



Clinical trial results:

A Randomized, Open-Label Study to Evaluate the Efficacy and Safety of ABT-450/Ritonavir/ABT-267 and ABT-333 Co-administered with and without Ribavirin Compared to Telaprevir Co-administered with Pegylated Interferon -2a and Ribavirin in Treatment-Naïve Adults with Chronic Hepatitis C Genotype 1 Virus Infection (MALACHITE I)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-003754-84 |
| Trial protocol | HU FI SK PL |
| Global end of trial date | 16 July 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 24 July 2016 |
| First version publication date | 24 July 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M13-774 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01854697 |
| 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 4UB |
| Public contact | Global Medical Services, AbbVie, 001 800-633-9110, |
| Scientific contact | Yan Luo, AbbVie, Yan.Luo@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 | 16 July 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 July 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a study to evaluate the efficacy and safety of three experimental drugs compared with telaprevir (a licensed product) in people with hepatitis C virus infection who have not had treatment before.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 28 March 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Argentina: 12 |
| Country: Number of subjects enrolled | Australia: 36 |
| Country: Number of subjects enrolled | Canada: 51 |
| Country: Number of subjects enrolled | Chile: 29 |
| Country: Number of subjects enrolled | Finland: 4 |
| Country: Number of subjects enrolled | Hungary: 32 |
| Country: Number of subjects enrolled | Norway: 16 |
| Country: Number of subjects enrolled | Poland: 43 |
| Country: Number of subjects enrolled | Romania: 83 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Worldwide total number of subjects | 311 |
| EEA total number of subjects | 183 |

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) | 308 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a Screening Period of up to 35 days.

Period 1

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

Arms

| | |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A: 3-DAA + RBV in GT1a |

Arm description:

ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-450/r/ABT-267 |
| Investigational medicinal product code | |
| Other name | Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

| | |
|--|---|
| Investigational medicinal product name | ABT-333 |
| Investigational medicinal product code | |
| Other name | dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267) |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

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

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

| | |
|------------------|-----------------------|
| Arm title | Arm B: TPV/PR in GT1a |
|------------------|-----------------------|

Arm description:

Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and

weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a)

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Telaprevir |
| Investigational medicinal product code | |
| Other name | INCIVO® |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

TPV 375 mg film-coated tablets, to be taken orally as 2 tablets every 8 hours, which corresponds to 750 mg TPV dose every 8 hours. Alternative dosing schedules for TPV (1,125 mg every 12 hours) were allowed per the prescribing information and only if approved by AbbVie.

| | |
|--|--|
| Investigational medicinal product name | Peginterferon alfa-2a |
| Investigational medicinal product code | |
| Other name | Pegasys® |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegylated interferon α-2a in kits of 1 prefilled syringe with 180 µg/0.5 mL per syringe. PegIFN was administered as an SC injection once per week.

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

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

| | |
|------------------|----------------------------|
| Arm title | Arm C: 3-DAA + RBV in GT1b |
|------------------|----------------------------|

Arm description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-450/r/ABT-267 |
| Investigational medicinal product code | |
| Other name | Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

| | |
|--|---|
| Investigational medicinal product name | ABT-333 |
| Investigational medicinal product code | |
| Other name | dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267) |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

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

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

| | |
|------------------|----------------------|
| Arm title | Arm D: 3-DAA in GT1b |
|------------------|----------------------|

Arm description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-450/r/ABT-267 |
| Investigational medicinal product code | |
| Other name | Viekirax, Viekira Pak (with ABT-333), Holkira Pak (with ABT-333), ABT-267 also known as ombitasvir, ABT-450 also known as paritaprevir |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-450/r/ABT-267 was to be taken orally as 2 tablets QD, which corresponds to a 150 mg ABT-450/100 mg ritonavir/25 mg ABT-267 dose QD.

| | |
|--|---|
| Investigational medicinal product name | ABT-333 |
| Investigational medicinal product code | |
| Other name | dasabuvir, Viekira Pak (with ABT-450/r/ABT-267), Holkira Pak (with ABT-450/r/ABT-267) |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-333 was to be taken orally as 1 tablet BID, which corresponds to a 250 mg dose BID.

| | |
|------------------|-----------------------|
| Arm title | Arm E: TPV/PR in GT1b |
|------------------|-----------------------|

Arm description:

Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b)

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Telaprevir |
| Investigational medicinal product code | |
| Other name | INCIVO® |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

TPV 375 mg film-coated tablets, to be taken orally as 2 tablets every 8 hours, which corresponds to 750 mg TPV dose every 8 hours. Alternative dosing schedules for TPV (1,125 mg every 12 hours) were allowed per the prescribing information and only if approved by AbbVie.

| | |
|--|--|
| Investigational medicinal product name | Peginterferon alfa-2a |
| Investigational medicinal product code | |
| Other name | Pegasys® |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegylated interferon α-2a in kits of 1 prefilled syringe with 180 µg/0.5 mL per syringe. PegIFN was

administered as an SC injection once per week.

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

Dosage and administration details:

Ribavirin has weight-based dosing 1,000 to 1,200 mg divided BID per prescribing information. Subjects weighing < 75 kg took RBV orally as 2 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,000 mg total daily dose. Subjects weighing ≥ 75 kg took RBV orally as 3 tablets in the morning and 3 tablets in the evening, which corresponds to a 1,200 mg total daily dose.

| Number of subjects in period 1 | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b |
|---------------------------------------|-----------------------------------|------------------------------|-----------------------------------|
| Started | 69 | 34 | 84 |
| Completed | 63 | 31 | 82 |
| Not completed | 6 | 3 | 2 |
| Withdrew Consent | - | 1 | - |
| To enter another AbbVie study | 1 | - | - |
| Not Specified | - | 1 | 1 |
| Adverse event | 1 | - | - |
| Lost to follow-up | 4 | 1 | 1 |

| Number of subjects in period 1 | Arm D: 3-DAA in GT1b | Arm E: TPV/PR in GT1b |
|---------------------------------------|-----------------------------|------------------------------|
| Started | 83 | 41 |
| Completed | 80 | 39 |
| Not completed | 3 | 2 |
| Withdrew Consent | 1 | - |
| To enter another AbbVie study | - | 1 |
| Not Specified | - | - |
| Adverse event | - | 1 |
| Lost to follow-up | 2 | - |

Baseline characteristics

Reporting groups

| | |
|---|----------------------------|
| Reporting group title | Arm A: 3-DAA + RBV in GT1a |
| Reporting group description: ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a) | |
| Reporting group title | Arm B: TPV/PR in GT1a |
| Reporting group description: Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a) | |
| Reporting group title | Arm C: 3-DAA + RBV in GT1b |
| Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b) | |
| Reporting group title | Arm D: 3-DAA in GT1b |
| Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b) | |
| Reporting group title | Arm E: TPV/PR in GT1b |
| Reporting group description: Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b) | |

| Reporting group values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b |
|--|----------------------------|-----------------------|----------------------------|
| Number of subjects | 69 | 34 | 84 |
| Age, Customized Units: participants | | | |
| < 55 years | 46 | 23 | 59 |
| >= 55 years | 23 | 11 | 25 |
| Age Continuous Units: years | | | |
| arithmetic mean | 46.1 | 44.5 | 46.2 |
| standard deviation | ± 12.25 | ± 14.1 | ± 11.34 |
| Gender, Male/Female Units: participants | | | |
| Female | 21 | 17 | 46 |
| Male | 48 | 17 | 38 |

| Reporting group values | Arm D: 3-DAA in GT1b | Arm E: TPV/PR in GT1b | Total |
|--|----------------------|-----------------------|-------|
| Number of subjects | 83 | 41 | 311 |
| Age, Customized Units: participants | | | |
| < 55 years | 60 | 31 | 219 |
| >= 55 years | 23 | 10 | 92 |

| | | | |
|---|-----------------|-----------------|-----|
| Age Continuous Units: years arithmetic mean standard deviation | 47.1 ± 11.33 | 45.9 ± 10.78 | - |
| Gender, Male/Female Units: participants | | | |
| Female | 43 | 24 | 151 |
| Male | 40 | 17 | 160 |

End points

End points reporting groups

| | |
|---|----------------------------|
| Reporting group title | Arm A: 3-DAA + RBV in GT1a |
| Reporting group description: ABT-450/ritonavir (r)/ABT-267 150 mg/100 mg/25 mg once daily (QD) and ABT-333 250 mg twice daily (BID) and weight-based ribavirin (RBV) for 12 weeks (3 direct-acting antivirals [DAAs] with RBV in genotype [GT] 1a) | |
| Reporting group title | Arm B: TPV/PR in GT1a |
| Reporting group description: Telaprevir (TPV) 750 mg every 8 hours (q8h) and pegylated interferon (pegIFN) 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV (PR) according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1a) | |
| Reporting group title | Arm C: 3-DAA + RBV in GT1b |
| Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks (3 DAAs with RBV in GT1b) | |
| Reporting group title | Arm D: 3-DAA in GT1b |
| Reporting group description: ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks (3 DAAs without RBV in GT1b) | |
| Reporting group title | Arm E: TPV/PR in GT1b |
| Reporting group description: Telaprevir 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir (telaprevir with pegIFN/RBV in GT1b) | |

Primary: Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment (SVR12) - Primary Efficacy Analyses

| | |
|--|---|
| End point title | Percentage of Subjects With Sustained Virologic Response 12 Weeks After Treatment (SVR12) - Primary Efficacy Analyses |
| 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. | |
| End point type | Primary |
| End point timeframe: 12 weeks after the last actual dose of active study drug | |

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|-------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 34 | 84 | 83 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 97.1 | 82.4 | 98.8 | 97.6 |

| | | | | |
|-------------------------------|-----------------------|--|--|--|
| End point values | Arm E: TPV/PR in GT1b | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 78 | | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference |
| Point estimate | 19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.4 |
| upper limit | 32.6 |

Notes:

[1] - The primary endpoint assessment comparison was made within each of the 2 HCV genotypes (GT1a and GT1b). Within HCV GT1a, the 3-DAA + RBV and TPV/PR arms were compared. Within HCV GT1b, the 3-DAA and TPV/PR arms were compared. The test treatment arm was considered noninferior to the TPV/PR arm in the respective HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Arm B: TPV/PR in GT1a v Arm A: 3-DAA + RBV in GT1a |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Difference |
| Point estimate | 14.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.3 |
| upper limit | 28.2 |

Notes:

[2] - The primary endpoint assessment comparison was made within each of the 2 HCV genotypes (GT1a and GT1b). Within HCV GT1a, the 3-DAA + RBV and TPV/PR arms were compared. Within HCV GT1b, the 3-DAA and TPV/PR arms were compared. The test treatment arm was considered noninferior to the TPV/PR arm in the respective HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Secondary: Mean Change From Baseline to the Final Treatment Visit in Short-Form 36 Version 2 Health Status Survey (SF-36V2) Mental Component Summary (MCS)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline to the Final Treatment Visit in Short-Form 36 Version 2 Health Status Survey (SF-36V2) Mental Component Summary (MCS) |
|-----------------|---|

End point description:

SF-36V2 is a generic 36-item questionnaire measuring health-related quality of life (HRQoL) covering 2 summary measures: physical component summary (PCS) and MCS; it consists of 8 subscales. The MCS is represented by 4 subscales: vitality, social function, role limitations due to emotional problems, and mental health. Subjects self-report on items in a subscale that have choices per item. Scoring is done for both MCS subscale scores and summary scores; for each, the range is 0 (worst HRQoL) to 100 (best HRQoL).

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

End point timeframe:

From Day 1 of treatment up to 12 weeks for Arms A, C and D and up to 24 or 48 weeks for Arms B and E

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|--------------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 32 | 84 | 83 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -4.2 (± 10.59) | -5.8 (± 12.18) | -0.3 (± 8.89) | -0.1 (± 7.73) |

| End point values | Arm E: TPV/PR in GT1b | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -6.4 (± 11.78) | | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.351 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 2.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.39 |
| upper limit | 6.65 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.28 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean of Difference |
| Point estimate | 5.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.19 |
| upper limit | 9.47 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.84 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean of Difference |
| Point estimate | 5.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.01 |
| upper limit | 8.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.65 |

Secondary: Mean Change From Baseline to the Final Treatment Visit in SF-36V2 Physical Component Summary (PCS)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline to the Final Treatment Visit in SF-36V2 Physical Component Summary (PCS) |
|-----------------|--|

End point description:

SF-36V2 is a generic 36-item questionnaire measuring HRQoL covering 2 summary measures: PCS and MCS; it consists of 8 subscales. The PCS is represented by 4 subscales: physical function, role limitations due to physical problems, bodily pain, and general health perception. Subjects self-report on items in a subscale that have choices per item. Scoring is done for both PCS subscale scores and summary scores; for each, the range is 0 (worst HRQoL) to 100 (best HRQoL).

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Day 1 of treatment up to 12 weeks for Arms A, C and D and up to 24 or 48 weeks for Arms B and E | |

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|--------------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 32 | 84 | 83 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 0.5 (± 8.63) | -5.5 (± 8.26) | 0.4 (± 5.8) | 2.2 (± 4.34) |

| End point values | Arm E: TPV/PR in GT1b | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -5.5 (± 11.46) | | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 6.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.72 |
| upper limit | 9.44 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.69 |

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|--|
| Comparison groups | Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 6.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.36 |
| upper limit | 9.37 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.27 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least Squares Mean Difference |
| Point estimate | 6.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.55 |
| upper limit | 8.85 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.34 |

Secondary: Percentage of Subjects With SVR12 - Secondary Efficacy Analyses

| | |
|--|---|
| End point title | Percentage of Subjects With SVR12 - Secondary Efficacy Analyses |
| End point description: The percentage of subjects with sustained virologic response (plasma HCV RNA level < LLOQ) 12 weeks after the last dose of study drug. | |
| End point type | Secondary |
| End point timeframe: 12 weeks after the last actual dose of active study drug | |

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|-------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 34 | 84 | 83 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 97.1 | 82.4 | 98.8 | 97.6 |

| End point values | Arm E: TPV/PR in GT1b | | | |
|-------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 78 | | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.021 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 7.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.4 |
| upper limit | 38 |

| Statistical analysis title | Statistical Analysis 2 |
|---|--|
| Comparison groups | Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Difference |
| Point estimate | 20.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.9 |
| upper limit | 33.6 |

Notes:

[3] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 28.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.3 |
| upper limit | 241.1 |

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 4 |
| Comparison groups | Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | Cochran-Mantel-Haenszel |
| Confidence interval | |
| sides | 2-sided |

Secondary: Percentage of Subjects with Virologic Failure During Treatment

| | |
|--|--|
| End point title | Percentage of Subjects with Virologic Failure During Treatment |
| End point description: | |
| Subjects in Arms A, C or D demonstrating any of the following were considered virologic failures and discontinued therapy: | |
| <ul style="list-style-type: none">• Confirmed increase from nadir in HCV RNA (defined as 2 consecutive HCV RNA measurements of >1 log₁₀ IU/mL above nadir) at any time point during treatment• Failure to achieve HCV RNA < LLOQ by Week 6 or• Confirmed HCV RNA ≥ LLOQ (defined as 2 consecutive HCV RNA measurements ≥ LLOQ) at any point after HCV RNA < LLOQ during treatment after HCV RNA < LLOQ. | |
| Subjects in Arms B and E followed virologic stopping criteria described in the TPV Summary of Product Characteristics; they were considered virologic failures and discontinued therapy as follows: | |
| <ul style="list-style-type: none">• HCV RNA > 1000 IU/mL at Week 4 to Week 12, discontinue TPV and pegIFN and RBV• HCV RNA > 1000 IU/mL at Week 12, discontinue pegIFN and RBV• Confirmed HCV RNA > lower limit of detection (LLOD) at Week 24, discontinue pegIFN and RBV• Confirmed HCV RNA > LLOD at Week 36, discontinue pegIFN and RBV. | |
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks for Arms A, C and D and 24 weeks or 48 weeks for Arms B and E | |

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|-------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 34 | 84 | 83 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 2.9 | 5.9 | 0 | 1.2 |

| End point values | Arm E: TPV/PR in GT1b | | | |
|-------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 12.2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Post-treatment Relapse

| | |
|--|--|
| End point title | Percentage of Subjects with Post-treatment Relapse |
| End point description: Hepatitis C virus (HCV) ribonucleic acid (RNA) confirmed greater than or equal to the lower limit of quantification (LLOQ) between the end of treatment and 24 weeks post treatment among subjects completing treatment and with HCV RNA less than the LLOQ at the end of treatment. | |
| End point type | Secondary |
| End point timeframe: Within 24 weeks post treatment | |

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|-------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 66 ^[4] | 28 ^[5] | 84 ^[6] | 81 ^[7] |
| Units: percentage of subjects | | | | |
| number (not applicable) | 0 | 0 | 1.2 | 0 |

Notes:

[4] - subjects with sustained virologic response at Week 24 (SVR24)

[5] - subjects with sustained virologic response at Week 24 (SVR24)

[6] - subjects with sustained virologic response at Week 24 (SVR24)

[7] - subjects with sustained virologic response at Week 24 (SVR24)81

| End point values | Arm E: TPV/PR in GT1b | | | |
|------------------|-----------------------|--|--|--|
|------------------|-----------------------|--|--|--|

| | | | | |
|-------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 ^[8] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 6.3 | | | |

Notes:

[8] - subjects with sustained virologic response at Week 24 (SVR24)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Virologic Response 24 Weeks After Treatment (SVR24)

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Sustained Virologic Response 24 Weeks After Treatment (SVR24) |
|-----------------|---|

End point description:

The percentage of subjects with sustained virologic response (plasma HCV RNA level < LLOQ) 24 weeks after the last dose of study drug.

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

End point timeframe:

24 weeks after the last actual dose of active study drug

| End point values | Arm A: 3-DAA + RBV in GT1a | Arm B: TPV/PR in GT1a | Arm C: 3-DAA + RBV in GT1b | Arm D: 3-DAA in GT1b |
|-------------------------------|----------------------------|-----------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 69 | 34 | 84 | 83 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 95.7 | 82.4 | 97.6 | 97.6 |

| End point values | Arm E: TPV/PR in GT1b | | | |
|-------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 78 | | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Arm A: 3-DAA + RBV in GT1a v Arm B: TPV/PR in GT1a |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[9] |
| Parameter estimate | Difference |
| Point estimate | 13.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 27 |

Notes:

[9] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1a HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Arm D: 3-DAA in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[10] |
| Parameter estimate | Difference |
| Point estimate | 19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.4 |
| upper limit | 32.6 |

Notes:

[10] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Arm C: 3-DAA + RBV in GT1b v Arm E: TPV/PR in GT1b |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[11] |
| Parameter estimate | Difference |
| Point estimate | 19.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.5 |
| upper limit | 32.7 |

Notes:

[11] - The test treatment arm was considered noninferior to the TPV/PR arm in the GT1b HCV subtype if the lower bound of the 2-sided 95% CI for the treatment arm difference was above the noninferiority margin of -10.5%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) collected from time of study drug administration until 30 days following discontinuation or completion of study drug administration, up to 96 weeks. Serious AEs collected from signing of informed consent until study completion.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | 3 DAA + RBV |
|-----------------------|-------------|

Reporting group description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID and weight-based RBV for 12 weeks

| | |
|-----------------------|--------------------|
| Reporting group title | TPV + PEGIFN + RBV |
|-----------------------|--------------------|

Reporting group description:

TPV 750 mg q8h and pegIFN 180 µg/week and weight-based RBV for 12 weeks followed by an additional 12 or 36 weeks of pegIFN and weight based RBV according to response guided therapy per the prescribing information for telaprevir

| | |
|-----------------------|-------|
| Reporting group title | 3 DAA |
|-----------------------|-------|

Reporting group description:

ABT-450/r/ABT-267 150 mg/100 mg/25 mg QD and ABT-333 250 mg BID for 12 weeks

| Serious adverse events | 3 DAA + RBV | TPV + PEGIFN + RBV | 3 DAA |
|---|-----------------|--------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 9 / 75 (12.00%) | 0 / 83 (0.00%) |
| number of deaths (all causes) | 2 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 75 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| ACCIDENTAL OVERDOSE | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|-----------------|----------------|----------------|
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 2 / 75 (2.67%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| RETINOPATHY | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| HAEMATOCHESIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| TOXIC SKIN ERUPTION | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CELLULITIS | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 75 (1.33%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | 3 DAA + RBV | TPV + PEGIFN + RBV | 3 DAA |
|---|--------------------|--------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 100 / 153 (65.36%) | 74 / 75 (98.67%) | 29 / 83 (34.94%) |
| Nervous system disorders | | | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 2 / 153 (1.31%) | 6 / 75 (8.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 2 | 6 | 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 7 / 153 (4.58%) | 13 / 75 (17.33%) | 2 / 83 (2.41%) |
| occurrences (all) | 7 | 14 | 2 |
| HEADACHE | | | |
| subjects affected / exposed | 41 / 153 (26.80%) | 23 / 75 (30.67%) | 16 / 83 (19.28%) |
| occurrences (all) | 48 | 30 | 17 |
| LETHARGY | | | |
| subjects affected / exposed | 6 / 153 (3.92%) | 4 / 75 (5.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 6 | 4 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 10 / 153 (6.54%) | 32 / 75 (42.67%) | 1 / 83 (1.20%) |
| occurrences (all) | 12 | 47 | 1 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 4 / 75 (5.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 14 / 75 (18.67%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 17 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |

| | | | |
|-----------------------------|-------------------|------------------|----------------|
| subjects affected / exposed | 11 / 153 (7.19%) | 15 / 75 (20.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 16 | 18 | 2 |
| CHILLS | | | |
| subjects affected / exposed | 3 / 153 (1.96%) | 7 / 75 (9.33%) | 3 / 83 (3.61%) |
| occurrences (all) | 3 | 7 | 3 |
| FATIGUE | | | |
| subjects affected / exposed | 21 / 153 (13.73%) | 23 / 75 (30.67%) | 4 / 83 (4.82%) |
| occurrences (all) | 21 | 25 | 5 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 3 / 153 (1.96%) | 7 / 75 (9.33%) | 1 / 83 (1.20%) |
| occurrences (all) | 3 | 7 | 1 |
| INJECTION SITE ERYTHEMA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 5 / 75 (6.67%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 4 / 153 (2.61%) | 16 / 75 (21.33%) | 2 / 83 (2.41%) |
| occurrences (all) | 5 | 17 | 2 |
| Eye disorders | | | |
| VISION BLURRED | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 5 / 75 (6.67%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 5 | 1 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 3 / 153 (1.96%) | 6 / 75 (8.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 3 | 7 | 1 |
| ANAL PRURITUS | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 10 / 75 (13.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 11 | 0 |
| ANORECTAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 4 / 75 (5.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 8 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 15 / 153 (9.80%) | 12 / 75 (16.00%) | 7 / 83 (8.43%) |
| occurrences (all) | 19 | 12 | 8 |
| DRY MOUTH | | | |

| | | | |
|--|-------------------------|------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 5 / 153 (3.27%) 5 | 4 / 75 (5.33%) 4 | 0 / 83 (0.00%) 0 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed occurrences (all) | 0 / 153 (0.00%) 0 | 4 / 75 (5.33%) 4 | 0 / 83 (0.00%) 0 |
| NAUSEA | | | |
| subjects affected / exposed occurrences (all) | 32 / 153 (20.92%) 37 | 30 / 75 (40.00%) 33 | 7 / 83 (8.43%) 7 |
| VOMITING | | | |
| subjects affected / exposed occurrences (all) | 11 / 153 (7.19%) 12 | 14 / 75 (18.67%) 17 | 1 / 83 (1.20%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed occurrences (all) | 11 / 153 (7.19%) 11 | 8 / 75 (10.67%) 8 | 1 / 83 (1.20%) 1 |
| DYSPNOEA | | | |
| subjects affected / exposed occurrences (all) | 7 / 153 (4.58%) 7 | 5 / 75 (6.67%) 5 | 0 / 83 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed occurrences (all) | 1 / 153 (0.65%) 1 | 10 / 75 (13.33%) 10 | 1 / 83 (1.20%) 1 |
| DRY SKIN | | | |
| subjects affected / exposed occurrences (all) | 3 / 153 (1.96%) 3 | 4 / 75 (5.33%) 5 | 1 / 83 (1.20%) 1 |
| ECZEMA | | | |
| subjects affected / exposed occurrences (all) | 1 / 153 (0.65%) 1 | 4 / 75 (5.33%) 5 | 0 / 83 (0.00%) 0 |
| ERYTHEMA | | | |
| subjects affected / exposed occurrences (all) | 1 / 153 (0.65%) 1 | 4 / 75 (5.33%) 4 | 0 / 83 (0.00%) 0 |
| PRURITUS | | | |
| subjects affected / exposed occurrences (all) | 19 / 153 (12.42%) 22 | 26 / 75 (34.67%) 30 | 5 / 83 (6.02%) 5 |
| RASH | | | |

| | | | |
|---|------------------------|------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 12 / 153 (7.84%) 13 | 17 / 75 (22.67%) 25 | 0 / 83 (0.00%) 0 |
| RASH PRURITIC subjects affected / exposed occurrences (all) | 1 / 153 (0.65%) 1 | 7 / 75 (9.33%) 11 | 0 / 83 (0.00%) 0 |
| Psychiatric disorders DEPRESSION subjects affected / exposed occurrences (all) | 3 / 153 (1.96%) 3 | 7 / 75 (9.33%) 7 | 0 / 83 (0.00%) 0 |
| INSOMNIA subjects affected / exposed occurrences (all) | 14 / 153 (9.15%) 14 | 7 / 75 (9.33%) 7 | 0 / 83 (0.00%) 0 |
| IRRITABILITY subjects affected / exposed occurrences (all) | 11 / 153 (7.19%) 11 | 7 / 75 (9.33%) 7 | 0 / 83 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) | 3 / 153 (1.96%) 3 | 6 / 75 (8.00%) 6 | 2 / 83 (2.41%) 2 |
| BACK PAIN subjects affected / exposed occurrences (all) | 4 / 153 (2.61%) 4 | 4 / 75 (5.33%) 5 | 1 / 83 (1.20%) 1 |
| MYALGIA subjects affected / exposed occurrences (all) | 7 / 153 (4.58%) 10 | 12 / 75 (16.00%) 17 | 2 / 83 (2.41%) 2 |
| Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all) | 13 / 153 (8.50%) 14 | 7 / 75 (9.33%) 8 | 4 / 83 (4.82%) 5 |
| UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all) | 10 / 153 (6.54%) 10 | 3 / 75 (4.00%) 3 | 1 / 83 (1.20%) 1 |
| URINARY TRACT INFECTION subjects affected / exposed occurrences (all) | 2 / 153 (1.31%) 2 | 5 / 75 (6.67%) 5 | 1 / 83 (1.20%) 1 |
| Metabolism and nutrition disorders | | | |

| | | | |
|-----------------------------|-----------------|------------------|----------------|
| DECREASED APPETITE | | | |
| subjects affected / exposed | 6 / 153 (3.92%) | 17 / 75 (22.67%) | 1 / 83 (1.20%) |
| occurrences (all) | 7 | 17 | 1 |
| HYPERTRIGLYCERIDAEMIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 4 / 75 (5.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 5 / 75 (6.67%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 4 / 75 (5.33%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 08 April 2013 | The purpose of this amendment was to: <ul style="list-style-type: none">• prohibit the use of hormonal contraceptives during study drug administration. |
| 18 June 2013 | The purpose of this amendment was to: <ul style="list-style-type: none">• specify screening criteria that should remain stable did not need to be re-tested if rescreening occurred within the initial 35-day screening window;• allow for additional rescreening if screening failure related to an eligibility criterion that was subsequently amended;• update Inclusion Criterion No. 3 to allow enrollment of subjects with a borderline pregnancy test result under certain circumstances;• amend Exclusion Criterion No. 9 to allow appropriate use of over-the-counter and prescription medication;• make minor language edits to clarify the eligibility criteria;• allow informed consent for optional samples to be performed at the Baseline Visit;• clarify language relating to pill-count requirements;• clarify that the IRT system should be used for drug accountability;• update the pregnancy section to be consistent with current AbbVie HCV safety language relating to pregnancy;• update addresses and contact details;• make minor edits for consistency and clarity throughout the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported