



Clinical trial results:

A Randomized, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Co-Administration of ABT-493 and ABT-530 (or ABT-493/ABT-530) With and Without Ribavirin in Adults With Chronic Hepatitis C Virus (HCV) Infection who Failed a Prior Direct-Acting Antiviral Agent (DAA)-Containing Therapy

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2015-002350-13 |
| Trial protocol | ES GB |
| Global end of trial date | 23 January 2017 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 15 December 2017 |
| First version publication date | 15 December 2017 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M15-410 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02446717 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AbbVie Deutschland GmbH & Co. KG |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact | Global Medical Services, Abbvie, 001 800-633-9110, |
| Scientific contact | Armen Asatryan, Abbvie, armen.asatryan@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 | 23 January 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 January 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the efficacy and safety of ABT-493 and ABT-530 with or without ribavirin (RBV) in participants with chronic hepatitis C virus, (HCV)-infection who previously failed treatment with a direct acting antiviral (DAA)-containing regimen.

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 | 23 April 2015 |
| 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 | Spain: 9 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | France: 9 |
| Country: Number of subjects enrolled | Australia: 24 |
| Country: Number of subjects enrolled | Puerto Rico: 3 |
| Country: Number of subjects enrolled | United States: 94 |
| Worldwide total number of subjects | 141 |
| EEA total number of subjects | 20 |

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) | 126 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a 42-day screening period.

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 |

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-493, ABT-530 |
| Investigational medicinal product code | |
| Other name | ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-493 (tablet) dosed with ABT-530 (tablet)

| | |
|------------------|-------|
| Arm title | ARM B |
|------------------|-------|

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-493, ABT-530 |
| Investigational medicinal product code | |
| Other name | ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-493 (tablet) dosed with ABT-530 (tablet)

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

Dosage and administration details:

Tablet

| | |
|------------------|-------|
| Arm title | ARM C |
|------------------|-------|

Arm description:
 ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-493, ABT-530 |
| Investigational medicinal product code | |
| Other name | ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, ABT-493/ABT-530 (ABT-493 coformulated with ABT-267) also known as MAVIRET |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-493 (tablet) dosed with ABT-530 (tablet)

| | |
|------------------|-------|
| Arm title | ARM D |
|------------------|-------|

Arm description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-493/ABT-530 |
| Investigational medicinal product code | |
| Other name | ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet; ABT-493 coformulated with ABT-530

| | |
|------------------|-------|
| Arm title | ARM E |
|------------------|-------|

Arm description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-493/ABT-530 |
| Investigational medicinal product code | |
| Other name | ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet; ABT-493 coformulated with ABT-530

| Number of subjects in period 1 | Arm A | ARM B | ARM C |
|---------------------------------------|-------|-------|-------|
| Started | 6 | 22 | 22 |
| Completed | 6 | 21 | 20 |
| Not completed | 0 | 1 | 2 |
| Adverse event | - | - | 1 |
| Lost to follow-up | - | 1 | 1 |
| Withdrew consent | - | - | - |

| Number of subjects in period 1 | ARM D | ARM E |
|---------------------------------------|-------|-------|
| Started | 44 | 47 |
| Completed | 43 | 46 |
| Not completed | 1 | 1 |
| Adverse event | - | - |
| Lost to follow-up | - | 1 |
| Withdrew consent | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|-------|
| Reporting group title | Arm A |
| Reporting group description: ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM B |
| Reporting group description: ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM C |
| Reporting group description: ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM D |
| Reporting group description: ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis. | |
| Reporting group title | ARM E |
| Reporting group description: ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis. | |

| Reporting group values | Arm A | ARM B | ARM C |
|------------------------------------|-------|-------|-------|
| Number of subjects | 6 | 22 | 22 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----------------|
| Age continuous Units: years arithmetic mean standard deviation | 53.5 ± 9.16 | 55.2 ± 6.29 | 58.5 ± 6.56 |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 2 | 4 |
| Male | 3 | 20 | 18 |

| Reporting group values | ARM D | ARM E | Total |
|------------------------------------|-------|-------|-------|
| Number of subjects | 44 | 47 | 141 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 55.6 ± 8.57 | 55.6 ± 8.31 | - |
| Gender categorical Units: Subjects | | | |
| Female | 13 | 14 | 36 |

| | | | |
|------|----|----|-----|
| Male | 31 | 33 | 105 |
|------|----|----|-----|

End points

End points reporting groups

| | |
|---|-------|
| Reporting group title | Arm A |
| Reporting group description: ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM B |
| Reporting group description: ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM C |
| Reporting group description: ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis. | |
| Reporting group title | ARM D |
| Reporting group description: ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis. | |
| Reporting group title | ARM E |
| Reporting group description: ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis. | |

Primary: Percentage of Participants With Sustained Virologic Response 12 Weeks Post-treatment (SVR12)

| | |
|--|---|
| End point title | Percentage of Participants With Sustained Virologic Response 12 Weeks Post-treatment (SVR12) ^[1] |
| End point description: SVR12 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 12 weeks after the last dose of study drug. Participants with missing data after backwards imputation were imputed as nonresponders. | |
| End point type | Primary |
| End point timeframe: 12 weeks after the last actual 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: Descriptive data are summarized for this end point per protocol.

| End point values | Arm A | ARM B | ARM C | ARM D |
|-----------------------------------|-------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[2] | 22 ^[3] | 22 ^[4] | 44 ^[5] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100 (61.0 to 100) | 95.5 (78.2 to 99.2) | 86.4 (66.7 to 95.3) | 88.6 (76.0 to 95.0) |

Notes:

[2] - Intent-to-treat population: all participants who received at least 1 dose of study drug

[3] - Intent-to-treat population: all participants who received at least 1 dose of study drug

[4] - Intent-to-treat population: all participants who received at least 1 dose of study drug

[5] - Intent-to-treat population: all participants who received at least 1 dose of study drug

| End point values | ARM E | | | |
|-----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 47 ^[6] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 91.5 (80.1 to 96.6) | | | |

Notes:

[6] - Intent-to-treat population: all participants who received at least 1 dose of study drug

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks Post-treatment (SVR4)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Sustained Virologic Response 4 Weeks Post-treatment (SVR4) |
|-----------------|--|

End point description:

SVR4 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 4 weeks after the last dose of study drug. Participants with missing data after backwards imputation were imputed as nonresponders.

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

End point timeframe:

4 weeks after the last actual dose of study drug

| End point values | Arm A | ARM B | ARM C | ARM D |
|-----------------------------------|-----------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[7] | 22 ^[8] | 22 ^[9] | 44 ^[10] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (61.0 to 100.0) | 95.5 (78.2 to 99.2) | 95.5 (78.2 to 99.2) | 90.9 (78.8 to 96.4) |

Notes:

[7] - ITT population

[8] - ITT population

[9] - ITT population

[10] - ITT population

| End point values | ARM E | | | |
|-----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 47 ^[11] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 91.5 (80.1 to 96.6) | | | |

Notes:

[11] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment Virologic Failure

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

End point description:

On-treatment virologic failure was defined as confirmed HCV RNA \geq 100 IU after HCV RNA < LLOQ during treatment; confirmed increase of > 1 log(subscript)10(subscript) IU/mL above the lowest value post-baseline in HCV RNA during treatment; or HCV RNA \geq LLOQ at end of treatment with at least 6 weeks of treatment.

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

End point timeframe:

Day 3, Treatment Weeks 1, 2, 4, 6, 8, 10, 12 (end of treatment for 12-week treatment arms), and 16 (end of treatment for 16-week treatment arm) or premature discontinuation from treatment

| End point values | Arm A | ARM B | ARM C | ARM D |
|-----------------------------------|-------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[12] | 22 ^[13] | 22 ^[14] | 44 ^[15] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 39.0) | 0.0 (0.0 to 14.9) | 4.5 (0.8 to 21.8) | 2.3 (0.4 to 11.8) |

Notes:

[12] - ITT population

[13] - ITT population

[14] - ITT population

[15] - ITT population

| End point values | ARM E | | | |
|-----------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 47 ^[16] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 8.5 (3.4 to 19.9) | | | |

Notes:

[16] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Post-treatment Relapse

| | |
|-----------------|--|
| End point title | Percentage of Participants With Post-treatment Relapse |
|-----------------|--|

End point description:

Post-treatment relapse was defined as confirmed HCV RNA \geq LLOQ between the end of treatment and 12 weeks after the last dose of study drug among participants with HCV RNA levels $<$ LLOQ at the end of treatment, excluding reinfection.

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

End point timeframe:

From the end of treatment through 12 weeks after the last dose of study drug

| End point values | Arm A | ARM B | ARM C | ARM D |
|-----------------------------------|-------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[17] | 21 ^[18] | 21 ^[19] | 43 ^[20] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 39.0) | 4.8 (0.8 to 22.7) | 0.0 (0.0 to 15.5) | 9.3 (3.7 to 21.6) |

Notes:

[17] - ITT population who completed treatment and had HCV RNA $<$ LLOQ at the final treatment visit

[18] - ITT population who completed treatment and had HCV RNA $<$ LLOQ at the final treatment visit

[19] - ITT population who completed treatment and had HCV RNA $<$ LLOQ at the final treatment visit

[20] - ITT population who completed treatment and had HCV RNA $<$ LLOQ at the final treatment visit

| End point values | ARM E | | | |
|-----------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 ^[21] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 8.2) | | | |

Notes:

[21] - ITT population who completed treatment and had HCV RNA $<$ LLOQ at the final treatment visit

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from the time of study drug administration until 30 days after the last dose of study drug (up to 20 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any AE or SAE with an onset date that is after the first dose of study drug until 30 days after the last dose of study drug and were collected whether elicited or spontaneously reported by the participant.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm A |
|-----------------------|-------|

Reporting group description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (80 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|-----------------------|-------|
| Reporting group title | ARM B |
|-----------------------|-------|

Reporting group description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD plus ribavirin (RBV) for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|-----------------------|-------|
| Reporting group title | ARM C |
|-----------------------|-------|

Reporting group description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in chronic HCV genotype 1- infected participants without cirrhosis.

| | |
|-----------------------|-------|
| Reporting group title | ARM D |
|-----------------------|-------|

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks in HCV genotypes 1- or 4-6- infected participants with or without cirrhosis.

| | |
|-----------------------|-------|
| Reporting group title | ARM E |
|-----------------------|-------|

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 16 weeks in HCV genotype 1- or 4-6- infected participants with or without cirrhosis.

| Serious adverse events | Arm A | ARM B | ARM C |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 22 (4.55%) | 0 / 22 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 22 (0.00%) | 0 / 22 (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 | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 22 (4.55%) | 0 / 22 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | ARM D | ARM E | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 2 / 47 (4.26%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 47 (2.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 47 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 47 (2.13%) | |
| 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 | Arm A | ARM B | ARM C |
|--|----------------|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 17 / 22 (77.27%) | 16 / 22 (72.73%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 5 / 22 (22.73%) | 8 / 22 (36.36%) |
| occurrences (all) | 1 | 7 | 9 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 22 (0.00%) 0 | 0 / 22 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 8 / 22 (36.36%) | 4 / 22 (18.18%) |
| occurrences (all) | 1 | 8 | 4 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 22 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 22 (9.09%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 2 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 22 (9.09%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 3 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 22 (4.55%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 22 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 22 (9.09%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 2 | 1 |
| Nausea | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 6 / 22 (27.27%) | 3 / 22 (13.64%) |
| occurrences (all) | 1 | 6 | 4 |
| Toothache | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 22 (0.00%) 0 | 2 / 22 (9.09%) 2 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 2 / 22 (9.09%) 3 | 1 / 22 (4.55%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 22 (13.64%) 3 | 0 / 22 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 22 (0.00%) 0 | 2 / 22 (9.09%) 2 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 22 (13.64%) 3 | 0 / 22 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 22 (4.55%) 1 | 2 / 22 (9.09%) 2 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 6 / 22 (27.27%) 6 | 0 / 22 (0.00%) 0 |
| Irritability subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 2 / 22 (9.09%) 2 | 0 / 22 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 0 / 22 (0.00%) 0 | 4 / 22 (18.18%) 5 |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 22 (0.00%) 0 | 0 / 22 (0.00%) 0 |
| Infections and infestations Nasopharyngitis | | | |

| | | | |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 22 (13.64%) 3 | 1 / 22 (4.55%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 22 (4.55%) 1 | 1 / 22 (4.55%) 1 |
| Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 22 (0.00%) 0 | 0 / 22 (0.00%) 0 |

| Non-serious adverse events | ARM D | ARM E | |
|--|----------------------|------------------------|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 23 / 44 (52.27%) | 27 / 47 (57.45%) | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 6 / 44 (13.64%) 8 | 11 / 47 (23.40%) 11 | |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 0 / 47 (0.00%) 0 | |
| Lethargy subjects affected / exposed occurrences (all) | 3 / 44 (6.82%) 3 | 1 / 47 (2.13%) 1 | |
| Somnolence subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 0 / 47 (0.00%) 0 | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 3 / 47 (6.38%) 6 | |
| Fatigue subjects affected / exposed occurrences (all) | 3 / 44 (6.82%) 3 | 5 / 47 (10.64%) 5 | |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 0 / 47 (0.00%) 0 | |

| | | | | |
|---|----------------------------------|----------------|----------------|--|
| Gastrointestinal disorders | Constipation | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 4 / 47 (8.51%) | |
| | occurrences (all) | 0 | 4 | |
| | Diarrhoea | | | |
| | subjects affected / exposed | 2 / 44 (4.55%) | 2 / 47 (4.26%) | |
| | occurrences (all) | 2 | 2 | |
| | Dyspepsia | | | |
| | subjects affected / exposed | 2 / 44 (4.55%) | 4 / 47 (8.51%) | |
| | occurrences (all) | 2 | 4 | |
| | Faeces discoloured | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 0 / 47 (0.00%) | |
| | occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | Flatulence | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 0 / 47 (0.00%) | |
| | occurrences (all) | 0 | 0 | |
| | Gastrooesophageal reflux disease | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 1 / 47 (2.13%) | |
| | occurrences (all) | 0 | 1 | |
| | Nausea | | | |
| | subjects affected / exposed | 4 / 44 (9.09%) | 3 / 47 (6.38%) | |
| | occurrences (all) | 5 | 4 | |
| | Toothache | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 0 / 47 (0.00%) | |
| | occurrences (all) | 0 | 0 | |
| Skin and subcutaneous tissue disorders | Cough | | | |
| | subjects affected / exposed | 1 / 44 (2.27%) | 0 / 47 (0.00%) | |
| | occurrences (all) | 1 | 0 | |
| | Dyspnoea | | | |
| | subjects affected / exposed | 1 / 44 (2.27%) | 0 / 47 (0.00%) | |
| | occurrences (all) | 1 | 0 | |
| | Oropharyngeal pain | | | |
| | subjects affected / exposed | 0 / 44 (0.00%) | 2 / 47 (4.26%) | |
| | occurrences (all) | 0 | 2 | |
| | | | | |
| Skin and subcutaneous tissue disorders | | | | |

| | | | |
|---|---------------------|---------------------|--|
| Pruritus subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 2 / 47 (4.26%) 2 | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 2 / 47 (4.26%) 2 | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 44 (4.55%) 2 | 2 / 47 (4.26%) 2 | |
| Irritability subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 2 / 47 (4.26%) 2 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 2 / 47 (4.26%) 2 | |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 0 / 47 (0.00%) 0 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 1 / 47 (2.13%) 1 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | 4 / 47 (8.51%) 4 | |
| Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | 0 / 47 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 23 March 2015 | The main purpose of this amendment was to update the dosage strength of ABT-530 from 120 mg QD to 80 mg QD in treatment Arm A and of ABT-493 from 200 mg QD to 300 mg QD in treatment Arm B; clarify inclusion criterion (permitted prior direct acting antiviral agent [DAA] treatment); clarify the definition of on-treatment failure in DAA-experienced subjects; and revise treatment extension (from additional 4 weeks [total duration of 16 weeks] to 12 weeks [total duration of 24 weeks], add ribavirin and sofosbuvir to the treatment regimen for the subjects to whom treatment extension criteria are applied, and classify NS3/4A/NS5A-experienced subjects as NS3/4A-experienced/NS5A-naïve for the purpose of treatment extension). |
| 24 April 2015 | The main purpose of this amendment was to update the definitions of on-treatment failure and post-treatment failure; clarify inclusion criteria (provide examples of prior DAA-containing therapies); update secondary objective to include evaluation of 2 dose levels of ABT-530; and clarify treatment extension criteria. |
| 16 June 2015 | The main purpose of this amendment was to clarify inclusion criteria (definition of true abstinence, clarify when additional assessments for liver cirrhosis need to be made based on the initial test results); stop enrollment in Arm A; update virologic stopping criterion (remove "Failure to achieve hepatitis C virus [HCV] ribonucleic acid [RNA] < LLOQ by Week 6"); and clarify adverse event (AE) collection period. |
| 10 September 2015 | The main purpose of this amendment was to add Part 2 of the study based upon meeting pre specified efficacy and safety criteria; include use of ABT-493/ABT-530 co-formulated tablet for Part 2; clarify rescreening for Part 2; update inclusion criteria (remove upper age limit for inclusion in Part 2; allow enrollment of GT4, 5, and 6 in Part 2; specify acceptable methods of contraception in Parts 1 and 2; clarify the accepted definitions of chronic HCV; specify eligible prior DAA regimens in Part 2; remove the upper BMI limit in Part 2; clarify accepted criteria of defining absence of cirrhosis and include criteria for defining presence of compensated cirrhosis in Part 2; exclude subjects with hepatocellular carcinoma [HCC] in Part 2) and exclusion criteria (exclude subjects with HCV RNA load of < 1000 IU/mL in Part 2); update prohibited therapy; clarify timing of study procedures; and clarify AE collection period. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported