# Clinical trial results:
# EXTEND: A 3-Year, Virology, Follow-up Study in Subjects Previously Treated With Telaprevir in Select Clinical Studies

## Summary

| | |
|---|---|
| EudraCT number | 2009-011464-11 |
| Trial protocol | DE FR |
| Global end of trial date | 23 December 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 28 June 2016 |
| First version publication date | 07 August 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | VX08-950-112 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00916474 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Vertex Pharmaceuticals Incorporated |
| Sponsor organisation address | 50 Northern Avenue, Boston, Boston, MA, United States, 02210-1862 |
| Public contact | Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |
| Scientific contact | Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 04 April 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 December 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Cohort A: To assess the durability of virologic response in subjects who achieved a sustained viral response (SVR) following telaprevir-based treatment in a previous study. Cohort B: To evaluate changes in hepatitis C virus (HCV) variants over time in subjects who did not achieve an SVR following telaprevir-based treatment in a previous study.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 June 2009 |
| 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 | Austria: 12 |
| Country: Number of subjects enrolled | France: 50 |
| Country: Number of subjects enrolled | Germany: 58 |
| Country: Number of subjects enrolled | Canada: 30 |
| Country: Number of subjects enrolled | Puerto Rico: 4 |
| Country: Number of subjects enrolled | United States: 254 |
| Worldwide total number of subjects | 408 |
| EEA total number of subjects | 120 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |

| | |
|---|---|
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 387 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects previously treated with at least 1 dose of telaprevir-based treatment in 1 of the following studies were enrolled: VX05-950-104, VX05-950-104EU, VX06-950-106, VX06-950-107, VX07-950-108, VX08-950-111, or VX-950-TiDP24-C216 (referred as Studies 104, 104EU, 106, 107, 108, 111, and C216).

### Pre-assignment

Screening details:

All subjects were divided into 2 cohorts: Cohort A: Subjects who achieved an SVR in the previous telaprevir study and Cohort B: Subjects who did not achieve SVR in the previous telaprevir study.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort A – Subjects with SVR |

Arm description:

Subjects who received at least 1 dose of telaprevir-based treatment and achieved an SVR in the previous telaprevir study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Telaprevir |
| Investigational medicinal product code | VX-950 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Telaprevir administered in previous study.

| | |
|---|---|
| **Arm title** | Cohort B – Subjects without SVR |

Arm description:

Subjects who received at least 1 dose of telaprevir-based treatment and who did not achieve an SVR in the previous telaprevir study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Telaprevir |
| Investigational medicinal product code | VX-950 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Telaprevir administered in previous study.

| **Number of subjects in period 1** | Cohort A – Subjects with SVR | Cohort B – Subjects without SVR |
|---|---|---|
| Started | 220 | 188 |
| Completed | 172 | 110 |
| Not completed | 48 | 78 |
| Consent withdrawn by subject | 9 | 13 |
| Death | 4 | 2 |
| Plan to Receive Investigational Treatment for HCV | - | 23 |
| Received Investigational Treatment for HCV | - | 10 |
| Unspecified | 1 | 4 |
| Study Terminated by Sponsor | - | 1 |
| Lost to follow-up | 34 | 25 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort A – Subjects with SVR |
| Reporting group description: | |
| Subjects who received at least 1 dose of telaprevir-based treatment and achieved an SVR in the previous telaprevir study. | |
| Reporting group title | Cohort B – Subjects without SVR |
| Reporting group description: | |
| Subjects who received at least 1 dose of telaprevir-based treatment and who did not achieve an SVR in the previous telaprevir study. | |

| Reporting group values | Cohort A – Subjects with SVR | Cohort B – Subjects without SVR | Total |
|---|---|---|---|
| Number of subjects | 220 | 188 | 408 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 53.3 | 53.8 | |
| standard deviation | ± 8.08 | ± 7.21 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 68 | 56 | 124 |
| Male | 152 | 132 | 284 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Cohort A – Subjects with SVR |
| Reporting group description: | |
| Subjects who received at least 1 dose of telaprevir-based treatment and achieved an SVR in the previous telaprevir study. | |
| Reporting group title | Cohort B – Subjects without SVR |
| Reporting group description: | |
| Subjects who received at least 1 dose of telaprevir-based treatment and who did not achieve an SVR in the previous telaprevir study. | |

### Primary: Cohort A: Percentage of Subjects Who Maintained Undetectable HCV RNA Over Time After Achieving SVR

| | |
|---|---|
| End point title | Cohort A: Percentage of Subjects Who Maintained Undetectable HCV RNA Over Time After Achieving SVR[1][2] |
| End point description: | |
| The plasma HCV RNA level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification (LLOQ) was 25 IU/mL and lower limit of detection was 10 international units per milliliter (IU/mL). Analysis was performed on the Efficacy Set defined as all subjects who were enrolled per entry criteria. | |
| End point type | Primary |
| End point timeframe: | |
| 36 months | |

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: No inferential statistics was planned.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was applicable for Cohort A only.

| End point values | Cohort A – Subjects with SVR | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 220 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 100 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Cohort B: Percentage of Subjects With Change of Resistant Mutation to Wild Type From Previous Study

| | |
|---|---|
| End point title | Cohort B: Percentage of Subjects With Change of Resistant Mutation to Wild Type From Previous Study[3][4] |
| End point description: | |
| Sequencing analyses were conducted on samples with total HCV RNA levels above the limit of detection | |

of the sequencing assay (1000 IU/mL). A subject's HCV population was considered to have changed to WT if a WT AA character was observed at all 6 resistance-associated mutation (RAM) positions in the subject's viral sequencing data. Analysis was performed on Evaluable for Resistance Profile Virology Population defined as all subjects who had resistant profile at baseline in previous study, had non-resistant profile at post-nadir visit, or lacked sequencing data after post-nadir visit.

| End point type | Primary |
|---|---|

End point timeframe:

36 months

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: No inferential statistics was planned.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was applicable for Cohort B only.

| **End point values** | Cohort B – Subjects without SVR | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139[5] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| HCV Genotype 1a (n=110) | 81.8 | | | |
| HCV Genotype 1b (n=29) | 89.7 | | | |

Notes:

[5] - n = subjects with specified resistant profile

### Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort A: Percentage of Subjects With Change of Resistant Mutation to Wild Type From Previous Study Among Subjects With Late Relapse

| End point title | Cohort A: Percentage of Subjects With Change of Resistant Mutation to Wild Type From Previous Study Among Subjects With Late Relapse[6] |
|---|---|

End point description:

Late relapse was defined as having detectable HCV RNA after achieving SVR.

| End point type | Secondary |
|---|---|

End point timeframe:

36 months

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was applicable for Cohort A only.

| **End point values** | Cohort A – Subjects with SVR | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[7] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[7] - The analysis was not performed as no subject in Cohort A had late relapse.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort A and B: Number of Subjects With Severe Liver Related Events

| End point title | Cohort A and B: Number of Subjects With Severe Liver Related Events |
|---|---|

End point description:

Severe liver related events included decompensation events (ascites, variceal bleed, and hepatic encephalopathy), hepatocellular carcinoma (HCC), liver transplant, and liver-related death. Analysis was performed on Efficacy Set.

| End point type | Secondary |
|---|---|

End point timeframe:

36 Months

| **End point values** | Cohort A – Subjects with SVR | Cohort B – Subjects without SVR | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 220 | 188 | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Subjects with Severe Liver related events | 1 | 6 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

36 months

Adverse event reporting additional description:

Due to observational nature of the study only SAEs related to study procedure were planned to be collected. No other safety data was collected.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | No Dictionary Coding |
| Dictionary version | 0.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Cohort A – Subjects with SVR |

Reporting group description:

Subjects who received at least 1 dose of telaprevir-based treatment and achieved an SVR in the previous telaprevir study.

| | |
|---|---|
| Reporting group title | Cohort B – Subjects without SVR |

Reporting group description:

Subjects who received at least 1 dose of telaprevir-based treatment and who did not achieve an SVR in the previous telaprevir study.

| Serious adverse events | Cohort A – Subjects with SVR | Cohort B – Subjects without SVR | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 220 (0.00%) | 0 / 188 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Cohort A – Subjects with SVR | Cohort B – Subjects without SVR | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 220 (0.00%) | 0 / 188 (0.00%) | |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Due to observational nature of the study only SAEs related to study procedure were planned to be collected. No other safety data was collected.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 June 2009 | subjects who had been retreated with an approved treatment for HCV were allowed to continue in this study and a new secondary objective to evaluate the incidence of clinical outcomes related to severe liver disease was added and sample sizes were reduced for Cohorts A and B. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported