Clinical trial results:
An Open-Label, Multicenter Study to Evaluate the Pharmacokinetics, Safety, and Efficacy of Ombitasvir (OBV), Paritaprevir (PTV), Ritonavir (RTV) With or Without Dasabuvir (DSV) and With or Without Ribavirin (RBV) in Pediatric Subjects With Genotype 1 or 4 Chronic Hepatitis C Virus (HCV) Infection (ZIRCON)

Summary

EudraCT number	2015-000111-41
Trial protocol	ES DE BE IT
Global end of trial date	19 November 2020

Results information

Result version number	v1 (current)
This version publication date	14 May 2021
First version publication date	14 May 2021

Trial information

Trial identification

Sponsor protocol code	M14-748

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02486406
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 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001440-PIP01-13, EMEA-001439-PIP01-13
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 November 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a Phase 2/3, open-label, multicenter study to evaluate the pharmacokinetics (PK), efficacy, and safety of ombitasvir/paritaprevir/ritonavir (OBV/PTV/RTV) with or without dasabuvir (DSV) and with or without ribavirin (RBV) in Hepatitis C virus (HCV) genotype 1 or 4 (GT1 or GT4)-infected pediatric subjects of ≥ 3 to 17 years of age. The study population for Part 1, the PK study, included GT1-infected subjects who were noncirrhotic and treatment-naïve (TN). Part 2, the safety and efficacy study, included GT-1 or GT4-infected subjects ≥ 12 to 17 yrs old who were TN or interferon ([IFN] or Pegylated-interferon alfa-2a or 2b [pegIFN] with or without RBV) treatment-experienced (TE) without cirrhosis or with compensated cirrhosis. In Part 1 and Part 2, the treatment regimen and duration were dependent on HCV GT, GT1 subtype, and cirrhosis status.

Protection of trial subjects:

The investigator or his/her representative explained the nature of the study to the subject's parent(s)/legal guardian(s) and answered all questions regarding the study. Pediatric subjects were to be included in all the discussions in order to obtain written assent. Prior to any study-related screening procedures being performed on the subject, the informed consent statement was to be reviewed and signed and dated by subject's parent(s)/legal guardian(s) and the person who administered the informed consent, and any other signatories according to local requirements. Additionally, in keeping with each institution's IEC requirements, if applicable, an informed assent form will also to be obtained by each subject, as appropriate for age and country, prior to any study-related procedures being performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 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	Puerto Rico: 2
Country: Number of subjects enrolled	United States: 44
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Spain: 9
Worldwide total number of subjects	64
EEA total number of subjects	18

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)	26
Adolescents (12-17 years)	38
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Safety population: all participants who received at least one dose of study drug in Part 1 or Part 2

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	Adult tablet, 12-17 yr, Part 1

Arm description:

Participants with HCV GT1b without cirrhosis received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75 mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label.

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

Dosage and administration details:

Participants received the adult OBV/PTV/RTV formulation: two 12.5 mg ombitasvir /75 mg paritaprevir/50 mg ritonavir tablets taken orally every morning (QD) for 12 weeks.

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	
Other name	Exviera, ABT-333
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin 200 mg tablets were administered orally for 12 weeks per local label for those participants with HCV GT1a.

Arm title	Adult tablet, 12-17 yr, Part 2

Arm description:

Participants with HCV GT1b received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one

dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT1a with compensated cirrhosis received 24-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT4 received 12-week treatment with the OBV/PTV/RTV formulation and ribavirin 200 mg tablets were administered orally per local label.

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

Dosage and administration details:

Participants received the adult OBV/PTV/RTV formulation: two 12.5 mg ombitasvir /75 mg paritaprevir/50 mg ritonavir tablets taken orally every morning (QD) for 12 weeks (HCV GT1b, GT1a without cirrhosis, and GT4) or 24 weeks (HCV GT1a with compensated cirrhosis).

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	
Other name	Exviera, ABT-333
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks (HCV GT1b, GT1a without cirrhosis) or 24 weeks (HCV GT1a with compensated cirrhosis).

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin 200 mg tablets were administered orally per local label for 12 weeks (HCV GT1a without cirrhosis and GT4) or 24 weeks (HCV GT1a with compensated cirrhosis).

Arm title	Mini tablet, 9-11 yr, Part 1

Arm description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir
Investigational medicinal product code	
Other name	ABT-267
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 0.3 mg mini-tablet formulation for 12 weeks, administered orally QD based on body weight.

Investigational medicinal product name	Paritaprevir
Investigational medicinal product code	
Other name	ABT-450

Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 1.0 mg mini-tablet formulation for 12 weeks, administered orally QD based on body weight.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 1.0 mg mini-tablet formulation for 12 weeks, administered orally QD based on body weight.

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	
Other name	Exviera, ABT-333
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 3.08 mg mini-tablet formulation for 12 weeks, administered orally BID based on body weight.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants with HCV GT1a received 40 mg/mL oral solution administered per local label for 12 weeks.

Arm title	Mini tablet, 3-8 yr, Part 1

Arm description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Arm type	Experimental
Investigational medicinal product name	Ombitasvir
Investigational medicinal product code	
Other name	ABT-267
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 0.3 mg mini-tablet formulation for 12 weeks, administered orally QD based on body weight.

Investigational medicinal product name	Paritaprevir
Investigational medicinal product code	
Other name	ABT-450
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 1.0 mg mini-tablet formulation for 12 weeks, administered orally QD based on

body weight.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 1.0 mg mini-tablet formulation for 12 weeks, administered orally QD based on body weight.

Investigational medicinal product name	Dasabuvir
Investigational medicinal product code	
Other name	Exviera, ABT-333
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received the 3.08 mg mini-tablet formulation for 12 weeks, administered orally BID based on body weight.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants with HCV GT1a received 40 mg/mL oral solution administered per local label for 12 weeks.

Number of subjects in period 1	Adult tablet, 12-17 yr, Part 1	Adult tablet, 12-17 yr, Part 2	Mini tablet, 9-11 yr, Part 1
Started	12	26	12
Completed	10	23	10
Not completed	2	3	2
Other, not specified	-	-	1
Withdrew consent	1	-	-
Lost to follow-up	1	3	1

Number of subjects in period 1	Mini tablet, 3-8 yr, Part 1
Started	14
Completed	10
Not completed	4
Other, not specified	-
Withdrew consent	1
Lost to follow-up	3

Baseline characteristics

Reporting groups	
Reporting group title	Adult tablet, 12-17 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75 mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Adult tablet, 12-17 yr, Part 2

Reporting group description:

Participants with HCV GT1b received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT1a with compensated cirrhosis received 24-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT4 received 12-week treatment with the OBV/PTV/RTV formulation and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Mini tablet, 9-11 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Reporting group title	Mini tablet, 3-8 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Reporting group values	Adult tablet, 12-17 yr, Part 1	Adult tablet, 12-17 yr, Part 2	Mini tablet, 9-11 yr, Part 1
Number of subjects	12	26	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15.4	15.0	9.8
standard deviation	± 1.73	± 1.68	± 0.83
Gender categorical Units: Subjects			
Female	9	16	6
Male	3	10	6

Reporting group values	Mini tablet, 3-8 yr, Part 1	Total	
Number of subjects	14	64	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	4.8		
standard deviation	± 1.67	-	
Gender categorical Units: Subjects			
Female	11	42	
Male	3	22	

End points

End points reporting groups

Reporting group title	Adult tablet, 12-17 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75 mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Adult tablet, 12-17 yr, Part 2

Reporting group description:

Participants with HCV GT1b received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT1a with compensated cirrhosis received 24-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT4 received 12-week treatment with the OBV/PTV/RTV formulation and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Mini tablet, 9-11 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Reporting group title	Mini tablet, 3-8 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Subject analysis set title	15 – 29 kg body weight
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in Part 1 of the study who weighed between 15-29 kg at the time of enrollment

Subject analysis set title	30 – 44 kg body weight
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in Part 1 of the study who weighed between 30-44 kg at the time of enrollment

Subject analysis set title	≥ 45 kg body weight
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in Part 1 of the study who weighed ≥ 45 kg at the time of enrollment

Subject analysis set title	Participants in Parts 1 and 2 of the study
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in Parts 1 and 2 who were part of the ITT population (those who received at least one dose of study drug in Part 1 or Part 2)

Subject analysis set title	Adult tablet, 12-17 YR, ≥ 45 kg

Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 12-17 years old who received the adult formulation and weighed ≥ 45 kg	
Subject analysis set title	Mini-tablet, 9-11 YR, 15 to 29 kg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 9-11 years old who received the mini-tablet formulation and weighed 15 to 29 kg	
Subject analysis set title	Mini-tablet, 9-11 YR, 30 to 44 kg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 9-11 years old who received the mini-tablet formulation and weighed 30 to 44 kg	
Subject analysis set title	Mini-tablet, 9-11 YR, ≥ 45 kg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 9-11 years old who received the mini-tablet formulation and weighed ≥ 45 kg	
Subject analysis set title	Mini-tablet, 3-8 YR, 15 to 29 kg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 3-8 years old who received the mini-tablet formulation and weighed 15 to 29 kg	
Subject analysis set title	Mini-tablet total
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants who received the mini-tablet formulation	
Subject analysis set title	Adult tablet,12-17 YR, ≥ 45 kg, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 12-17 years old with alanine aminotransferase > upper limit of normal at baseline who received the adult formulation and weighed ≥ 45 kg	
Subject analysis set title	Mini-tablet, 9-11 YR, 15 to 29 kg, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 9-11 years old with alanine aminotransferase > upper limit of normal at baseline who received the mini-tablet formulation and weighed 15 to 29 kg	
Subject analysis set title	Mini-tablet, 9-11 YR, 30 to 44 kg, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 9-11 years old with alanine aminotransferase > upper limit of normal at baseline who received the mini-tablet formulation and weighed 30 to 44 kg	
Subject analysis set title	Mini-tablet, 3-8 YR, 15 to 29 kg, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants age 3-8 years old with alanine aminotransferase > upper limit of normal at baseline who received the mini-tablet formulation and weighed 15 to 29 kg	
Subject analysis set title	Mini-tablet total, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants with alanine aminotransferase > upper limit of normal at baseline who received the mini-tablet formulation	
Subject analysis set title	Participants in Parts 1 and 2 of the study, ALT normalization
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants with with alanine aminotransferase > upper limit of normal at baseline	

Primary: Part 1: Maximum plasma concentration (Cmax) of ombitasvir (OBV)

End point title	Part 1: Maximum plasma concentration (Cmax) of ombitasvir (OBV)[1]

End point description:

Cmax is the peak concentration that a drug or drug metabolite achieves in a specified compartment after the drug has been administrated and before administration of a second dose.

End point type	Primary

End point timeframe:

At Week 2

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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[2]	9[3]	13[4]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	99.6 (± 27)	116 (± 14)	83.7 (± 39)	

Notes:

[2] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[3] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[4] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Maximum plasma concentration (Cmax) of paritaprevir (PTV)

End point title	Part 1: Maximum plasma concentration (Cmax) of paritaprevir (PTV)[5]

End point description:

Cmax is the peak concentration that a drug or drug metabolite achieves in a specified compartment after the drug has been administrated and before administration of a second dose.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[5] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[6]	9[7]	13[8]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	294 (± 152)	1540 (± 71)	870 (± 125)	

Notes:

[6] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[7] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[8] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Lowest plasma concentration (Ctrough) of ombitasvir (OBV)

End point title	Part 1: Lowest plasma concentration (Ctrough) of ombitasvir (OBV)[9]

End point description:

Minimum plasma concentration (C trough; measured in ng/mL) was directly determined from the concentration-time data.

End point type	Primary

End point timeframe:

At Weeks 2 and 8

Notes:

[9] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[10]	8[11]	12[12]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 2 (n= 12, 8, 12)	24.7 (± 32)	28.2 (± 16)	21.8 (± 39)	
Week 8 (n= 11, 7, 11)	29.6 (± 78)	30.4 (± 24)	20.9 (± 58)	

Notes:

[10] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[11] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[12] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of ombitasvir (OBV)

End point title	Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of ombitasvir (OBV)[13]

End point description:

AUC is a measure of how long and how much drug is present in the body after dosing. The amount of ombitasvir present was measured up to 24 hours after dosing.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[13] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[14]	8[15]	12[16]	
Units: ng•h/mL				
geometric mean (geometric coefficient of variation)	1270 (± 26)	1490 (± 12)	1060 (± 43)	

Notes:

[14] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[15] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[16] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of ritonavir (RTV)

End point title	Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of ritonavir (RTV)[17]

End point description:

AUC is a measure of how long and how much drug is present in the body after dosing. The amount of ritonavir present was measured up to 24 hours after dosing.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[17] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[18]	9[19]	12[20]	
Units: ng•h/mL				
geometric mean (geometric coefficient of variation)	6570 (± 60)	14100 (± 49)	8900 (± 37)	

Notes:

[18] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[19] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[20] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Maximum plasma concentration (Cmax) of dasabuvir (DSV)

End point title	Part 1: Maximum plasma concentration (Cmax) of dasabuvir (DSV)[21]

End point description:

Cmax is the peak concentration that a drug or drug metabolite achieves in a specified compartment after the drug has been administrated and before administration of a second dose.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[21] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[22]	9[23]	13[24]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	579 (± 44)	830 (± 45)	671 (± 48)	

Notes:

[22] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[23] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[24] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of paritaprevir (PTV)

End point title	Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of paritaprevir (PTV)[25]

End point description:

AUC is a measure of how long and how much drug is present in the body after dosing. The amount of paritaprevir present was measured up to 24 hours after dosing.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[25] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[26]	8[27]	12[28]	
Units: ng•h/mL				
geometric mean (geometric coefficient of variation)	2180 (± 136)	8640 (± 90)	5770 (± 152)	

Notes:

[26] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[27] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[28] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Lowest plasma concentration (Ctrough) of dasabuvir (DSV)

End point title	Part 1: Lowest plasma concentration (Ctrough) of dasabuvir (DSV)[29]

End point description:

Minimum plasma concentration (C trough; measured in ng/mL) was directly determined from the concentration-time data.

End point type	Primary

End point timeframe:

At Weeks 2 and 8

Notes:

[29] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[30]	9[31]	13[32]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 2 (n= 12, 9, 13)	110 (± 57)	215 (± 54)	165 (± 56)	
Week 8 (n= 12, 7 ,11)	168 (± 82)	264 (± 65)	191 (± 60)	

Notes:

[30] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[31] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[32] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of dasabuvir (DSV)

End point title	Part 1: Concentration of drug in blood plasma over time [Area under the curve (AUC)] of dasabuvir (DSV)[33]

End point description:

AUC is a measure of how long and how much drug is present in the body after dosing. The amount of dasabuvir present was measured up to 12 hours after dosing. For two subjects in the 15-29 kg group, the 24 h concentration was used as the 12 h concentration due to the significant sampling time deviation. For one subject in the 30-44 kg group, the 24 h concentration was used as the 12 h concentration due to the significant sampling time deviation.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[33] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[34]	9[35]	13[36]	
Units: ng•h/mL				
geometric mean (geometric coefficient of variation)	3960 (± 44)	5960 (± 47)	4630 (± 49)	

Notes:

[34] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[35] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[36] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Maximum plasma concentration (Cmax) of ritonavir (RTV)

End point title	Part 1: Maximum plasma concentration (Cmax) of ritonavir (RTV)[37]

End point description:

Cmax is the peak concentration that a drug or drug metabolite achieves in a specified compartment after the drug has been administrated and before administration of a second dose.

End point type	Primary

End point timeframe:

At Week 2

Notes:

[37] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[38]	9[39]	13[40]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1090 (± 67)	1830 (± 42)	1180 (± 35)	

Notes:

[38] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[39] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[40] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Lowest plasma concentration (Ctrough) of paritaprevir (PTV)

End point title	Part 1: Lowest plasma concentration (Ctrough) of paritaprevir (PTV)[41]

End point description:

Minimum plasma concentration (C trough; measured in ng/mL) was directly determined from the concentration-time data.

End point type	Primary

End point timeframe:

At Weeks 2 and 8

Notes:

[41] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[42]	8[43]	12[44]	
Units: : ng/mL				
geometric mean (geometric coefficient of variation)				
Week 2 (n= 12, 8, 12)	9.86 (± 113)	16.1 (± 112)	18.0 (± 78)	
Week 8 (n= 12, 7 ,11)	17.3 (± 136)	18.4 (± 89)	23.5 (± 86)	

Notes:

[42] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[43] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

[44] - ITT: all subjects who received at least one dose of study drug in Part 1 with available data

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Lowest plasma concentration (Ctrough) of ritonavir (RTV)

End point title	Part 1: Lowest plasma concentration (Ctrough) of ritonavir (RTV)[45]

End point description:

Minimum plasma concentration (C trough; measured in ng/mL) was directly determined from the concentration-time data.

End point type	Primary

End point timeframe:

At Weeks 2 and 8

Notes:

[45] - 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: Per protocol no statistical analyses are planned for pharmacokinetic endpoints

End point values	15 – 29 kg body weight	30 – 44 kg body weight	≥ 45 kg body weight	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[46]	9[47]	12[48]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 2 (n= 12, 9, 12)	16.1 (± 72)	32.1 (± 63)	29.8 (± 54)	
Week 8 (n= 12, 7 ,11)	91.8 (± 268)	38.1 (± 112)	58.2 (± 138)	

Notes:

[46] - The statistical analysis data per protocol are presented in the Endpoint Data Table.

[47] - The statistical analysis data per protocol are presented in the Endpoint Data Table.

[48] - The statistical analysis data per protocol are presented in the Endpoint Data Table.

Statistical analyses

No statistical analyses for this end point

Primary: Parts 1 and 2: Percentage of participants with sustained virologic response 12 weeks after the last actual dose of study drug (SVR12)

End point title	Parts 1 and 2: Percentage of participants with sustained virologic response 12 weeks after the last actual dose of study drug (SVR12)[49]

End point description:

SVR12 is defined as hepatitis C virus ribonucleic acid (HCV RNA) < lower limit of quantification (LLOQ) 12 weeks after the last actual dose of study drug.

End point type	Primary

End point timeframe:

12 weeks after last dose of study drug (Week 24 or 36 depending on treatment duration)

Notes:

[49] - 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: According to the Highlights of Prescribing Information of PEGASYS, the SVR24 rate was 47% among 45 treatment-naïve pediatric participants with HCV GT1 in the NV17424 trial. To show that the DAA regimen is superior to this current standard of care by 20%, the lower bound of the 2-sided 95% confidence interval of the SVR12 rate across all participants in the study must be greater than 67%. The Wilson's score method was used to calculate the confidence interval.

End point values	Participants in Parts 1 and 2 of the study			
Subject group type	Subject analysis set			
Number of subjects analysed	64[50]			
Units: percentage of participants				
number (confidence interval 95%)	98.4 (91.7 to 99.7)			

Notes:

[50] - ITT population: missing data after backwards imputation = nonresponders

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of participants with sustained virologic response 12 weeks after the last actual dose of study drug (SVR12) summarized by formulation, age and weight group, and across all subjects on the adult formulations

End point title	Parts 1 and 2: Percentage of participants with sustained virologic response 12 weeks after the last actual dose of study drug (SVR12) summarized by formulation, age and weight group, and across all subjects on the adult formulations

End point description:

SVR12 is defined as hepatitis C virus ribonucleic acid (HCV RNA) < lower limit of quantification (LLOQ) 12 weeks after the last actual dose of study drug.

End point type	Secondary

End point timeframe:

12 weeks after last dose of study drug (Week 24 or 36 depending on treatment duration)

End point values	Adult tablet, 12-17 YR, ≥ 45 kg	Mini-tablet, 9-11 YR, 15 to 29 kg	Mini-tablet, 9-11 YR, 30 to 44 kg	Mini-tablet, 9-11 YR, ≥ 45 kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38[51]	1[52]	9[53]	2[54]
Units: percentage of participants				
number (confidence interval 95%)	100 (90.8 to 100.0)	100 (20.7 to 100.0)	100 (70.1 to 100.0)	100 (34.2 to 100.0)

Notes:

[51] - ITT population: missing data after backwards imputation = nonresponders

[52] - ITT population: missing data after backwards imputation = nonresponders

[53] - ITT population: missing data after backwards imputation = nonresponders

[54] - ITT population: missing data after backwards imputation = nonresponders

End point values	Mini-tablet, 3-8 YR, 15 to 29 kg	Mini-tablet total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[55]	26[56]		
Units: percentage of participants				
number (confidence interval 95%)	92.9 (68.5 to 98.7)	96.2 (81.1 to 99.3)		

Notes:

[55] - ITT population: missing data after backwards imputation = nonresponders

[56] - ITT population: missing data after backwards imputation = nonresponders

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of participants with sustained virologic response 24 weeks after the last actual dose of study drug (SVR24), summarized by formulation, age and weight group, across all subjects, and across all subjects on the adult formulations

End point title	Parts 1 and 2: Percentage of participants with sustained virologic response 24 weeks after the last actual dose of study drug (SVR24), summarized by formulation, age and weight group, across all subjects, and across all subjects on the adult formulations

End point description:

SVR24 is defined as hepatitis C virus ribonucleic acid (HCV RNA) < lower limit of quantification (LLOQ) 24 weeks after the last actual dose of study drug.

End point type	Secondary

End point timeframe:

24 weeks after last dose of study drug (Week 36 or 48 depending on treatment duration)

End point values	Participants in Parts 1 and 2 of the study	Adult tablet, 12-17 YR, ≥ 45 kg	Mini-tablet, 9-11 YR, 15 to 29 kg	Mini-tablet, 9-11 YR, 30 to 44 kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64[57]	38[58]	1[59]	9[60]
Units: percentage of participants				
number (confidence interval 95%)	96.9 (89.3 to 99.1)	100 (90.8 to 100.0)	100.0 (20.7 to 100.0)	88.9 (56.5 to 98.0)

Notes:

[57] - ITT population: missing data after backwards imputation = nonresponders

[58] - ITT population: missing data after backwards imputation = nonresponders

[59] - ITT population: missing data after backwards imputation = nonresponders

[60] - ITT population: missing data after backwards imputation = nonresponders

End point values	Mini-tablet, 9-11 YR, ≥ 45 kg	Mini-tablet, 3-8 YR, 15 to 29 kg	Mini-tablet total	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	2[61]	14[62]	26[63]	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (34.2 to 100.0)	92.9 (68.5 to 98.7)	92.3 (75.9 to 97.9)	

Notes:

[61] - ITT population: missing data after backwards imputation = nonresponders

[62] - ITT population: missing data after backwards imputation = nonresponders

[63] - ITT population: missing data after backwards imputation = nonresponders

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of participants with alanine aminotransferase (ALT) normalization during treatment by formulation, age and weight group, across all subjects, and across all subjects on the adult formulations

End point title	Parts 1 and 2: Percentage of participants with alanine aminotransferase (ALT) normalization during treatment by formulation, age and weight group, across all subjects, and across all subjects on the adult formulations

End point description:

Alanine aminotransferase (ALT) normalization during treatment is defined as ALT ≤ the upper limit of normal (ULN) at the final treatment visit for participants with ALT > ULN at baseline.

End point type	Secondary

End point timeframe:

12 or 24 weeks after starting study drug, depending on treatment duration

End point values	Adult tablet,12-17 YR, ≥ 45 kg, ALT	Mini-tablet, 9-11 YR, 15 to 29 kg, ALT normalization	Mini-tablet, 9-11 YR, 30 to 44 kg, ALT normalization	Mini-tablet, 3-8 YR, 15 to 29 kg, ALT normalization
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[64]	1[65]	5[66]	10[67]
Units: percentage of participants				
number (confidence interval 95%)	87.5 (69.0 to 95.7)	100 (20.7 to 100.0)	100 (56.6 to 100.0)	80.0 (49.0 to 94.3)

Notes:

[64] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

[65] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

[66] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

[67] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

End point values	Mini-tablet total, ALT	Participants in Parts 1 and 2		

	normalization	of the study, ALT normalization		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[68]	40[69]		
Units: percentage of participants				
number (confidence interval 95%)	87.5 (64.0 to 96.5)	87.5 (73.9 to 94.5)		

Notes:

[68] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

[69] - ITT population with ALT > ULN at baseline and available on-treatment ALT data

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) collected from 1st dose of study drug until 30 d after last dose, up to 37 wks. SAEs and protocol-related nonserious AEs were collected from the time the subject signed consent

Adverse event reporting additional description:

TEAEs and SAEs are defined as any AE or SAE with onset or worsening reported by a participant from the time that the first dose of study drug is administered until 30 days have elapsed following discontinuation of study drug. TEAEs were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Adult tablet, 12-17 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75 mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Adult tablet, 12-17 yr, Part 2

Reporting group description:

Participants with HCV GT1b received the adult 3-DAA (OBV/PTV/RTV and DSV) regimen: two 12.5 mg ombitasvir /75mg paritaprevir /50 mg ritonavir tablets taken orally every morning (QD) and one dasabuvir 250 mg tablet taken orally twice a day (BID) for 12 weeks. Participants with HCV GT1a without cirrhosis received 12-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT1a with compensated cirrhosis received 24-week treatment with the adult 3-DAA regimen and ribavirin 200 mg tablets were administered orally per local label. Participants with HCV GT4 received 12-week treatment with the OBV/PTV/RTV formulation and ribavirin 200 mg tablets were administered orally per local label.

Reporting group title	Adult tablet, 12-17 yr, Total

Reporting group description:

Participants age 12-17 years old who received at least one dose of the adult formulation

Reporting group title	Mini tablet, 9-11 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Reporting group title	Mini tablet, 3-8 yr, Part 1

Reporting group description:

Participants with HCV GT1b without cirrhosis were to receive the mini-tablet 3-DAA (OBV, PTV, RTV, and DSV) regimen for 12 weeks: ombitasvir 0.3 mg, paritaprevir 1.0 mg, and ritonavir 1.0 mg mini-tablets administered orally QD based on body weight and dasabuvir taken orally BID as 3.08 mg mini-tablets based on body weight. Participants with HCV GT1a without cirrhosis received 12-week treatment with the mini-tablet 3-DAA regimen and ribavirin was provided as a 40 mg/mL oral solution and administered per local label.

Reporting group title	Mini tablet, Total

Reporting group description:

Participants who received at least one dose of the mini-tablet formulation

Reporting group title	All participants, Total

Reporting group description:

All participants who received at least one dose of study drug in Part 1 or Part 2

Serious adverse events	Adult tablet, 12-17 yr, Part 1	Adult tablet, 12-17 yr, Part 2	Adult tablet, 12-17 yr, Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Mini tablet, 9-11 yr, Part 1	Mini tablet, 3-8 yr, Part 1	Mini tablet, Total
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All participants, Total		
Total subjects affected by serious adverse events			

subjects affected / exposed	1 / 64 (1.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIA			
subjects affected / exposed	1 / 64 (1.56%)		
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 %

Non-serious adverse events	Adult tablet, 12-17 yr, Part 1	Adult tablet, 12-17 yr, Part 2	Adult tablet, 12-17 yr, Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	17 / 26 (65.38%)	28 / 38 (73.68%)
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
CHEST PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 26 (3.85%)	2 / 38 (5.26%)
occurrences (all)	1	1	2
CHILLS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
FATIGUE			
subjects affected / exposed	2 / 12 (16.67%)	5 / 26 (19.23%)	7 / 38 (18.42%)
occurrences (all)	2	5	7
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	2 / 12 (16.67%)	1 / 26 (3.85%)	3 / 38 (7.89%)
occurrences (all)	2	1	3
VESSEL PUNCTURE SITE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	2 / 12 (16.67%)	0 / 26 (0.00%)	2 / 38 (5.26%)
occurrences (all)	2	0	2
BEHAVIOURAL INSOMNIA OF CHILDHOOD			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
MOOD SWINGS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
NIGHTMARE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
SLEEP TERROR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
SUICIDAL IDEATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

DYSMENORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	3 / 26 (11.54%)	3 / 38 (7.89%)
occurrences (all)	0	3	3
PRURITUS GENITAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 12 (0.00%)	2 / 26 (7.69%)	2 / 38 (5.26%)
occurrences (all)	0	2	2
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM CHANGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)

occurrences (all)	0	3	3
NASAL CONGESTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 12 (16.67%)	1 / 26 (3.85%)	3 / 38 (7.89%)
occurrences (all)	2	1	3
RHINORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	2	0	2
HAEMOLYSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 12 (0.00%)	2 / 26 (7.69%)	2 / 38 (5.26%)
occurrences (all)	0	2	2
HEADACHE			
subjects affected / exposed	3 / 12 (25.00%)	5 / 26 (19.23%)	8 / 38 (21.05%)
occurrences (all)	3	5	8
PARAESTHESIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	2	0	2

Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 12 (16.67%)	0 / 26 (0.00%)	2 / 38 (5.26%)
occurrences (all)	2	0	2
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
CONSTIPATION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
DIARRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
FLATULENCE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
LIP ULCERATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
NAUSEA			
subjects affected / exposed	3 / 12 (25.00%)	0 / 26 (0.00%)	3 / 38 (7.89%)
occurrences (all)	3	0	3
VOMITING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Hepatobiliary disorders			

HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ECZEMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
PRURITUS			
subjects affected / exposed	1 / 12 (8.33%)	4 / 26 (15.38%)	5 / 38 (13.16%)
occurrences (all)	1	4	5
RASH			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
RASH PAPULAR			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
BACK PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 26 (3.85%)	2 / 38 (5.26%)
occurrences (all)	1	1	2
NECK PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 26 (3.85%)	2 / 38 (5.26%)
occurrences (all)	1	1	2
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
PAIN IN JAW			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	1 / 12 (8.33%)	1 / 26 (3.85%)	2 / 38 (5.26%)
occurrences (all)	1	1	2
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
INCREASED APPETITE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
ACUTE SINUSITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
IMPETIGO			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
INFLUENZA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 26 (3.85%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
NASOPHARYNGITIS			
subjects affected / exposed	1 / 12 (8.33%)	4 / 26 (15.38%)	5 / 38 (13.16%)
occurrences (all)	1	5	6
ORAL HERPES			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
OTITIS MEDIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)

occurrences (all)	1	0	1
SINUSITIS			
subjects affected / exposed	2 / 12 (16.67%)	0 / 26 (0.00%)	2 / 38 (5.26%)
occurrences (all)	2	0	2
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
TRACHEITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 26 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 12 (16.67%)	2 / 26 (7.69%)	4 / 38 (10.53%)
occurrences (all)	3	3	6
VIRAL INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 26 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Mini tablet, 9-11 yr, Part 1	Mini tablet, 3-8 yr, Part 1	Mini tablet, Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	9 / 14 (64.29%)	21 / 26 (80.77%)
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	2 / 12 (16.67%)	0 / 14 (0.00%)	2 / 26 (7.69%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	5 / 12 (41.67%)	1 / 14 (7.14%)	6 / 26 (23.08%)

occurrences (all)	5	1	6
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
PYREXIA			
subjects affected / exposed	3 / 12 (25.00%)	2 / 14 (14.29%)	5 / 26 (19.23%)
occurrences (all)	4	2	6
VESSEL PUNCTURE SITE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
BEHAVIOURAL INSOMNIA OF CHILDHOOD			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
DEPRESSION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
MOOD SWINGS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
NIGHTMARE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
SLEEP TERROR			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
SUICIDAL IDEATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1

Reproductive system and breast disorders			
DYSMENORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
PRURITUS GENITAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
ELECTROCARDIOGRAM CHANGE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Cardiac disorders			
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	2 / 12 (16.67%)	2 / 14 (14.29%)	4 / 26 (15.38%)
occurrences (all)	2	2	4
EPISTAXIS			

subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
NASAL CONGESTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	2 / 12 (16.67%)	0 / 14 (0.00%)	2 / 26 (7.69%)
occurrences (all)	2	0	2
SNEEZING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
HAEMOLYSIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
LYMPHOPENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
NEUTROPENIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	5 / 12 (41.67%)	2 / 14 (14.29%)	7 / 26 (26.92%)
occurrences (all)	6	2	8
PARAESTHESIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)

occurrences (all)	0	0	0

Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
ABDOMINAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 12 (16.67%)	0 / 14 (0.00%)	2 / 26 (7.69%)
occurrences (all)	2	0	2
CONSTIPATION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
DIARRHOEA			
subjects affected / exposed	3 / 12 (25.00%)	0 / 14 (0.00%)	3 / 26 (11.54%)
occurrences (all)	3	0	3
FLATULENCE			
subjects affected / exposed	2 / 12 (16.67%)	0 / 14 (0.00%)	2 / 26 (7.69%)
occurrences (all)	2	0	2
GASTRITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
LIP ULCERATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	3 / 12 (25.00%)	1 / 14 (7.14%)	4 / 26 (15.38%)
occurrences (all)	3	1	4
VOMITING			
subjects affected / exposed	4 / 12 (33.33%)	1 / 14 (7.14%)	5 / 26 (19.23%)

occurrences (all)	4	1	5

Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
ECZEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
RASH			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
RASH PAPULAR			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
BACK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
PAIN IN JAW			

subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
INCREASED APPETITE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Infections and infestations			
ACUTE SINUSITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
GASTROENTERITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 12 (0.00%)	2 / 14 (14.29%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
IMPETIGO			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
INFLUENZA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
NASOPHARYNGITIS			
subjects affected / exposed	2 / 12 (16.67%)	1 / 14 (7.14%)	3 / 26 (11.54%)
occurrences (all)	2	2	4
ORAL HERPES			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)

occurrences (all)	0	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
SINUSITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
TRACHEITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 14 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	3 / 14 (21.43%)	4 / 26 (15.38%)
occurrences (all)	1	3	4
VIRAL INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2

Non-serious adverse events	All participants, Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 64 (76.56%)		
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
CHEST PAIN			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
CHILLS			
subjects affected / exposed	1 / 64 (1.56%)		

occurrences (all)	1			
FATIGUE				
subjects affected / exposed	13 / 64 (20.31%)			
occurrences (all)	13			
INFLUENZA LIKE ILLNESS				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
PAIN				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences (all)	2			
PYREXIA				
subjects affected / exposed	8 / 64 (12.50%)			
occurrences (all)	9			
VESSEL PUNCTURE SITE PAIN				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
Psychiatric disorders				
ANXIETY				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences (all)	2			
BEHAVIOURAL INSOMNIA OF CHILDHOOD				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
DEPRESSION				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
MOOD SWINGS				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
NIGHTMARE				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			
SLEEP TERROR				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences (all)	1			

SUICIDAL IDEATION subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Reproductive system and breast disorders DYSMENORRHOEA subjects affected / exposed occurrences (all) PRURITUS GENITAL subjects affected / exposed occurrences (all) VAGINAL DISCHARGE subjects affected / exposed occurrences (all)	 3 / 64 (4.69%) 3 1 / 64 (1.56%) 1 2 / 64 (3.13%) 2		
Injury, poisoning and procedural complications ARTHROPOD BITE subjects affected / exposed occurrences (all)	 1 / 64 (1.56%) 1		
Investigations BLOOD BILIRUBIN INCREASED subjects affected / exposed occurrences (all) ELECTROCARDIOGRAM ABNORMAL subjects affected / exposed occurrences (all) ELECTROCARDIOGRAM CHANGE subjects affected / exposed occurrences (all) HAEMOGLOBIN DECREASED subjects affected / exposed occurrences (all)	 1 / 64 (1.56%) 1 1 / 64 (1.56%) 1 1 / 64 (1.56%) 1 1 / 64 (1.56%) 1		
Cardiac disorders ATRIOVENTRICULAR BLOCK FIRST DEGREE subjects affected / exposed occurrences (all)	 1 / 64 (1.56%) 1		
Respiratory, thoracic and mediastinal disorders			

COUGH			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
EPISTAXIS			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	4		
NASAL CONGESTION			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
OROPHARYNGEAL PAIN			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
RHINORRHOEA			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
SNEEZING			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	3		
HAEMOLYSIS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
LYMPHOPENIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
NEUTROPENIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
HEADACHE			
subjects affected / exposed	15 / 64 (23.44%)		

occurrences (all)	16		
PARAESTHESIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	2		
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
ABDOMINAL PAIN			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
CONSTIPATION			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
DIARRHOEA			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
FLATULENCE			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
GASTRITIS			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
LIP ULCERATION			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
NAUSEA			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	7		

VOMITING subjects affected / exposed occurrences (all)	6 / 64 (9.38%) 6		
Hepatobiliary disorders HYPERBILIRUBINAEMIA subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Skin and subcutaneous tissue disorders ECZEMA subjects affected / exposed occurrences (all) PRURITUS subjects affected / exposed occurrences (all) RASH subjects affected / exposed occurrences (all) RASH PAPULAR subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1 7 / 64 (10.94%) 7 2 / 64 (3.13%) 2 1 / 64 (1.56%) 1		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all) MUSCULOSKELETAL PAIN subjects affected / exposed occurrences (all) NECK PAIN subjects affected / exposed occurrences (all) PAIN IN EXTREMITY subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1 1 / 64 (1.56%) 1 2 / 64 (3.13%) 2 2 / 64 (3.13%) 2 1 / 64 (1.56%) 1		

PAIN IN JAW			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
INCREASED APPETITE			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Infections and infestations			
ACUTE SINUSITIS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
GASTROENTERITIS			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
GASTROENTERITIS VIRAL			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
IMPETIGO			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
INFLUENZA			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
NASOPHARYNGITIS			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	10		
ORAL HERPES			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
OTITIS MEDIA			
subjects affected / exposed	1 / 64 (1.56%)		

occurrences (all)	1		
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
SINUSITIS			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
STREPTOCOCCAL INFECTION			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
TRACHEITIS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	10		
VIRAL INFECTION			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2015	Amendment 1 • Modified language regarding fibrosis assessments at screening • Added longitudinal FibroTest to study procedures • Added an additional virologic failure criterion • Edited ALT monitoring and management parameters • Added information regarding drug storage • Added Medical Complaint language • Added an additional efficacy endpoint in Part 2 of the study
07 July 2016	Amendment 2 • Reduced the sample size in Part 2 • Changed treatment of GT1b-infected patients with compensated cirrhosis to OBV/PTV/RTV and DSV without RBV for 12 weeks • Changed treatment of GT4-infected patients with compensated cirrhosis to OBV/PTV/RTV and RBV for 12 weeks • Updated contraceptive language in the protocol • Added the guidelines that were followed regarding total blood loss per patient during the study • Provided additional details for alternate management for subjects meeting virologic failure criteria • Incorporated Administrative Change 1.0 to update the DSV strength concentration
21 August 2017	Amendment 3 • Removed pellets formulation from the study, and changed all endpoints to remove the pellet formulation • Removed aspartate aminotransferase-to-platelet ratio index (APRI) from study procedures • Updated contraceptive language in the protocol • Updated virologic failure criteria • Reduced the duration of LTFU Period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported