



## Clinical trial results:

### A Single-Arm, Open-Label, Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Renally-Impaired Adults with Chronic Hepatitis C Virus Genotype 1 – 6 Infection (EXPEDITION-4)

#### Summary

EudraCT number	2015-002353-35
Trial protocol	GB BE GR IT
Global end of trial date	26 January 2017

#### Results information

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

#### Trial information

##### Trial identification

Sponsor protocol code	M15-462
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02651194
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	David Pugatch, Abbvie, david.pugatch@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	26 January 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 January 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the efficacy and safety of 12 weeks of treatment with the ABT-493/ABT-530 combination regimen in adults with chronic HCV genotype 1 - 6 infection and chronic severe renal impairment.

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	21 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Greece: 18
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	104
EEA total number of subjects	65

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	76
From 65 to 84 years	28
85 years and over	0

## 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
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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	104
Completed	99
Not completed	5
Not specified	2
Lost to follow-up	3

## Baseline characteristics

### Reporting groups

Reporting group title	ABT-493/ABT-530
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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	104	104	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	57.52		
standard deviation	± 11.14	-	
Gender categorical			
Units: Subjects			
Female	25	25	
Male	79	79	

## End points

### End points 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.	

### 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>
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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. Participants with missing data after backwards imputation were imputed as nonresponders.

End point type	Primary
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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	104 <sup>[2]</sup>			
Units: percentage of participants				
number (confidence interval 95%)	98.1 (95.4 to 100)			

Notes:

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With 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 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
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End point timeframe:

up to 12 weeks

<b>End point values</b>	ABT-493/ABT-530			
Subject group type	Reporting group			
Number of subjects analysed	104 <sup>[3]</sup>			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 3.6)			

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, excluding reinfection.

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

<b>End point values</b>	ABT-493/ABT-530			
Subject group type	Reporting group			
Number of subjects analysed	100 <sup>[4]</sup>			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 3.7)			

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 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	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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### Reporting groups

Reporting group title	ABT-493/ABT-530
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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	25 / 104 (24.04%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Patella fracture			



subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural haemorrhage			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Superior vena cava occlusion			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypertensive cardiomyopathy			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mitral valve stenosis			

subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Facial paresis			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haematoma			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal			

disorders			
Pulmonary oedema			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
End stage renal disease			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal haemorrhage			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			

subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected fistula			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal abscess			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			

subjects affected / exposed	1 / 104 (0.96%)		
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	54 / 104 (51.92%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 104 (6.73%)		
occurrences (all)	7		
Headache			
subjects affected / exposed	9 / 104 (8.65%)		
occurrences (all)	11		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 104 (9.62%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	15 / 104 (14.42%)		
occurrences (all)	16		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 104 (9.62%)		
occurrences (all)	11		
Nausea			
subjects affected / exposed	11 / 104 (10.58%)		
occurrences (all)	15		
Vomiting			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	6 / 104 (5.77%) 6		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	21 / 104 (20.19%) 27		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	9 / 104 (8.65%) 10		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2015	The main purpose of this amendment was to update the introduction and benefit/risk sections with newly available safety and efficacy information, clarify that all patient populations with severe renal-impairment were to be included, with the exception of GT3 noncirrhotic treatment-experienced subjects and GT3 cirrhotic subjects; and clarify assessments of concomitant medications.
17 March 2016	The main purpose of this amendment was to update inclusion (clarify contraception use during the study) and exclusion criteria (allow subjects on peritoneal dialysis, organ transplant if subject was stable without immunosuppressive medications); and clarify study procedures.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported