



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
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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
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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
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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 Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	59.19 ± 7.68	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	75	75	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	17	17	
Not Hispanic or Latino	83	83	
Unknown or Not Reported	0	0	
Race (NIH/OMB) 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]
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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 $\geq 96\%$, 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
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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.

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
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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 in HCV RNA during treatment; confirmed HCV RNA ≥ 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
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End point timeframe:

Up to 12 weeks

End point values	Glecaprevir/Pib rentasvir			
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
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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.

End point type	Secondary
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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/Pib rentasvir			
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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

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

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