



## Clinical trial results:

### An Open-Label, Single-Arm Study to Evaluate the Safety and Efficacy of Ombitasvir/ABT-450/Ritonavir and Dasabuvir in Adults with Genotype 1b Chronic Hepatitis C Virus (HCV) Infection and Cirrhosis (TURQUOISE-III)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-001953-18   |
| Trial protocol           | BE               |
| Global end of trial date | 06 November 2015 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 05 August 2016 |
| First version publication date | 05 August 2016 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | M14-490 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02219503 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | AbbVie Deutschland GmbH & Co. KG                                                                  |
| Sponsor organisation address | Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE |
| Public contact               | Global Medical Information, AbbVie, 001 800-633-9110,                                             |
| Scientific contact           | Roger Trinh, AbbVie, roger.trinh@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                       | 06 November 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 June 2015     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 06 November 2015 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and efficacy of ombitasvir/ paritaprevir/ ritonavir and dasabuvir in adults with genotype 1b chronic hepatitis C virus (HCV) infection and cirrhosis.

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 15 September 2014 |
| 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 | Belgium: 18       |
| Country: Number of subjects enrolled | Canada: 18        |
| Country: Number of subjects enrolled | United States: 24 |
| Worldwide total number of subjects   | 60                |
| EEA total number of subjects         | 18                |

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)                      | 45 |
| From 65 to 84 years                       | 15 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 60 subjects were enrolled and all the subjects completed the study. All 60 subjects were analyzed for both efficacy (included all subjects who received at least 1 dose of study drug (ITT)) and safety.

### 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> | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |
|------------------|--------------------------------------------------|

Arm description:

Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.

|                                        |                                                                                                    |
|----------------------------------------|----------------------------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                                       |
| Investigational medicinal product name | Ombitasvir/Paritaprevir/Ritonavir                                                                  |
| Investigational medicinal product code |                                                                                                    |
| Other name                             | ABT-267 also know as ombitasvir, ABT-450 also know as paritaprevir, Ritonavir also known as norvir |
| Pharmaceutical forms                   | Film-coated tablet                                                                                 |
| Routes of administration               | Oral use                                                                                           |

Dosage and administration details:

Ombitasvir/Paritaprevir/Ritonavir 25/150/100 mg milligram(s), administered for oral use.

|                                        |                    |
|----------------------------------------|--------------------|
| Investigational medicinal product name | Dasabuvir          |
| Investigational medicinal product code |                    |
| Other name                             | ABT-333            |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dasabuvir 500 mg milligram(s), administered for oral use

|                                       |                                                  |
|---------------------------------------|--------------------------------------------------|
| <b>Number of subjects in period 1</b> | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |
| Started                               | 60                                               |
| Completed                             | 60                                               |

## Baseline characteristics

### Reporting groups

|                                                                                                                            |                                                  |
|----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| Reporting group title                                                                                                      | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |
| Reporting group description:                                                                                               |                                                  |
| Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks. |                                                  |

| Reporting group values                             | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir | Total |  |
|----------------------------------------------------|--------------------------------------------------|-------|--|
| Number of subjects                                 | 60                                               | 60    |  |
| Age categorical                                    |                                                  |       |  |
| Units: Subjects                                    |                                                  |       |  |
| In utero                                           | 0                                                | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                                                | 0     |  |
| Newborns (0-27 days)                               | 0                                                | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                                                | 0     |  |
| Children (2-11 years)                              | 0                                                | 0     |  |
| Adolescents (12-17 years)                          | 0                                                | 0     |  |
| Adults (18-64 years)                               | 45                                               | 45    |  |
| From 65-84 years                                   | 15                                               | 15    |  |
| 85 years and over                                  | 0                                                | 0     |  |
| Age Continuous                                     |                                                  |       |  |
| Units: years                                       |                                                  |       |  |
| arithmetic mean                                    | 59.5                                             |       |  |
| standard deviation                                 | ± 9.53                                           | -     |  |
| Gender, Male/Female                                |                                                  |       |  |
| Units: participants                                |                                                  |       |  |
| Female                                             | 23                                               | 23    |  |
| Male                                               | 37                                               | 37    |  |
| Interleukin 28B (IL28B) Genotype                   |                                                  |       |  |
| Units: Subjects                                    |                                                  |       |  |
| CC                                                 | 10                                               | 10    |  |
| CT                                                 | 36                                               | 36    |  |
| TT                                                 | 14                                               | 14    |  |
| Missing                                            | 0                                                | 0     |  |

## End points

### End points reporting groups

|                                                                                                                                                            |                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| Reporting group title                                                                                                                                      | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |
| Reporting group description:<br>Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks. |                                                  |

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

|                                                                                                                                                                                                                                                  |                                                                                                         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                  | Percentage of Subjects With Sustained Virologic Response 12 Weeks (SVR12) Post-treatment <sup>[1]</sup> |
| End point description:<br>Sustained Virologic Response 12 (SVR12) is defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) less than the lower limit of quantification (< LLOQ; < 25 IU/mL) 12 weeks after the last dose of study drug. |                                                                                                         |
| End point type                                                                                                                                                                                                                                   | Primary                                                                                                 |
| End point timeframe:<br>Post-treatment Day 1 to Post-treatment Week 12                                                                                                                                                                           |                                                                                                         |

Notes:

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

Justification: The percentage of subjects (95% CI, calculated using Wilson score method) from post-treatment day 1 to post-treatment week 12 was 100 (94.0 to 100.0). Non-inferiority was to be declared if the lower confidence bound was greater than 72.7% and superiority was to be declared if the lower confidence bound was greater than 83.2%.

|                                   |                                                  |  |  |  |
|-----------------------------------|--------------------------------------------------|--|--|--|
| End point values                  | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |  |  |  |
| Subject group type                | Reporting group                                  |  |  |  |
| Number of subjects analysed       | 60                                               |  |  |  |
| Units: percentage of participants |                                                  |  |  |  |
| number (confidence interval 95%)  | 100 (94 to 100)                                  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with On-Treatment Virologic Failure

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Percentage of Subjects with On-Treatment Virologic Failure |
| End point description:<br>On-Treatment Virologic Failure is defined as confirmed HCV RNA $\geq$ LLOQ after HCV RNA < LLOQ during treatment, or confirmed increase from nadir (local minimum value) in HCV RNA [2 consecutive HCV RNA measurements > 1 log <sub>10</sub> IU/mL above nadir] at any time point during treatment, or failure to suppress during treatment [all on-treatment values of HCV RNA $\geq$ LLOQ] with at least 6 weeks [defined as active study drug duration $\geq$ 36 days] of treatment. |                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Secondary                                                  |

End point timeframe:  
Day 1 through Week 12

|                                   |                                                  |  |  |  |
|-----------------------------------|--------------------------------------------------|--|--|--|
| <b>End point values</b>           | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |  |  |  |
| Subject group type                | Reporting group                                  |  |  |  |
| Number of subjects analysed       | 60                                               |  |  |  |
| Units: percentage of participants |                                                  |  |  |  |
| number (confidence interval 95%)  | 0 (0 to 6)                                       |  |  |  |

### 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:<br>Post- Treatment Relapse is defined as confirmed HCV RNA >= LLOQ between end of treatment and 12 weeks after last actual dose of active study drug [up to and including the SVR12 assessment time point] for a subject with HCV RNA < LLOQ at Final Treatment Visit who completes treatment. |                                                    |
| End point type                                                                                                                                                                                                                                                                                                        | Secondary                                          |
| End point timeframe:<br>Post-treatment Day 1 to Post-treatment Week 12                                                                                                                                                                                                                                                |                                                    |

|                                   |                                                  |  |  |  |
|-----------------------------------|--------------------------------------------------|--|--|--|
| <b>End point values</b>           | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |  |  |  |
| Subject group type                | Reporting group                                  |  |  |  |
| Number of subjects analysed       | 60                                               |  |  |  |
| Units: percentage of participants |                                                  |  |  |  |
| number (confidence interval 95%)  | 0 (0 to 6)                                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from the time of study drug administration to 30 days after last dose of study drug (12 weeks); SAEs were also collected from the time that informed consent was obtained until the end of the study (up to 42 weeks).

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

### Dictionary used

|                    |      |
|--------------------|------|
| Dictionary name    | 18.0 |
| Dictionary version | 18.0 |

### Reporting groups

|                       |                                                  |
|-----------------------|--------------------------------------------------|
| Reporting group title | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |
|-----------------------|--------------------------------------------------|

Reporting group description:

Ombitasvir/Paritaprevir/Ritonavir (25/150/100 mg once daily) and Dasabuvir (250 mg twice daily) administered for 12 weeks.

|                                                   |                                                  |  |  |
|---------------------------------------------------|--------------------------------------------------|--|--|
| <b>Serious adverse events</b>                     | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |  |  |
| Total subjects affected by serious adverse events |                                                  |  |  |
| subjects affected / exposed                       | 1 / 60 (1.67%)                                   |  |  |
| number of deaths (all causes)                     | 0                                                |  |  |
| number of deaths resulting from adverse events    |                                                  |  |  |
| Vascular disorders                                |                                                  |  |  |
| HYPOTENSION                                       |                                                  |  |  |
| subjects affected / exposed                       | 1 / 60 (1.67%)                                   |  |  |
| occurrences causally related to treatment / all   | 1 / 1                                            |  |  |
| deaths causally related to treatment / all        | 0 / 0                                            |  |  |
| Nervous system disorders                          |                                                  |  |  |
| SYNCOPE                                           |                                                  |  |  |
| subjects affected / exposed                       | 1 / 60 (1.67%)                                   |  |  |
| occurrences causally related to treatment / all   | 1 / 1                                            |  |  |
| deaths causally related to treatment / all        | 0 / 0                                            |  |  |

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

|                                                       |                                                  |  |  |
|-------------------------------------------------------|--------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                     | Ombitasvir/Paritaprevir/Ritonavir plus Dasabuvir |  |  |
| Total subjects affected by non-serious adverse events |                                                  |  |  |
| subjects affected / exposed                           | 39 / 60 (65.00%)                                 |  |  |

|                                                                                                                                                                                                                                                                                                                    |                                                                                                         |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|--|--|
| Vascular disorders<br>HYPERTENSION<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                             | 3 / 60 (5.00%)<br>3                                                                                     |  |  |
| Nervous system disorders<br>DIZZINESS<br>subjects affected / exposed<br>occurrences (all)<br><br>HEADACHE<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                      | 6 / 60 (10.00%)<br>7<br><br>11 / 60 (18.33%)<br>11                                                      |  |  |
| General disorders and administration site conditions<br>FATIGUE<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                | 13 / 60 (21.67%)<br>13                                                                                  |  |  |
| Gastrointestinal disorders<br>ABDOMINAL PAIN UPPER<br>subjects affected / exposed<br>occurrences (all)<br><br>DIARRHOEA<br>subjects affected / exposed<br>occurrences (all)<br><br>DYSPEPSIA<br>subjects affected / exposed<br>occurrences (all)<br><br>NAUSEA<br>subjects affected / exposed<br>occurrences (all) | 3 / 60 (5.00%)<br>3<br><br>12 / 60 (20.00%)<br>13<br><br>4 / 60 (6.67%)<br>4<br><br>4 / 60 (6.67%)<br>5 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>COUGH<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                       | 4 / 60 (6.67%)<br>4                                                                                     |  |  |
| Skin and subcutaneous tissue disorders<br>PRURITUS<br>subjects affected / exposed<br>occurrences (all)<br><br>PRURITUS GENERALISED                                                                                                                                                                                 | 6 / 60 (10.00%)<br>6                                                                                    |  |  |

|                                                                                                                                                                                      |                                                 |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                     | 3 / 60 (5.00%)<br>3                             |  |  |
| Psychiatric disorders<br>INSOMNIA<br>subjects affected / exposed<br>occurrences (all)                                                                                                | 6 / 60 (10.00%)<br>6                            |  |  |
| Musculoskeletal and connective tissue disorders<br>ARTHRALGIA<br>subjects affected / exposed<br>occurrences (all)<br><br>MYALGIA<br>subjects affected / exposed<br>occurrences (all) | 6 / 60 (10.00%)<br>6<br><br>4 / 60 (6.67%)<br>4 |  |  |
| Infections and infestations<br>INFLUENZA<br>subjects affected / exposed<br>occurrences (all)<br><br>NASOPHARYNGITIS<br>subjects affected / exposed<br>occurrences (all)              | 4 / 60 (6.67%)<br>4<br><br>4 / 60 (6.67%)<br>4  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 01 July 2014      | The purpose of this amendment was to update inclusion/exclusion criteria and language related to hormonal contraceptives for female subjects of childbearing potential; update the way the date and time of the second-to-last dose and the date and time of last dose before each pharmacokinetic visit will be recorded; and to update Investigator Brochures version numbers for ombitasvir, paritaprevir, and dasabuvir in Reference section.                                                                                                                                                                                    |
| 17 September 2014 | The purpose of this amendment was to update the primary objective and primary endpoints to include comparison of the SVR12 rate of the ombitasvir/paritaprevir/r and dasabuvir treated subjects to a threshold based on the historical SVR12 rates of sofosbuvir plus pegIFN/RBV in the same patient population; to show the derivation of the thresholds on which the primary endpoints are based; to exclude sofosbuvir treatment-experienced patients; and to update determination of the sample size, to show the power of the study for the comparisons to the threshold based on the SVR12 rate of sofosbuvir plus pegIFN/RBV. |
| 02 March 2015     | The purpose of this amendment was to update the approximate number of subjects to be enrolled into the study; to align with the current product label; and to update exclusion criteria to clarify subject exclusion based on current or past clinical evidence of Child-Pugh B or C classification or clinical history of liver decompensation at time of screening.                                                                                                                                                                                                                                                                |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported