



Clinical trial results:

A Randomized, Double-Blind, Controlled Study to Evaluate the Efficacy and Safety of the Combination of ABT-450/Ritonavir/ABT-267 (ABT 450/r/ABT-267) and ABT-333 With and Without Ribavirin (RBV) in Treatment-Naïve Adults with Genotype 1b Chronic Hepatitis C Virus (HCV) Infection (PEARL-III)

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 | 2012-003687-52 |
| Trial protocol | PT BE HU AT IT ES PL |
| Global end of trial date | 19 August 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 May 2016 |
| First version publication date | 13 May 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M13-961 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01767116 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AbbVie Deutschland GmbH & Co. KG |
| Sponsor organisation address | Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE |
| Public contact | Global Medical Information, AbbVie, 001 800-633-9110, |
| Scientific contact | Dan Cohen, MD, AbbVie, daniel.cohen@abbvie.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 | 19 August 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 August 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and antiviral activity of ABT-450/ritonavir/ABT-267 (ABT-450/r/ABT-267; ABT-450 also known as paritaprevir; ABT-267 also known as ombitasvir) and ABT-333 (also known as dasabuvir) with and without ribavirin (RBV) in patients with chronic hepatitis C virus genotype 1b (HCV GT1b) infection without cirrhosis.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 December 2012 |
| 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 | Poland: 39 |
| Country: Number of subjects enrolled | Portugal: 16 |
| Country: Number of subjects enrolled | Spain: 31 |
| Country: Number of subjects enrolled | Austria: 21 |
| Country: Number of subjects enrolled | Belgium: 26 |
| Country: Number of subjects enrolled | Hungary: 21 |
| Country: Number of subjects enrolled | Italy: 26 |
| Country: Number of subjects enrolled | Israel: 58 |
| Country: Number of subjects enrolled | Romania: 48 |
| Country: Number of subjects enrolled | Russian Federation: 38 |
| Country: Number of subjects enrolled | United States: 95 |
| Worldwide total number of subjects | 419 |
| EEA total number of subjects | 228 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|-----|
| wk | |
| 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) | 386 |
| From 65 to 84 years | 33 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a screening period of 35 days.

Period 1

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

Arms

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

| | |
|------------------|---|
| Arm title | ABT-450/r/ABT-267 and ABT-333, Plus RBV |
|------------------|---|

Arm description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily), plus weight-based RBV (dosed 1,000 or 1,200 mg daily divided twice a day) for 12 weeks

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-450/r/ABT-267 |
| Investigational medicinal product code | |
| Other name | ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir, Viekirax |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-450 (150 mg) coformulated with ritonavir (100 mg) and ABT-267 (25 mg)

| | |
|--|--------------------|
| Investigational medicinal product name | ABT-333 |
| Investigational medicinal product code | |
| Other name | dasabuvir, Exviera |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

250 mg twice daily

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

Dosage and administration details:

Weight-based (dosed 1,000 or 1,200 mg daily divided twice a day)

| | |
|------------------|---|
| Arm title | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
|------------------|---|

Arm description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily) for 12 weeks plus placebo RBV (twice daily) for 12 weeks

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

| | |
|--|--|
| Investigational medicinal product name | ABT-450/r/ABT-267 |
| Investigational medicinal product code | |
| Other name | ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir, Viekirax |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-450 (150 mg) coformulated with ritonavir (100 mg) and ABT-267 (25 mg)

| | |
|--|--------------------|
| Investigational medicinal product name | ABT-333 |
| Investigational medicinal product code | |
| Other name | dasabuvir, Exviera |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

250 mg twice daily

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

Dosage and administration details:

Twice daily

| Number of subjects in period 1 | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
|---------------------------------------|---|---|
| Started | 210 | 209 |
| Completed | 208 | 207 |
| Not completed | 2 | 2 |
| Lost to follow-up | 2 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus RBV |
|-----------------------|---|

Reporting group description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily), plus weight-based RBV (dosed 1,000 or 1,200 mg daily divided twice a day) for 12 weeks

| | |
|-----------------------|---|
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
|-----------------------|---|

Reporting group description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily) for 12 weeks plus placebo RBV (twice daily) for 12 weeks

| Reporting group values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | Total |
|------------------------------------|---|---|-------|
| Number of subjects | 210 | 209 | 419 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----------------|-----------------|-----|
| Age continuous Units: years arithmetic mean standard deviation | 48.4 ± 11.94 | 49.2 ± 12.03 | - |
| Gender categorical Units: Subjects | | | |
| Female | 104 | 123 | 227 |
| Male | 106 | 86 | 192 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus RBV |
| Reporting group description: ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily), plus weight-based RBV (dosed 1,000 or 1,200 mg daily divided twice a day) for 12 weeks | |
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
| Reporting group description: ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily) for 12 weeks plus placebo RBV (twice daily) for 12 weeks | |

Primary: Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Noninferiority Analyses of Each Treatment Arm Compared to Historical Rate

| | |
|---|---|
| End point title | Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Noninferiority Analyses of Each Treatment Arm Compared to Historical Rate ^[1] |
| End point description: The percentage of subjects with sustained virologic response (plasma Hepatitis C virus ribonucleic acid [HCV RNA] level less than the lower limit of quantitation [$< \text{LLOQ}$]) 12 weeks after the last dose of study drug. The LLOQ for the assay was 25 IU/mL. Subjects with missing data were counted as non-responders. The primary endpoints were noninferiority of the percentage of subjects who achieved sustained virologic response 12 weeks after treatment in each treatment arm compared with the historical control rate for noncirrhotic, treatment-naïve subjects with HCV GT1b infection treated with telaprevir and peginterferon/RBV (pegIFN). Based on a 2-sided significance level of 0.05 and an underlying rate of $\geq 92\%$ in each arm, a sample size of 200 subjects per treatment arm provides $>95\%$ power to demonstrate noninferiority of each regimen to the historical rate (84%) (based on the normal approximation of a single binomial proportion in a one-sample test for superiority) | |
| End point type | Primary |
| End point timeframe: 12 weeks after last dose of study drug | |

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: The lower confidence bound of the 2-sided 95% CI must exceed 73% to achieve noninferiority.

ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV: 95% CI calculated using the Wilson score method for the single proportion; ABT-450/r/ABT-267 and ABT-333, Plus RBV: 95% CI calculated using the normal approximation to the binomial distribution.

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 210 ^[2] | 209 ^[3] | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 99.5 (98.6 to 100) | 100 (98.2 to 100) | | |

Notes:

[2] - All randomized subjects who received at least 1 dose of study drug (intent-to-treat [ITT])

[3] - All randomized subjects who received at least 1 dose of study drug (intent-to-treat [ITT])

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Noninferiority Analysis of ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV Compared With ABT-450/r/ABT-267 and ABT-333, Plus RBV

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Noninferiority Analysis of ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV Compared With ABT-450/r/ABT-267 and ABT-333, Plus RBV |
|-----------------|---|

End point description:

The percentage of subjects with sustained virologic response (plasma Hepatitis C virus ribonucleic acid [HCV RNA] level less than the lower limit of quantitation [$< \text{LLOQ}$]) 12 weeks after the last dose of study drug. Subjects with missing data were counted as non-responders.

The secondary endpoint was the noninferiority of the percentage of subjects who achieved sustained virologic response 12 weeks after treatment who received ABT-450/r/ABT-267 and ABT-333, plus placebo RBV compared with those who received ABT-450/r/ABT-267 and ABT-333, plus RBV.

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

End point timeframe:

12 weeks after last dose of study drug

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 210 ^[4] | 209 ^[5] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 99.5 | 100 | | |

Notes:

[4] - ITT population

[5] - ITT population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

For the secondary efficacy endpoint of sustained virologic response at 12 weeks after treatment, based on a -10% margin, a 2-sided significance level of 0.05 and an underlying rate of 92% or higher in each arm, a sample size of 200 subjects per arm provides >95% power to demonstrate noninferiority of ABT-450/r/ABT-267 and ABT-333, plus Placebo RBV compared with ABT-450/r/ABT-267 and ABT-333, plus RBV (normal approximation of a single binomial proportion in a 1-sample test for superiority).

| | |
|-------------------|---|
| Comparison groups | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV v ABT-450/r/ABT-267 and ABT-333, Plus RBV |
|-------------------|---|

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 419 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[6] |
| Parameter estimate | difference in percentage of subjects |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.5 |
| upper limit | 1.4 |

Notes:

[6] - Noninferiority of the rate of sustained virologic response at 12 weeks after treatment for the ABT-450/r/ABT-267 and ABT-333, plus placebo RBV treatment group as compared with the ABT-450/r/ABT-267 and ABT-333, plus RBV treatment group was analyzed using a noninferiority margin of -10.5%. The lower confidence bound of the 2-sided 95% CI for the difference in percentage of subjects with sustained virologic response at 12 weeks after treatment must exceed -10.5% to achieve noninferiority.

Secondary: Percentage of Subjects With Hemoglobin Decrease to Below the Lower Limit of Normal (LLN) At End of Treatment

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Hemoglobin Decrease to Below the Lower Limit of Normal (LLN) At End of Treatment |
|-----------------|--|

End point description:

The percentage of subjects with a decrease in hemoglobin from greater than or equal to the lower limit of normal (\geq LLN) at baseline to $<$ LLN at the end of treatment.

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

End point timeframe:

Baseline (Day 1) and Week 12 (End of Treatment)

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 207 ^[7] | 205 ^[8] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 51.2 | 3.4 | | |

Notes:

[7] - Subjects in ITT population who had hemoglobin \geq LLN reference range at baseline

[8] - Subjects in ITT population who had hemoglobin \geq LLN reference range at baseline

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | ABT-450/r/ABT-267 and ABT-333, Plus RBV v ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
| Number of subjects included in analysis | 412 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Fisher exact |

Secondary: Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Superiority Analyses of Each Treatment Arm Compared to Historical Rate

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment; Superiority Analyses of Each Treatment Arm Compared to Historical Rate |
|-----------------|---|

End point description:

The percentage of subjects with sustained virologic response (plasma HCV RNA less than the lower limit of quantitation [$<$ LLOQ]) 12 weeks after the last dose of study drug. Subjects with missing data were counted as non-responders.

The secondary endpoints were superiority of the percentage of subjects who achieved sustained virologic response 12 weeks after treatment in each treatment arm compared with the historical control rate for noncirrhotic, treatment-naïve subjects with HCV GT1b treated with telaprevir and pegIFN/RBV. 95% CI (plus RBV arm: calculated using the normal approximation to the binomial distribution; plus placebo RBV arm: calculated using the Wilson score method for the single proportion); the lower confidence bound for the percentage of subjects with sustained virologic response at 12 weeks after treatment must exceed 84% to achieve superiority.

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

End point timeframe:

12 weeks after last dose of study drug

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 210 ^[9] | 209 ^[10] | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 99.5 (98.6 to 100) | 100 (98.2 to 100) | | |

Notes:

[9] - ITT population

[10] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Virologic Failure During Treatment

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Virologic Failure During Treatment |
|-----------------|--|

End point description:

Virologic failure during treatment was defined as rebound (confirmed HCV RNA greater than or equal to the lower limit of quantitation [\geq LLOQ] after HCV RNA $<$ LLOQ during treatment, or confirmed increase from the lowest value post baseline in HCV RNA [2 consecutive HCV RNA measurements $>$ 1 log₁₀ IU/mL above the lowest value post baseline] at any time point during treatment), or failure to suppress (HCV RNA \geq LLOQ persistently during treatment with at least 6 weeks [\geq 36 days] of treatment).

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

End point timeframe:

Baseline (Day 1), and Treatment Weeks 1, 2, 4, 6, 8, 10, and 12

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 210 ^[11] | 209 ^[12] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Rebound | 0.5 | 0 | | |
| Failure to suppress | 0 | 0 | | |

Notes:

[11] - ITT population

[12] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Virologic Relapse After Treatment

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Virologic Relapse After Treatment |
|-----------------|---|

End point description:

Subjects who completed treatment with plasma HCV RNA less than the lower limit of quantification (<LLOQ) at the end of treatment were considered to have virologic relapse if they had confirmed HCV RNA \geq LLOQ during the post-treatment period.

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

End point timeframe:

Between End of Treatment (Week 12) and Post-treatment (up to Week 12 Post-treatment)

| End point values | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 208 ^[13] | 207 ^[14] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 0 | 0 | | |

Notes:

[13] - ITT population with HCV RNA < LLOQ at the final treatment visit and completed treatment

[14] - ITT population with HCV RNA < LLOQ at the final treatment visit and completed treatment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of study drug administration to 30 days after last dose of study drug (16 weeks); SAEs were also collected from the time that informed consent was obtained until the end of participation in the study (up to 65 weeks)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus RBV |
|-----------------------|---|

Reporting group description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily), plus weight-based RBV (dosed 1,000 or 1,200 mg daily divided twice a day) for 12 weeks

| | |
|-----------------------|---|
| Reporting group title | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV |
|-----------------------|---|

Reporting group description:

ABT-450/r/ABT-267 (150 mg/ 100 mg/ 25 mg once daily) and ABT-333 (250 mg twice daily) for 12 weeks plus placebo RBV (twice daily) for 12 weeks

| Serious adverse events | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 210 (1.90%) | 4 / 209 (1.91%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 210 (0.00%) | 1 / 209 (0.48%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 210 (0.48%) | 0 / 209 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 210 (0.48%) | 0 / 209 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Epididymitis | | | |
| subjects affected / exposed | 1 / 210 (0.48%) | 0 / 209 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 210 (0.00%) | 1 / 209 (0.48%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 210 (0.48%) | 0 / 209 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 210 (0.00%) | 1 / 209 (0.48%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 210 (0.00%) | 1 / 209 (0.48%) | |
| 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 | ABT-450/r/ABT-267 and ABT-333, Plus RBV | ABT-450/r/ABT-267 and ABT-333, Plus Placebo RBV | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 133 / 210 (63.33%) | 97 / 209 (46.41%) | |

| | | | |
|--|---|---|--|
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 51 / 210 (24.29%) 61 | 49 / 209 (23.44%) 58 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 14 / 210 (6.67%) 15 | 1 / 209 (0.48%) 1 | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) | 22 / 210 (10.48%) 26 45 / 210 (21.43%) 48 | 12 / 209 (5.74%) 13 49 / 209 (23.44%) 52 | |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 11 / 210 (5.24%) 12 9 / 210 (4.29%) 9 14 / 210 (6.67%) 14 23 / 210 (10.95%) 23 | 6 / 209 (2.87%) 7 13 / 209 (6.22%) 15 9 / 209 (4.31%) 9 9 / 209 (4.31%) 11 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 19 / 210 (9.05%) 19 | 5 / 209 (2.39%) 5 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash | 25 / 210 (11.90%) 28 | 11 / 209 (5.26%) 14 | |

| | | | |
|---|------------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 12 / 210 (5.71%) 12 | 8 / 209 (3.83%) 11 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 19 / 210 (9.05%) 21 | 7 / 209 (3.35%) 7 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 12 November 2012 | <p>The purpose of the amendment is to</p> <ul style="list-style-type: none">• update the introduction to provide more current data from ongoing clinical trials.• update the thresholds for the primary and secondary endpoints to be based on historical sustained virologic response (SVR) rates from telaprevir plus pegIFN and RBV therapy.• update primary and secondary endpoints to remove rapid virologic response (RVR) and end of treatment response (EOTR), which are irrelevant in the absence of SVR, and to include rebound and relapse rates, which are relevant in clinical practice when using direct-acting antiviral agent (DAAs).• clarify inclusion/exclusion criteria to ensure the appropriate subject population was enrolled.• update plan for resistance analysis throughout the protocol to clarify and more accurately reflect plans for assessing resistance development.• update RBV toxicity management to align better with the RBV label.• address inconsistencies throughout the protocol. |
| 08 April 2013 | <p>The purpose of the amendment is to prohibit the use of hormonal contraceptives during study drug administration.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported