



## Clinical trial results:

### A Single Arm, Open-label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Adults with Chronic Hepatitis C Virus Genotype 1, 2, 4, 5 or 6 Infection and Compensated Cirrhosis (EXPEDITION-1)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-003797-32   |
| Trial protocol           | DE BE ES         |
| Global end of trial date | 10 February 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 | M14-172 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02642432 |
| 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           | Joaquin Valdes, Abbvie, joaquin.m.valdes@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:

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**Results analysis stage**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 10 February 2017 |
| Is this the analysis of the primary completion data? | No               |

|                                  |                  |
|----------------------------------|------------------|
| Global end of trial reached?     | Yes              |
| Global end of trial date         | 10 February 2017 |
| Was the trial ended prematurely? | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of ABT-493/ABT-530 following 12 weeks of treatment in adults with chronic Hepatitis C Virus Infection genotype 1, 2, 4, 5 or 6 infection and compensated 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                          | 07 December 2015 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 29        |
| Country: Number of subjects enrolled | South Africa: 3   |
| Country: Number of subjects enrolled | United States: 69 |
| Country: Number of subjects enrolled | Spain: 17         |
| Country: Number of subjects enrolled | Belgium: 12       |
| Country: Number of subjects enrolled | Germany: 16       |
| Worldwide total number of subjects   | 146               |
| EEA total number of subjects         | 45                |

Notes:

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**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) | 105 |
| From 65 to 84 years  | 40  |
| 85 years and over    | 1   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

This study included a 35-day screening period.

### Period 1

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

### Arms

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | ABT-493/ABT-530 |
|------------------|-----------------|

Arm description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

|  |  |
|--|--|
| 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

| <b>Number of subjects in period 1</b> | ABT-493/ABT-530 |
|---------------------------------------|-----------------|
| Started                               | 146             |
| Completed                             | 138             |
| Not completed                         | 8               |
| Not specified                         | 3               |
| Adverse event                         | 2               |
| Withdrew consent                      | 1               |
| Lost to follow-up                     | 2               |

## Baseline characteristics

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | ABT-493/ABT-530 |
|-----------------------|-----------------|

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

| Reporting group values | ABT-493/ABT-530 | Total |  |
|------------------------|-----------------|-------|--|
| Number of subjects     | 146             | 146   |  |
| Age categorical        |                 |       |  |
| Units: Subjects        |                 |       |  |
| Age continuous         |                 |       |  |
| Units: years           |                 |       |  |
| arithmetic mean        | 60.12           |       |  |
| standard deviation     | ± 10.43         | -     |  |
| Gender categorical     |                 |       |  |
| Units: Subjects        |                 |       |  |
| Female                 | 56              | 56    |  |
| Male                   | 90              | 90    |  |

## End points

### End points reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | ABT-493/ABT-530 |
| Reporting group description:<br>ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks. |                 |

### 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) <sup>[1]</sup> |
|-----------------|---|

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.

|                                   |                      |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| <b>End point values</b>           | ABT-493/ABT-530      |  |  |  |
| Subject group type                | Reporting group      |  |  |  |
| Number of subjects analysed       | 146 <sup>[2]</sup>   |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (confidence interval 95%)  | 99.3 (98.0 to 100.0) |  |  |  |

Notes:

[2] - Intent-to-treat (ITT) 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 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 increase of  $> 1 \log(\text{subscript})_{10}(\text{subscript})$  IU/mL above the lowest value post-baseline HCV RNA during treatment; confirmed HCV RNA  $\geq 100$  IU/mL after HCV RNA  $< LLOQ$  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:

Treatment Weeks 1, 2, 4, 8, and 12 (end of treatment) or premature discontinuation from treatment

|                                   |                    |  |  |  |
|-----------------------------------|--------------------|--|--|--|
| <b>End point values</b>           | ABT-493/ABT-530    |  |  |  |
| Subject group type                | Reporting group    |  |  |  |
| Number of subjects analysed       | 146 <sup>[3]</sup> |  |  |  |
| Units: percentage of participants |                    |  |  |  |
| number (confidence interval 95%)  | 0 (0 to 2.6)       |  |  |  |

Notes:

[3] - All participants who received at least 1 dose of study drug (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 who completed treatment 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

|                                   |                    |  |  |  |
|-----------------------------------|--------------------|--|--|--|
| <b>End point values</b>           | ABT-493/ABT-530    |  |  |  |
| Subject group type                | Reporting group    |  |  |  |
| Number of subjects analysed       | 144 <sup>[4]</sup> |  |  |  |
| Units: percentage of participants |                    |  |  |  |
| number (confidence interval 95%)  | 0.7 (0.1 to 3.8)   |  |  |  |

Notes:

[4] - 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 16 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any AE or SAE event 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 | ABT-493/ABT-530 |
|-----------------------|-----------------|

Reporting group description:

ABT-493/ABT-530 (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

| Serious adverse events  | ABT-493/ABT-530  |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed   | 11 / 146 (7.53%) |  |  |
| number of deaths (all causes)                                       | 3                |  |  |
| number of deaths resulting from adverse events                      |                  |  |  |
| Investigations  |                  |  |  |
| Tumour marker increased   |                  |  |  |
| subjects affected / exposed   | 1 / 146 (0.68%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Hepatocellular carcinoma  |                  |  |  |
| subjects affected / exposed   | 2 / 146 (1.37%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 2            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Nervous system disorders  |                  |  |  |
| Syncope   |                  |  |  |
| subjects affected / exposed   | 1 / 146 (0.68%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Gastrointestinal disorders  |                  |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| Gastric ulcer                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Oesophageal varices haemorrhage                 |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Epistaxis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Alcohol abuse                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Rectal abscess                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary tract infection                         |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endophthalmitis                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Hyperglycaemia                                  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypoglycaemia                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

|   |                   |  |  |
|---|-------------------|--|--|
| <b>Non-serious adverse events</b>                     | ABT-493/ABT-530   |  |  |
| Total subjects affected by non-serious adverse events |                   |  |  |
| subjects affected / exposed                           | 63 / 146 (43.15%) |  |  |
| Nervous system disorders                              |                   |  |  |
| Headache  |                   |  |  |
| subjects affected / exposed                           | 20 / 146 (13.70%) |  |  |
| occurrences (all)                                     | 20                |  |  |
| General disorders and administration site conditions  |                   |  |  |
| Fatigue   |                   |  |  |
| subjects affected / exposed                           | 27 / 146 (18.49%) |  |  |
| occurrences (all)                                     | 27                |  |  |
| Gastrointestinal disorders                            |                   |  |  |
| Diarrhoea   |                   |  |  |
| subjects affected / exposed                           | 12 / 146 (8.22%)  |  |  |
| occurrences (all)                                     | 12                |  |  |
| Nausea  |                   |  |  |
| subjects affected / exposed                           | 13 / 146 (8.90%)  |  |  |
| occurrences (all)                                     | 14                |  |  |
| Skin and subcutaneous tissue disorders                |                   |  |  |
| Pruritus  |                   |  |  |
| subjects affected / exposed                           | 14 / 146 (9.59%)  |  |  |
| occurrences (all)                                     | 14                |  |  |
| Infections and infestations                           |                   |  |  |
| Urinary tract infection                               |                   |  |  |
| subjects affected / exposed                           | 9 / 146 (6.16%)   |  |  |
| occurrences (all)                                     | 11                |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 17 September 2015 | The main purpose of this amendment was to update the introduction with safety and efficacy data in cirrhotic subjects; update inclusion (clarify contraception use during the study, expand the categories of treatment-experienced subjects allowed [SOF plus RBV with or without pegIFN treatment failures]) and update the protocol to align with the addition of this subject population); and clarify the period of AE collection after completion of study treatment. |
| 23 November 2015  | The main purpose of this amendment was to update the introduction and benefit/risk sections with newly available safety and efficacy information; increase the number of genotype (GT) 5 and GT6 subjects to approximately 30 and the overall total number of subjects to approximately 175; update inclusion criteria (clarify contraception use during the study); and clarify that the primary analysis was to be conducted in the intent-to-treat (ITT) population.     |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported