

**Clinical trial results:****An Open-Label, Single Arm Study to Evaluate the Safety and Efficacy of Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir in Treatment-Naïve Adults With Genotype 1b Hepatitis C Virus (HCV) Without Cirrhosis (GARNET)****Summary**

EudraCT number	2015-003370-33
Trial protocol	DE GB ES IT
Global end of trial date	01 December 2016

**Results information**

Result version number	v1 (current)
This version publication date	02 December 2017
First version publication date	02 December 2017

**Trial information****Trial identification**

Sponsor protocol code	M15-684
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02582632
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	Daniel E. Cohen, MD, AbbVie, 001 847-938-1494, daniel.cohen@abbvie.com
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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	01 December 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 December 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy (the percentage of subjects achieving SVR12 [HCV ribonucleic acid {RNA} < lower limit of quantification {LLOQ} 12 weeks following treatment]) of coformulated ombitasvir/paritaprevir/ritonavir and dasabuvir for 8 weeks in treatment-naïve adults with HCV GT1b infection without cirrhosis.

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 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	Canada: 17
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Israel: 21
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Spain: 27
Worldwide total number of subjects	166
EEA total number of subjects	111

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)	137
From 65 to 84 years	29
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Eligible subjects had up to 35 days following the Screening Visit to enroll into the study.

### 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 and Dasabuvir
Arm description:	ombitasvir/paritaprevir/ritonavir (25 mg/150 mg/100 mg once daily) and dasabuvir (250 mg twice daily) administered for 8 weeks
Arm type	Experimental
Investigational medicinal product name	Ombitasvir/Paritaprevir/Ritonavir 12.5 mg/75 mg/50 mg Film-Coated Tablets
Investigational medicinal product code	
Other name	ABT-267/ABT-450/r, ombitasvir also known as ABT-267, paritaprevir also known as ABT-450
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ombitasvir/paritaprevir/ritonavir will be taken orally as 2 tablets once daily which corresponds to a 25 mg ombitasvir/150 mg paritaprevir/100 mg ritonavir dose once daily.

Investigational medicinal product name	Dasabuvir 250 mg Film-Coated Tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Dasabuvir will be taken orally as 1 tablet twice daily, which corresponds to a 250 mg dose twice daily.

<b>Number of subjects in period 1</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir
Started	166
Completed	165
Not completed	1
Not specified	1



## Baseline characteristics

### Reporting groups

Reporting group title	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir
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Reporting group description:

ombitasvir/paritaprevir/ritonavir (25 mg/150 mg/100 mg once daily) and dasabuvir (250 mg twice daily) administered for 8 weeks

Reporting group values	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir	Total	
Number of subjects	166	166	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	51.3 ± 13.42	-	
Gender categorical Units: Subjects			
Female	94	94	
Male	72	72	

## End points

### End points reporting groups

Reporting group title	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir
Reporting group description:	ombitasvir/paritaprevir/ritonavir (25 mg/150 mg/100 mg once daily) and dasabuvir (250 mg twice daily) administered for 8 weeks

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

End point title	Percentage of Subjects Who Achieve Sustained Virologic Response 12 Weeks Post-treatment (SVR12) <sup>[1]</sup>
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End point description:

SVR12 is defined as hepatitis C virus (HCV) ribonucleic acid (RNA) < lower limit of quantification (LLOQ) 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

Intent to Treat population: all enrolled subjects who received at least 1 dose of study drug. Flanking imputation.

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 statistics and confidence interval are presented, per protocol.

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	166			
Units: percentage of subjects				
number (confidence interval 95%)	97.6 (95.3 to 99.9)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With On-Treatment Virologic Failure During Treatment Period

End point title	Percentage of Subjects With On-Treatment Virologic Failure During Treatment Period
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End point description:

On-treatment virologic failure is defined as breakthrough (confirmed HCV RNA  $\geq$  LLOQ after HCV RNA < LLOQ during treatment, or confirmed increase from nadir in HCV RNA (two consecutive HCV rna measurements  $> 1 \log^{10}$  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 study drug duration  $\geq 36$  days) of treatment. Confidence interval calculated using the normal approximation to the binomial distribution.

Intent to Treat population: all enrolled subjects who received at least 1 dose of study drug.

End point type	Secondary
End point timeframe:	
Up to 8 weeks while on treatment	

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	166			
Units: percentage of subjects				
number (confidence interval 95%)	0.6 (0.0 to 1.8)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Post-Treatment Relapse12

End point title	Percentage of Subjects With Post-Treatment Relapse12
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End point description:

Relapse12 is defined as confirmed HCV RNA  $\geq$  LLOQ between end of treatment and 12 weeks after last actual dose of active study drug (up to and including the SVR12 window) excluding reinfection among subjects with HCV RNA  $<$  LLOQ at final treatment visit who complete treatment and have post-treatment HCV RNA data. Completion of treatment is defined as a study drug duration  $\geq 51$  days for subjects who receive 8 weeks of treatment. HCV reinfection is defined as confirmed HCV RNA  $\geq$  LLOQ after the end of treatment in a subject who had HCV RNA  $<$  LLOQ at final treatment visit, along with the post treatment detection of a different HCV genotype, subtype, or clade compared with baseline, as determined by phylogenetic analysis of the NS3 or NS5A, and/or NS5B gene sequences. Confidence interval calculated using the normal approximation to the binomial distribution.

Intent to Treat population: all enrolled participants who received at least 1 dose of study drug.

End point type	Secondary
End point timeframe:	
Up to 12 weeks after last dose of study drug	

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: percentage of subjects				
number (confidence interval 95%)	1.2 (0.0 to 2.9)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Female Subjects Responding With SVR12

End point title	Percentage of Female Subjects Responding With SVR12
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End point description:

SVR12 is defined as HCV RNA < LLOQ 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

Intent to Treat population: all enrolled female subjects who received at least 1 dose of study drug. Flanking imputation.

End point type	Secondary
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End point timeframe:

12 weeks after the last actual dose of study drug

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	94			
Units: percentage of subjects				
number (confidence interval 95%)	97.9 (95.0 to 100.0)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Baseline HCV RNA < 6,000,000 IU/mL Responding With SVR12

End point title	Percentage of Subjects With Baseline HCV RNA < 6,000,000 IU/mL Responding With SVR12
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End point description:

SVR12 is defined as HCV RNA < LLOQ 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

Intent to Treat population: all enrolled subjects who received at least 1 dose of study drug and with baseline HCV RNA < 6,000,000 IU/mL. Flanking imputation.

End point type	Secondary
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End point timeframe:

Baseline and 12 weeks after the last actual dose of study drug

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: percentage of subjects				
number (confidence interval 95%)	98.1 (95.9 to 100.0)			

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Subjects Who Achieve SVR12: mITT-GT Population

End point title	Percentage of Subjects Who Achieve SVR12: mITT-GT Population
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End point description:

SVR12 is defined as HCV RNA < LLOQ 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

The modified ITT (mITT)-GT population includes subjects who received at least 1 dose of study drug but excludes the subjects who do not have HCV GT1b infection. Flanking imputation.

End point type	Other pre-specified
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End point timeframe:

12 weeks after the last actual dose of study drug

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: percentage of subjects				
number (confidence interval 95%)	98.2 (96.1 to 100.0)			

### Statistical analyses

No statistical analyses for this end point

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**Other pre-specified: Percentage of Subjects With On-Treatment Virologic Failure During Treatment Period: mITT-GT Population**

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End point title	Percentage of Subjects With On-Treatment Virologic Failure During Treatment Period: mITT-GT Population
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End point description:

On-treatment virologic failure is defined as breakthrough (confirmed HCV RNA  $\geq$  LLOQ after HCV RNA  $<$  LLOQ during treatment, or confirmed increase from nadir in HCV RNA (two consecutive HCV rna measurements  $>$   $1 \log^{10}$  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 study drug duration  $\geq$  36 days) of treatment. Confidence interval calculated using the Wilson score method.

The mITT-GT population includes subjects who received at least 1 dose of study drug but excludes the subjects who do not have HCV GT1b infection.

End point type	Other pre-specified
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End point timeframe:

Up to 8 weeks while on treatment

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<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 2.3)			

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**Statistical analyses**

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No statistical analyses for this end point

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**Other pre-specified: Percentage of Subjects With Post-Treatment Relapse12: mITT-GT Population**

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End point title	Percentage of Subjects With Post-Treatment Relapse12: mITT-GT Population
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End point description:

Relapse12 is defined as confirmed HCV RNA  $\geq$  LLOQ between end of treatment and 12 weeks after last actual dose of active study drug (up to and including the SVR12 window) excluding reinfection among subjects with HCV RNA  $<$  LLOQ at final treatment visit who complete treatment and have post-treatment HCV RNA data. Completion of treatment is defined as a study drug duration  $\geq$  51 days for subjects who receive 8 weeks of treatment. HCV reinfection is defined as confirmed HCV RNA  $\geq$  LLOQ after the end of treatment in a subject who had HCV RNA  $<$  LLOQ at final treatment visit, along with the post treatment detection of a different HCV genotype, subtype, or clade compared with baseline, as determined by phylogenetic analysis of the NS3 or NS5A, and/or NS5B gene sequences. Confidence interval calculated using the normal approximation to the binomial distribution. Subjects who did not complete treatment, had no post treatment data, or had HCV RNA  $\geq$  LLOQ at Final Treatment Visit were not included.

End point type	Other pre-specified
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End point timeframe:

Up to 12 weeks after last dose of study drug

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<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	161 <sup>[2]</sup>			
Units: percentage of subjects				
number (confidence interval 95%)	1.2 (0.0 to 3.0)			

Notes:

[2] - mITT population

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Female Subjects Responding With SVR12: mITT-GT Population

End point title	Percentage of Female Subjects Responding With SVR12: mITT-GT Population
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End point description:

SVR12 is defined as HCV RNA < LLOQ 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

The mITT-GT population includes subjects who received at least 1 dose of study drug but excludes the subjects who do not have HCV GT1b infection; female subjects. Flanking imputation.

End point type	Other pre-specified
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End point timeframe:

12 weeks after the last actual dose of study drug

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: percentage of subjects				
number (confidence interval 95%)	97.8 (94.9 to 100.0)			

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Subjects With Baseline HCV RNA < 6,000,000 IU/mL Responding With SVR12: mITT-GT Population

End point title	Percentage of Subjects With Baseline HCV RNA < 6,000,000 IU/mL Responding With SVR12: mITT-GT Population
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End point description:

SVR12 is defined as HCV RNA < LLOQ 12 weeks after the last dose of study drugs without any confirmed quantifiable ( $\geq$  LLOQ) post-treatment value before or during that SVR window. Confidence interval calculated using the normal approximation to the binomial distribution.

The mITT-GT population includes subjects who received at least 1 dose of study drug but excludes the subjects who do not have HCV GT1b infection; subjects with baseline HCV RNA < 6,000,000 IU/mL. Flanking imputation.

End point type	Other pre-specified
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End point timeframe:

Baseline and 12 weeks after the last actual dose of study drug

<b>End point values</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir			
Subject group type	Reporting group			
Number of subjects analysed	151			
Units: percentage of subjects				
number (confidence interval 95%)	98.7 (96.9 to 100.0)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs (TEAEs) were collected from first dose of study drug until 30 days after the last dose of study drug (up to 12 weeks); SAEs were collected from the time informed consent was obtained (up to 35 days prior to first dose of study drug)

Adverse event reporting additional description:

A TEAE is defined as any AE from the first dose of study drug to 30 days after the last dose.

Assessment type	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	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir
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Reporting group description:

ombitasvir/paritaprevir/ritonavir (25 mg/150 mg/100 mg once daily) and dasabuvir (250 mg twice daily) administered for 8 weeks

<b>Serious adverse events</b>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 166 (1.20%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 166 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 166 (0.60%)		
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>	Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir		
Total subjects affected by non-serious adverse events subjects affected / exposed	70 / 166 (42.17%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	35 / 166 (21.08%) 36		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)  Fatigue subjects affected / exposed occurrences (all)	9 / 166 (5.42%) 11  28 / 166 (16.87%) 30		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	11 / 166 (6.63%) 12		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	14 / 166 (8.43%) 15		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 166 (8.43%) 14		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported