



Clinical trial results:

An Open-Label Study to Evaluate the Safety and Efficacy of Ombitasvir/Paritaprevir/Ritonavir With or Without Dasabuvir in Adults With Genotype 1a or Genotype 4 Chronic Hepatitis C Virus (HCV) Infection, With Severe Renal Impairment or End-Stage Renal Disease (RUBY-II)

Summary

EudraCT number	2015-002012-33
Trial protocol	ES
Global end of trial date	05 December 2016

Results information

Result version number	v1 (current)
This version publication date	20 December 2017
First version publication date	20 December 2017

Trial information

Trial identification

Sponsor protocol code	M15-461
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02487199
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	Eric Cohen, MD, AbbVie, eric.cohen@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	05 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluates the efficacy and safety of ombitasvir/paritaprevir/ritonavir with or without dasabuvir in adults with hepatitis C virus (HCV) genotype 1a (GT1a) or genotype 4 (GT4) infection and with severe kidney impairment or end-stage kidney disease.

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	01 October 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	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	New Zealand: 4
Worldwide total number of subjects	18
EEA total number of subjects	9

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)	16
From 65 to 84 years	2

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a 42-day screening period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	HCV GT1a (3-DAA)

Arm description:

Participants with hepatitis C virus (HCV) genotype 1a (GT1a) infection received 3-direct-acting antiviral agent (3-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily] and dasabuvir [250 mg twice daily]) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ombitasvir/paritaprevir/ritonavir
Investigational medicinal product code	
Other name	Viekirax, ombitasvir also known as ABT-267, paritaprevir also known as ABT-450
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ombitasvir (25 mg) coformulated with paritaprevir (150 mg) and ritonavir (100 mg) twice daily

Investigational medicinal product name	dasabuvir
Investigational medicinal product code	
Other name	Exviera, ABT-333
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

dasabuvir 250 mg twice daily

Arm title	HCV GT4 (2-DAA)
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Arm description:

Participants with hepatitis C virus (HCV) genotype 4 (GT4) infection received 2-direct-acting antiviral agent (2-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	ombitasvir/paritaprevir/ritonavir
Investigational medicinal product code	
Other name	Viekirax, ombitasvir also known as ABT-267, paritaprevir also known as ABT-450
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ombitasvir (25 mg) coformulated with paritaprevir (150 mg) and ritonavir (100 mg) twice daily

Number of subjects in period 1	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)
Started	13	5
Completed	13	4
Not completed	0	1
Withdrew consent	-	1

Baseline characteristics

Reporting groups

Reporting group title	HCV GT1a (3-DAA)
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Reporting group description:

Participants with hepatitis C virus (HCV) genotype 1a (GT1a) infection received 3-direct-acting antiviral agent (3-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily] and dasabuvir [250 mg twice daily]) for 12 weeks.

Reporting group title	HCV GT4 (2-DAA)
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Reporting group description:

Participants with hepatitis C virus (HCV) genotype 4 (GT4) infection received 2-direct-acting antiviral agent (2-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) for 12 weeks.

Reporting group values	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)	Total
Number of subjects	13	5	18
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	54.8	53.6	
standard deviation	± 10	± 14.08	-
Gender categorical			
Units: Subjects			
Female	4	2	6
Male	9	3	12

End points

End points reporting groups

Reporting group title	HCV GT1a (3-DAA)
Reporting group description: Participants with hepatitis C virus (HCV) genotype 1a (GT1a) infection received 3-direct-acting antiviral agent (3-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily] and dasabuvir [250 mg twice daily]) for 12 weeks.	
Reporting group title	HCV GT4 (2-DAA)
Reporting group description: Participants with hepatitis C virus (HCV) genotype 4 (GT4) infection received 2-direct-acting antiviral agent (2-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) 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. Participants with missing data after backward imputation were imputed as nonresponders.	
End point type	Primary
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.

End point values	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: percentage of participants				
number (confidence interval 95%)	100 (77.2 to 100)	80.0 (37.6 to 96.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events ^[2]
End point description: An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either reasonable possibility or no reasonable possibility. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event	

that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity from first dose of study drug until 30 days after the last dose. For more details on AEs please see the Adverse Event section.

End point type	Primary
End point timeframe:	
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)	

Notes:

[2] - 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.

End point values	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[3]	5 ^[4]		
Units: participants				
Any TEAE	13	5		
Any TESAE	3	1		

Notes:

[3] - Safety population: All participants who received at least 1 dose of study drug.

[4] - Safety 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 HCV RNA $\geq$ LLOQ after HCV RNA $<$ LLOQ during treatment or confirmed increase of $> 1 \log(\text{subscript})_{10}(\text{subscript})$ IU/mL above the lowest value post-baseline in HCV RNA during treatment with at least 6 weeks of treatment.		
End point type	Secondary	
End point timeframe:		
12 weeks		

End point values	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	5		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 22.8)	0.0 (0.0 to 43.4)		

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

End point values	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[5]	4 ^[6]		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 22.8)	0 (0 to 49.0)		

Notes:

[5] - Participants received ≥ 1 dose, completed treatment, had HCV RNA $<$ LLOQ at the final treatment visit

[6] - Participants received ≥ 1 dose, completed treatment, 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 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 TESAEs are defined as any adverse event or serious adverse event 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	19.1
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Reporting groups

Reporting group title	HCV GT1a (3-DAA)
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Reporting group description:

Participants with hepatitis C virus (HCV) genotype 1a (GT1a) infection received 3-direct-acting antiviral agent (3-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily] and dasabuvir [250 mg twice daily]) for 12 weeks.

Reporting group title	HCV GT4 (2-DAA)
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Reporting group description:

Participants with hepatitis C virus (HCV) genotype 4 (GT4) infection received 2-direct-acting antiviral agent (2-DAA: ombitasvir/paritaprevir/ritonavir [25 mg/150 mg/100 mg once daily]) for 12 weeks.

Serious adverse events	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)	1 / 5 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			

subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
End stage renal disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Folliculitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HCV GT1a (3-DAA)	HCV GT4 (2-DAA)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	5 / 5 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 13 (15.38%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Chest pain			

subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	3 / 13 (23.08%)	1 / 5 (20.00%)	
occurrences (all)	4	1	
Oedema peripheral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Euphoric mood			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Insomnia			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	0 / 5 (0.00%) 0	
Sleep disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Investigations Transaminases increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 5 (20.00%) 1	
Nervous system disorders Burning sensation subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 5 (20.00%) 1	
Dizziness subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 5	0 / 5 (0.00%) 0	
Sciatica subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Vision blurred subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	3 / 13 (23.08%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 13 (15.38%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	4 / 13 (30.77%)	0 / 5 (0.00%)	
occurrences (all)	6	0	
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 13 (15.38%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	4 / 13 (30.77%)	0 / 5 (0.00%)	
occurrences (all)	6	0	
Salivary gland calculus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 13 (15.38%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			

Dermatitis contact subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	0 / 5 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Swelling face subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Endocrine disorders Cushing's syndrome subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Hyperparathyroidism subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 5 (20.00%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Muscular weakness subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 5 (20.00%) 1	
Neck pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 5 (0.00%) 0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Kidney infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported