# Clinical trial results:
# A Single-Arm, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of ABT-493/ABT-530 in Adult Post-Liver or Post-Renal Transplant Recipients With Chronic Hepatitis C Virus Genotype 1 - 6 Infection (MAGELLAN-2)

## Summary

| | |
|---|---|
| EudraCT number | 2015-005616-14 |
| Trial protocol | GB ES |
| Global end of trial date | 29 June 2017 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 April 2018 |
| First version publication date | 19 April 2018 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | M13-596 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02692703 |
| 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, 011 800-633-9110, |
| Scientific contact | Susan Rhee, MD, AbbVie, susan.rhee@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 | 29 June 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 June 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 safety and efficacy of 12 weeks of treatment of ABT-493/ABT-530 (glecaprevir/
pibrentasvir) in adults who are post primary orthotopic liver or renal transplant with chronic hepatitis C virus (HCV) infection.

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 | 22 April 2016 |
| 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 | Australia: 8 |
| Country: Number of subjects enrolled | Canada: 9 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | New Zealand: 8 |
| Country: Number of subjects enrolled | Puerto Rico: 6 |
| Country: Number of subjects enrolled | Spain: 13 |
| Country: Number of subjects enrolled | Taiwan: 9 |
| Country: Number of subjects enrolled | United Kingdom: 16 |
| Country: Number of subjects enrolled | United States: 27 |
| Worldwide total number of subjects | 100 |
| EEA total number of subjects | 33 |

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) | 74 |
| From 65 to 84 years | 26 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study included a 36-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

| | |
|---|---|
| **Arm title** | Glecaprevir/Pibrentasvir |

Arm description:

Glecaprevir/pibrentasvir (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

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

Dosage and administration details:

glecaprevir coformulated with pibrentasvir

| **Number of subjects in period 1** | Glecaprevir/Pibrentasvir |
|---|---|
| Started | 100 |
| Completed | 98 |
| Not completed | 2 |
| Not specified | 1 |
| Lost to follow-up | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Glecaprevir/Pibrentasvir |
| Reporting group description: | |
| Glecaprevir/pibrentasvir (300 mg/120 mg) coformulated once daily (QD) for 12 weeks. | |

| Reporting group values | Glecaprevir/Pibrentasvir | Total | |
|---|---|---|---|
| Number of subjects | 100 | 100 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 59.19 | | |
| standard deviation | ± 7.68 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 25 | 25 | |
| Male | 75 | 75 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 17 | 17 | |
| Not Hispanic or Latino | 83 | 83 | |
| Unknown or Not Reported | 0 | 0 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 10 | 10 | |
| Native Hawaiian or Other Pacific Islander | 3 | 3 | |
| Black or African American | 8 | 8 | |
| White | 78 | 78 | |
| More than one race | 1 | 1 | |
| Unkown or Not Reported | 0 | 0 | |

## End points

### End points reporting groups

| Reporting group title | Glecaprevir/Pibrentasvir |
|---|---|
| Reporting group description: | |
| Glecaprevir/pibrentasvir (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)[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. The primary efficacy endpoint was noninferiority of the percentage of participants who achieved SVR12 compared with the historical SVR12 rate for the current standard of care regimens (sofosbuvir [SOF]/ledipasvir [LDV] + ribavirin [RBV] OR SOF + daclatasvir [DCV] + RBV). Participants with missing data after backward imputation were counted as non-responders. Based on a 2-sided significance level of 0.05 and an underlying rate of ≥96%, 90 participants provides >90% power to demonstrate noninferiority of the regimen to the historical rate for current standard of care regimens (94%) (based on the normal approximation of a single binomial proportion in a one-sample test for superiority). | |
| End point type | Primary |
| End point timeframe: | |
| 12 weeks after the last dose of study drug (up to 24 weeks) | |
| 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.<br>Justification: The lower confidence bound of the 2-sided 95% confidence interval (95% CI) for the percentage of participants with SVR12 must exceed 86% to achieve noninferiority. | |

| End point values | Glecaprevir/Pibrentasvir | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100[2] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 98 (95.3 to 100) | | | |

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(subscript)10(subscript) IU/mL above the<br>lowest value post-baseline in HCV RNA during treatment; confirmed HCV RNA ≥ 100 IU/mL after HCV RNA < LLOQ<br>during treatment; or HCV RNA ≥ LLOQ at end of treatment with at least 6 weeks of treatment. | |
| End point type | Secondary |

End point timeframe:

Up to 12 weeks

| End point values | Glecaprevir/Pibrentasvir | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100[3] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | | | |

Notes:

[3] - 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 ≥ 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.

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

End point timeframe:

From the end of treatment through 12 weeks after the last dose of study drug (up to 12 weeks)

| End point values | Glecaprevir/Pibrentasvir | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 99[4] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 1 | | | |

Notes:

[4] - ITT; completed treatment; HCV RNA <LLOQ at final treatment; data available; excluding reinfection

### 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 first dose of study drug until 30 days after the last dose of study drug (up to 16 weeks).

Adverse event reporting additional description:

TEAEs and SAEs are defined as any AE or SAE that begins or worsens in severity after initiation of study drug until 30 days after the last dose of study drug.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Glecaprevir/Pibrentasvir |

Reporting group description:

Glecaprevir/pibrentasvir (300 mg/120 mg) coformulated once daily (QD) for 12 weeks.

| Serious adverse events | Glecaprevir/Pibrentasvir | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| IMMUNOSUPPRESSANT DRUG LEVEL INCREASED | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LIVER FUNCTION TEST INCREASED | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| VASCULAR PSEUDOANEURYSM RUPTURED | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| ARTERIOVENOUS MALFORMATION | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| RENAL FAILURE | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RENAL IMPAIRMENT | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| GROIN INFECTION | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HEPATITIS E | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SEPSIS | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Glecaprevir/Pibrentasvir | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 67 / 100 (67.00%) | | |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 6 / 100 (6.00%) | | |
| occurrences (all) | 7 | | |
| HEADACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 22 / 100 (22.00%) | | |
| occurrences (all) | 26 | | |
| General disorders and administration site conditions | | | |
| FATIGUE | | | |
| subjects affected / exposed | 22 / 100 (22.00%) | | |
| occurrences (all) | 26 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | | |
| occurrences (all) | 5 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 10 / 100 (10.00%) | | |
| occurrences (all) | 11 | | |
| NAUSEA | | | |
| subjects affected / exposed | 12 / 100 (12.00%) | | |
| occurrences (all) | 13 | | |
| VOMITING | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | | |
| occurrences (all) | 8 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | | |
| occurrences (all) | 9 | | |
| Skin and subcutaneous tissue disorders | | | |
| PRURITUS | | | |
| subjects affected / exposed | 12 / 100 (12.00%) | | |
| occurrences (all) | 13 | | |
| Psychiatric disorders | | | |
| INSOMNIA | | | |
| subjects affected / exposed | 6 / 100 (6.00%) | | |
| occurrences (all) | 6 | | |
| Musculoskeletal and connective tissue disorders | | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | | |
| occurrences (all) | 7 | | |
| ARTHRALGIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 100 (7.00%) | | |
| occurrences (all) | 7 | | |
| Infections and infestations | | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | | |
| occurrences (all) | 10 | | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | | |
| occurrences (all) | 6 | | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | | |
| occurrences (all) | 10 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 26 May 2016 | The main purpose of this amendment was to include a comparison of the overall sustained virologic response at 12 weeks after treatment (SVR12) with a historical threshold for the current standard of care; increase enrollment to 90 subjects; and clarify study inclusion and exclusion criteria, study procedures, and timing (including adding mycophenolic acid as an allowed immunosuppressant medication). |
| 21 June 2016 | The main purpose of this amendment was to clarify cyclosporine dose adjustment during treatment for subjects requiring maintenance titration as per usual transplant standard of care and clarify that concurrent liver disease other than hepatitis C virus as an exclusionary criteria is applicable in the post-transplant period |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported