October 2014 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 30 January 2016 |
| First version publication date | 30 January 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | P05063 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|--|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00689390 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | MK-3034-021: Merck Registration Number |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 October 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 October 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 October 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Study P05063 is a 3-year long-term follow-up (LTFU) study in participants previously treated with boceprevir (BOC) or narlaprevir (NAR) in a Phase 1, 2, or 3 clinical study. Participants will be followed for up to 3.5 years after the end of their participation in the treatment protocol to document maintenance of the antiviral response (for sustained responders) and to characterize the long-term safety after use of this therapeutic regimen. LTFU procedures include collection of plasma samples for measuring Hepatitis C Virus ribonucleic acid (HCV-RNA) by polymerase chain reaction (PCR) and HCV sequence analysis. No drug therapy will be administered as part of this study.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 February 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Argentina: 24 |
| Country: Number of subjects enrolled | Belgium: 30 |
| Country: Number of subjects enrolled | Brazil: 3 |
| Country: Number of subjects enrolled | Canada: 91 |
| Country: Number of subjects enrolled | France: 146 |
| Country: Number of subjects enrolled | Germany: 103 |
| Country: Number of subjects enrolled | Italy: 102 |
| Country: Number of subjects enrolled | Netherlands: 13 |
| Country: Number of subjects enrolled | Poland: 4 |
| Country: Number of subjects enrolled | Spain: 64 |
| Country: Number of subjects enrolled | United States: 1369 |
| Country: Number of subjects enrolled | Portugal: 5 |
| Worldwide total number of subjects | 1954 |
| EEA total number of subjects | 467 |

Notes:

| Subjects enrolled per age group | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 1871 |
| From 65 to 84 years | 83 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 9 boceprevir studies (P03523 [NCT00423670], P03659 [NCT00160251], P04487 [No NCT], P05101 [NCT00708500], P05216 [NCT00705432], P05411 [NCT00959699], P05514 [NCT00910624], P05685 [NCT00845065], and P06086 [NCT01023035]) and 1 narlaprevir study (P05104 [NCT00797745]).

Pre-assignment

Screening details:

1954 participants enrolled in this long-term follow-up (LTFU) study, with 1907 participants from 9 boceprevir studies and 47 participants from 1 narlaprevir study.

Period 1

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

Arms

| | |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Participants from Boceprevir Studies |

Arm description:

Participants who previously participated in treatment studies in which boceprevir was administered were subsequently enrolled in Part 1 of the current follow-up study P05063 (NCT00689390). Participants may have received boceprevir or control peginterferon plus ribavirin (PR) in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|--|------------|
| Arm type | Follow-up |
| Investigational medicinal product name | Boceprevir |
| Investigational medicinal product code | |
| Other name | VICTRELIS® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

In previous treatment studies, boceprevir was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

| | |
|--|-------------------------|
| Investigational medicinal product name | Peginterferon alfa-2b |
| Investigational medicinal product code | |
| Other name | PEG-Intron®, SCH 054031 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

In previous treatment studies, peginterferon alfa-2b was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

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

Dosage and administration details:

In previous treatment studies, ribavirin was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

| | |
|------------------|---------------------------------------|
| Arm title | Participants from Narlaprevir Studies |
|------------------|---------------------------------------|

Arm description:

Participants who previously participated in treatment studies in which narlaprevir was administered were subsequently enrolled in Part 2 of the current follow-up study P05063 (NCT00689390). Participants may have received narlaprevir or control PR in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|--|---------------------|
| Arm type | Follow-up |
| Investigational medicinal product name | Narlaprevir |
| Investigational medicinal product code | |
| Other name | SCH 900518, MK-8515 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

In previous treatment studies, narlaprevir was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

| | |
|--|-------------------------|
| Investigational medicinal product name | Peginterferon alfa-2b |
| Investigational medicinal product code | |
| Other name | PEG-Intron®, SCH 054031 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

In previous treatment studies, peginterferon alfa-2b was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

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

Dosage and administration details:

In previous treatment studies, ribavirin was administered as specified by the protocol. No treatment was administered in the current follow-up study (P05063, NCT00689390, 2006-006529-25).

| Number of subjects in period 1 | Participants from Boceprevir Studies | Participants from Narlaprevir Studies |
|--|---|--|
| Started | 1907 | 47 |
| Completed | 1481 | 37 |
| Not completed | 426 | 10 |
| Adverse event, serious fatal | 14 | - |
| Consent withdrawn by subject | 117 | 3 |
| Administrative | 37 | - |
| Adverse event, non-fatal | 5 | - |
| Did Not Meet Protocol Eligibility | 1 | - |
| Non-Compliance With Protocol | 21 | - |
| Lost to follow-up | 179 | 7 |
| Withdrew Consent-Retreatment Opportunity | 52 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Participants from Boceprevir Studies |
|-----------------------|--------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which boceprevir was administered were subsequently enrolled in Part 1 of the current follow-up study P05063 (NCT00689390). Participants may have received boceprevir or control peginterferon plus ribavirin (PR) in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Participants from Narlaprevir Studies |
|-----------------------|---------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which narlaprevir was administered were subsequently enrolled in Part 2 of the current follow-up study P05063 (NCT00689390). Participants may have received narlaprevir or control PR in the previous treatment study. No treatment was administered in the current follow-up study.

| Reporting group values | Participants from Boceprevir Studies | Participants from Narlaprevir Studies | Total |
|--|--------------------------------------|---------------------------------------|-------|
| Number of subjects | 1907 | 47 | 1954 |
| Age categorical Units: Subjects | | | |
| <40 years | 173 | 5 | 178 |
| 40 to <65 years | 1651 | 42 | 1693 |
| ≥65 years | 83 | 0 | 83 |
| Gender, Male/Female Units: participants | | | |
| Female | 785 | 19 | 804 |
| Male | 1122 | 28 | 1150 |

End points

End points reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Participants from Boceprevir Studies |
|-----------------------|--------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which boceprevir was administered were subsequently enrolled in Part 1 of the current follow-up study P05063 (NCT00689390). Participants may have received boceprevir or control peginterferon plus ribavirin (PR) in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Participants from Narlaprevir Studies |
|-----------------------|---------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which narlaprevir was administered were subsequently enrolled in Part 2 of the current follow-up study P05063 (NCT00689390). Participants may have received narlaprevir or control PR in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | Previous SVR on Boceprevir + PR |
|----------------------------|---------------------------------|

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

Subject analysis set description:

Participants who previously received boceprevir plus PR in treatment studies and achieved sustained virologic response (SVR). No treatment was administered in the current follow-up study.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Previous SVR on Narlaprevir + PR |
|----------------------------|----------------------------------|

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

Subject analysis set description:

Participants who previously received narlaprevir plus PR in treatment studies and achieved SVR. No treatment was administered in the current follow-up study.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Previous SVR on PR Only |
|----------------------------|-------------------------|

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

Subject analysis set description:

Participants who previously received PR only in boceprevir or narlaprevir treatment studies and achieved SVR. No treatment was administered in the current follow-up study.

| | |
|----------------------------|---|
| Subject analysis set title | Participants from Boceprevir Studies with TE-RAVs |
|----------------------------|---|

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

Subject analysis set description:

Participants who previously participated in treatment studies in which boceprevir was administered were subsequently enrolled in Part 1 of the current follow-up study P05063 (NCT00689390). Participants may have received boceprevir or control peginterferon plus ribavirin (PR) in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|----------------------------|--|
| Subject analysis set title | Participants from Narlaprevir Studies with TE-RAVs |
|----------------------------|--|

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

Subject analysis set description:

Participants who previously participated in treatment studies in which narlaprevir was administered were subsequently enrolled in Part 2 of the current follow-up study P05063 (NCT00689390). Participants may have received narlaprevir or control PR in the previous treatment study. No treatment was administered in the current follow-up study.

Primary: Number of participants with relapse during the LTFU among sustained responders from previous treatment studies with boceprevir or narlaprevir (Durability of virologic response)

| | |
|-----------------|---|
| End point title | Number of participants with relapse during the LTFU among sustained responders from previous treatment studies with boceprevir or narlaprevir (Durability of virologic response) ^[1] |
|-----------------|---|

End point description:

Durability of response was assessed by the number of participants who relapsed during the LTFU among those that had achieved sustained virologic response (SVR) by 24 weeks after treatment with boceprevir or narlaprevir in a previous Phase 1, 2, or 3 treatment study. In the current LTFU, participants were classified based on the last Hepatitis C Virus ribonucleic acid (HCV-RNA) result available at the time of the data cut-off date as follows: A participant was classified as a sustained virologic responder at a given

time point if serum HCV-RNA was undetectable at that time point and there had not been a positive HCV-RNA since the participant was determined to have achieved SVR in the previous study. A participant was classified as a relapser if they were a sustained virologic responder in the previous treatment study and became serum HCV-RNA positive with no subsequent negative results during LTFU.

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

End point timeframe:

From End Of Treatment (EOT) date in the previous treatment study to the first date of a positive HCV RNA result for relapsers or the last contact date for non-relapsers in the LTFU (up to 3.5 years)

Notes:

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

Justification: Only descriptive statistics were reported for this endpoint. No statistical analyses were performed.

| End point values | Previous SVR on Boceprevir + PR | Previous SVR on Narlaprevir + PR | Previous SVR on PR Only | |
|-----------------------------|---------------------------------|----------------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1116 ^[2] | 40 ^[3] | 144 ^[4] | |
| Units: participants | 8 | 0 | 1 | |

Notes:

[2] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

[3] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

[4] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier exposure-adjusted relapse rate

| | |
|-----------------|--|
| End point title | Kaplan-Meier exposure-adjusted relapse rate ^[5] |
|-----------------|--|

End point description:

The distribution of time to relapse was summarized using Kaplan-Meier estimates for all participants who were sustained responders at 24 weeks post-treatment in the previous study. Exposure Adjusted Relapse Rate = $1000 \times (\text{number of relapses}) / (\text{Total exposure time in years})$. Total exposure time in years = $[(\text{total number of days from last day of treatment to the last follow-up day for all subjects who did not relapse}) + (\text{total number of days from last day of treatment to the day of relapse for those who relapsed})] / 365.25 \text{ days [for 1 year]}$.

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

End point timeframe:

From EOT date in the previous treatment study to the first date of a positive HCV RNA result for relapsers or the last contact date for non-relapsers in the LTFU (up to 3.5 years)

Notes:

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

Justification: Only descriptive statistics were reported for this endpoint. No statistical analyses were performed.

| End point values | Previous SVR on Boceprevir + PR | Previous SVR on Narlaprevir + PR | Previous SVR on PR Only | |
|--|---------------------------------|----------------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1116 ^[6] | 40 ^[7] | 144 ^[8] | |
| Units: relapses per 1,000 person-years | | | | |
| number (not applicable) | 2.3 | 0 | 2.2 | |

Notes:

[6] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

[7] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

[8] - All sustained responders at 24 weeks post-treatment in the previous study with available data.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with HCV Treatment-Emergent Resistance Associated Variants (TE-RAVs) of NS3/4A protease loci

| | |
|-----------------|--|
| End point title | Number of participants with HCV Treatment-Emergent Resistance Associated Variants (TE-RAVs) of NS3/4A protease loci ^[9] |
|-----------------|--|

End point description:

Plasma samples of all participants receiving at least one dose of study medication in a previous treatment protocol were evaluated by population sequencing and analyzed to detect amino acid variants in the NS3/4A protease known to be associated with reduced susceptibility to boceprevir and narlaprevir. RAVs in the NS3/4A protease gene were evaluated at 12 loci (V36, Q41, F43, T54, V55, V107, R155, A156, V158, D168, I/V170 and M175) on the basis of in vitro studies. A TE-RAV was defined as a RAV not present at baseline and that had not returned to wild type (WT) while the participant was still on treatment. The number of participants with TE-RAVs detected at the EOT in the previous treatment study are reported below, followed by those participants with TE-RAVs that returned to WT during the LTFU (among those with detected TE-RAVs).

Participants could have had more than one TE-RAV. All TE-RAVs were observed in participants in the boceprevir studies.

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

End point timeframe:

From EOT in the previous treatment study to the last available date in the LTFU (up to 3.5 years)

Notes:

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

Justification: Only descriptive statistics were reported for this endpoint. No statistical analyses were performed.

| End point values | Participants from Boceprevir Studies with TE-RAVs | Participants from Narlaprevir Studies with TE-RAVs | | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 308 ^[10] | 0 ^[11] | | |
| Units: participants | | | | |
| V36A TE-RAVs detected | 6 | | | |
| __V36A TE-RAVs returned to WT (out of 6) | 6 | | | |
| V36G TE-RAVs detected | 1 | | | |
| __V36G TE-RAVs returned to WT (out of 1) | 1 | | | |
| V36L TE-RAVs detected | 9 | | | |
| __V36L TE-RAVs returned to WT (out of 9) | 8 | | | |
| V36M TE-RAVs detected | 142 | | | |
| __V36M TE-RAVs returned to WT (out of 142) | 135 | | | |
| F43C TE-RAVs detected | 3 | | | |

| | | | | |
|---|-----|--|--|--|
| __F43C TE-RAVs returned to WT (out of 3) | 3 | | | |
| T54A TE-RAVs detected | 40 | | | |
| __T54A TE-RAVs returned to WT (out of 40) | 40 | | | |
| T54C TE-RAVs detected | 2 | | | |
| __T54C TE-RAVs returned to WT (out of 2) | 2 | | | |
| T54S TE-RAVs detected | 143 | | | |
| __T54S TE-RAVs returned to WT (out of 143) | 104 | | | |
| V55A TE-RAVs detected | 5 | | | |
| __V55A TE-RAVs returned to WT (out of 5) | 3 | | | |
| V107I TE-RAVs detected | 3 | | | |
| __V107I TE-RAVs returned to WT (out of 3) | 2 | | | |
| R155K TE-RAVs detected | 183 | | | |
| __R155K TE-RAVs returned to WT (out of 183) | 154 | | | |
| R155T TE-RAVs detected | 22 | | | |
| __R155T TE-RAVs returned to WT (out of 22) | 20 | | | |
| A156S TE-RAVs detected | 37 | | | |
| __A156S TE-RAVs returned to WT (out of 37) | 35 | | | |
| A156T TE-RAVs detected | 4 | | | |
| __A156T TE-RAVs returned to WT (out of 4) | 4 | | | |
| V158I TE-RAVs detected | 18 | | | |
| __V158I TE-RAVs returned to WT (out of 16) | 16 | | | |
| V158M TE-RAVs detected | 1 | | | |
| __V158M TE-RAVs returned to WT (out of 1) | 1 | | | |
| D168N TE-RAVs detected | 12 | | | |
| __D168N TE-RAVs returned to WT (out of 12) | 11 | | | |
| I170T TE-RAVs detected | 3 | | | |
| __I170T TE-RAVs returned to WT (out of 3) | 3 | | | |
| V170A TE-RAVs detected | 27 | | | |
| __V170A TE-RAVs returned to WT (out of 27) | 24 | | | |
| M175L TE-RAVs detected | 5 | | | |
| __M175L TE-RAVs returned to WT (out of 5) | 2 | | | |

Notes:

[10] - Participants with TE-RAVs receiving ≥ 1 dose of study drug in a previous boceprevir clinical study.

[11] - No participants in this treatment group had a TE-RAV.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with serious adverse events (SAEs) reported during the LTFU

| | |
|-----------------|--|
| End point title | Number of participants with serious adverse events (SAEs) reported during the LTFU ^[12] |
|-----------------|--|

End point description:

Long-term safety was assessed based on the SAEs reported during the LTFU period. An SAE was any adverse drug or biologic or device experience occurring at any dose that resulted in any of the following outcomes: death, life-threatening AE, persistent or significant disability/incapacity, required in-patient hospitalization or prolongs hospitalization, congenital anomaly or birth defect. Important medical events that did not result in any of these outcomes could still be considered SAEs if they jeopardized the participant and/or required medical/surgical intervention, based on appropriate medical judgment. Grade 4 laboratory abnormalities and out of normal range liver function tests that were not accompanied by clinical manifestations were NOT considered SAEs.

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

End point timeframe:

From enrollment in the LTFU study to the last available date in the LTFU study (up to 3 years)

Notes:

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

Justification: Only descriptive statistics were reported for this endpoint. No statistical analyses were performed.

| End point values | Participants from Boceprevir Studies | Participants from Narlaprevir Studies | | |
|-----------------------------|--------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1907 ^[13] | 47 ^[14] | | |
| Units: participants | 136 | 2 | | |

Notes:

[13] - All enrolled participants were included in safety analyses.

[14] - All enrolled participants were included in safety analyses.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants that discontinued the LTFU due to SAEs

| | |
|-----------------|--|
| End point title | Number of participants that discontinued the LTFU due to |
|-----------------|--|

End point description:

An SAE was any adverse drug or biologic or device experience occurring at any dose that resulted in any of the following outcomes: death, life-threatening AE, persistent or significant disability/incapacity, required in-patient hospitalization or prolongs hospitalization, congenital anomaly or birth defect. Important medical events that did not result in any of these outcomes could still be considered SAEs if they jeopardized the participant and/or required medical/surgical intervention, based on appropriate medical judgment. Grade 4 laboratory abnormalities and out of normal range liver function tests that were not accompanied by clinical manifestations were NOT considered SAEs.

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

End point timeframe:

From enrollment in the LTFU study to the last available date in the LTFU study (up to 3 years)

Notes:

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

Justification: Only descriptive statistics were reported for this endpoint. No statistical analyses were performed.

| End point values | Participants from Boceprevir Studies | Participants from Narlaprevir Studies | | |
|-----------------------------|--------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1907 ^[16] | 47 ^[17] | | |
| Units: participants | 19 | 0 | | |

Notes:

[16] - All enrolled participants were included in safety analyses.

[17] - All enrolled participants were included in safety analyses.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From enrollment in the LTFU study to the last available date in the LTFU study (up to 3 years)

Adverse event reporting additional description:

As specified in the protocol, only serious adverse events (SAEs) were collected. Other Adverse Events were not monitored and not collected, thus no participants were at risk for these events. All enrolled participants were included in safety analyses.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Participants from Narlaprevir Studies |
|-----------------------|---------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which narlaprevir was administered were subsequently enrolled in Part 2 of the current follow-up study P05063 (NCT00689390, 2006-006529-25). Participants may have received narlaprevir or control PR in the previous treatment study. No treatment was administered in the current follow-up study.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Participants from Boceprevir Studies |
|-----------------------|--------------------------------------|

Reporting group description:

Participants who previously participated in treatment studies in which boceprevir was administered were subsequently enrolled in Part 1 of the current follow-up study P05063 (NCT00689390, 2006-006529-25). Participants may have received boceprevir or control peginterferon plus ribavirin (PR) in the previous treatment study. No treatment was administered in the current follow-up study.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: As specified in the protocol, long-term safety was assessed based on the SAEs reported during the long-term follow-up period. No non-serious AEs were collected or reported on this study.

| Serious adverse events | Participants from Narlaprevir Studies | Participants from Boceprevir Studies | |
|---|---------------------------------------|--------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 136 / 1907 (7.13%) | |
| number of deaths (all causes) | 0 | 14 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenoma Benign | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Cancer Stage 0 | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder Cancer | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain Neoplasm | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchioloalveolar Carcinoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Diffuse Large B-Cell Lymphoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hepatocellular Carcinoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 9 / 1907 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive Ductal Breast Carcinoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Adenocarcinoma | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Adenocarcinoma Stage IV | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lung Neoplasm Malignant | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases To Liver | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic Carcinoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Prostate Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Cell Carcinoma | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salivary Gland Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous Cell Carcinoma Of Head And Neck | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid Cancer | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic Aneurysm | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Arterial Occlusive Disease | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Artery Thrombosis | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Coronary Artery Bypass | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Finger Amputation | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip Arthroplasty | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Knee Arthroplasty | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver Transplant | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shoulder Arthroplasty | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgery | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Valvuloplasty Cardiac | | | |

| | | | |
|--|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest Pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 4 / 1907 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multi-Organ Failure | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Uterovaginal Prolapse | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Distress Syndrome | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Disorder | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Fibrosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Completed Suicide | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Confusional State | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Alcohol Poisoning | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ankle Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head Injury | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Limb Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road Traffic Accident | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Scapula Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stab Wound | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural Haematoma | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia Fracture | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity To Various Agents | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Wound Complication | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Endocardial Fibroelastosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Huntington's Disease | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Coronary Syndrome | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute Myocardial Infarction | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|------------------|--|
| Angina Unstable | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 3 / 1907 (0.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac Arrest | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-Respiratory Arrest | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiopulmonary Failure | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Coronary Artery Disease | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 3 / 1907 (0.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary Artery Stenosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial Infarction | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 9 / 1907 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular Tachycardia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Arachnoid Cyst | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic Stroke | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tension Headache | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |

| | | | |
|---|----------------|------------------|--|
| Corneal Oedema | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Fistula | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis Ischaemic | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 1907 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular Perforation | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 1907 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Ulcer Haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Haemorrhage | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernial Eventration | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal Perforation | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large Intestine Polyp | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal Varices Haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Palatal Disorder | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis Acute | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Haemorrhage | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varices Oesophageal | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 5 / 1907 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Cirrhosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |
| Calculus Ureteric | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Failure | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Failure Acute | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Cervical Spinal Stenosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Spinal Stenosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|------------------|--|
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 5 / 1907 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Acute Hepatitis B | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis Perforated | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis C | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Simplex Pneumonia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 5 / 1907 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Postoperative Wound Infection | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinitis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 3 / 1907 (0.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic Shock | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 1907 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metabolism and nutrition disorders | | | |
| Diabetic Complication | | | |

| | | | |
|---|----------------|------------------|--|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Diabetic Ketoacidosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic Acidosis | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 1907 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Participants from Narlaprevir Studies | Participants from Boceprevir Studies | |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 0 / 1907 (0.00%) | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 21 December 2009 | General amendment 1 (AM1) included changes to allow for the inclusion of participants who previously participated in boceprevir AND narlaprevir clinical studies, including Phase 1 studies and participants who received peginterferon alfa-2a as part of their therapeutic regimen. Changes included revisions to the protocol title, number of study sites, overall duration, background, rationale, primary objectives, statistical methods, and the addition of new methods for pharmacogenetic sampling and IL-28 genotype. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|--|--------------|
| 10 July 2014 | The study was terminated due to satisfaction of postmarketing commitments. | - |

Notes:

Limitations and caveats

None reported