



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 |
|-----------------------|--------|

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 |
|-----------|--|

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 (AUC0-∞)

| | |
|--|--|
| End point title | Area Under the Plasma Concentration-Time Curve from Time 0 to Infinity (AUC0-∞) ^[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 (Cmax)

| | |
|--|--|
| End point title | Maximum Plasma Concentration (Cmax) ^[2] |
| End point description: Cmax 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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

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

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) Syncope subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 3 / 16 (18.75%) 3 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 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