



Clinical trial results:

Assessment of the Pharmacokinetics of Boceprevir in Pediatric Subjects with Chronic Hepatitis C Genotype 1 (Phase 1b); Protocol No. P07614

Summary

EudraCT number	2010-023498-20
Trial protocol	GB PL ES DE Outside EU/EEA
Global end of trial date	21 January 2014

Results information

Result version number	v1 (current)
This version publication date	05 April 2016
First version publication date	05 July 2015

Trial information

Trial identification

Sponsor protocol code	P07614
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01425190
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000583-PIP09-05
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	20 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2013
Global end of trial reached?	Yes
Global end of trial date	21 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to determine weight based doses of boceprevir for children 3 to 17 years of age in 3 separate age-based cohorts.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2012
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	Poland: 6
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	16
EEA total number of subjects	15

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)	16
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was designed to assess the pharmacokinetics (PK) of boceprevir in pediatric participants infected with Hepatitis C virus (HCV) genotype (GT) 1 across 3 age-based cohorts (Cohort 1: 17 to ≥ 13 years; Cohort 2: >13 to ≥ 7 years; Cohort 3: >3 to ≥ 7 years).

Pre-assignment

Screening details:

This study enrolled pediatric participants between the ages of 3 to 17 years who were infected with HCV GT1.

Period 1

Period 1 title	Boceprevir Administration (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study.

Arms

Arm title	Cohort 1: Children <17 to ≥ 13 Years of Age
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Arm description:

Pediatric HCV-infected participants <17 to ≥ 13 years of age were administered a single weight-based dose of boceprevir on Day 1.

Arm type	Experimental
Investigational medicinal product name	Boceprevir
Investigational medicinal product code	
Other name	Victrelis™
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Boceprevir was supplied as a powder to be dispensed in a suitable dosing vehicle (e.g., applesauce, Nutella, pudding). For each participant, dose was calculated by multiplying body weight on Day 1 by 11.4 mg/kg and rounding up or down to the nearest 50 mg. The maximum possible dose was 800 mg.

Number of subjects in period 1	Cohort 1: Children <17 to ≥ 13 Years of Age
Started	16
Completed	15
Not completed	1
Full dose not consumed.	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Children <17 to ≥13 Years of Age
Reporting group description: Pediatric HCV-infected participants <17 to ≥13 years of age were administered a single weight-based dose of boceprevir on Day 1.	

Reporting group values	Cohort 1: Children <17 to ≥13 Years of Age	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Adolescents (12-17 years)	16	16	
Age continuous Units: years			
arithmetic mean	14.9		
standard deviation	± 1.2	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	9	9	

End points

End points reporting groups

Reporting group title	Cohort 1: Children <17 to ≥13 Years of Age
Reporting group description:	Pediatric HCV-infected participants <17 to ≥13 years of age were administered a single weight-based dose of boceprevir on Day 1.

Primary: Area Under the Plasma Concentration-Time Curve from Time 0 to Infinity (AUC_{0-∞})

End point title	Area Under the Plasma Concentration-Time Curve from Time 0 to Infinity (AUC _{0-∞}) ^[1]
End point description:	AUC(0-∞) was assessed pre-dose, 0.5, 1, 2, 2.5, 4.5, 5.5, 8, and 10 hours post-dose.
End point type	Primary
End point timeframe:	Pre-dose to 10 hours Post-dose

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: Only summary statistics for the primary PK measures for Cohort 1 are provided.

End point values	Cohort 1: Children <17 to ≥13 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ng hr/mL				
arithmetic mean (full range (min-max))	6660 (3860 to 10500)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (C_{max})

End point title	Maximum Plasma Concentration (C _{max}) ^[2]
End point description:	C _{max} was assessed pre-dose, 0.5, 1, 2, 2.5, 4.5, 5.5, 8, and 10 hours post-dose.
End point type	Primary
End point timeframe:	From Pre-dose to 10 hours Post-dose

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: Only summary statistics for the primary PK measures for Cohort 1 are provided.

End point values	Cohort 1: Children <17 to ≥13 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ng/mL				
arithmetic mean (full range (min-max))	1710 (985 to 2320)			

Statistical analyses

No statistical analyses for this end point

Primary: Time of Maximum Plasma Concentration (Tmax)

End point title	Time of Maximum Plasma Concentration (Tmax) ^[3]
End point description:	Tmax was assessed pre-dose, 0.5, 1, 2, 2.5, 4.5, 5.5, 8, and 10 hours post-dose.
End point type	Primary
End point timeframe:	From Pre-dose to 10 hours Post-dose

Notes:

[3] - 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: Only summary statistics for the primary PK measures for Cohort 1 are provided.

End point values	Cohort 1: Children <17 to ≥13 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: hour				
arithmetic mean (full range (min-max))	1.87 (0.4 to 4.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Cohort 1: Children <17 to ≥13 Years of Age
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Reporting group description:

All participants who received study drug in the study are included.

Serious adverse events	Cohort 1: Children <17 to ≥13 Years of Age		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: Children <17 to ≥13 Years of Age		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)		
Investigations			
Blood pressure systolic increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hepatic enzyme increased			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Syncope subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Malaise subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2010	This amendment indicated that dosing should be conducted immediately prior to breakfast to ensure consumption of the entire dose, clarified that water could be consumed after dosing, and clarified the blood sampling intervals.
17 June 2011	This amendment added a new clinical monitor to replace an outgoing monitor, indicated that two instead of one 5mL blood sample should be collected, and indicated that fasting would not be required for the blood sample collected at follow-up.
27 June 2011	This amendment indicated that a second barrier method of birth control was required and prohibited use of oral contraceptives containing drospirenone.
28 March 2012	This amendment removed the requirement that participants be naive antiviral/immunomodulatory treatment for HCV infection, clarified that participants with mixed GT HCV infection were not eligible, and indicated that use of ribavirin 90 days prior or interferon-alpha 30 days prior to screening was not allowed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 March 2013	The oldest age cohort of 17 to ≥ 13 years of age was completed on 20MAR2013. The trial was terminated prior to enrollment of participants in the two younger age cohorts. In view of the shift in therapy to interferon-free regimens, the FDA and the EMA have been reassessing treatment regimens for pediatric studies of HCV infection. Following discussion with the agencies, in which both concurred that priority should be given to interferon-free regimens, P07614 was terminated and study sites were closed out. For this reason, the end of trial date of 21JAN2014 was the date of official study termination.	-

Notes:

Limitations and caveats

None reported