



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
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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
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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
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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
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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 standard deviation	53.3 ± 8.08	53.8 ± 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
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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]
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End point description:

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

End point type	Secondary
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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
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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
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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
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Dictionary used

Dictionary name	No Dictionary Coding
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Dictionary version	0.0
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Reporting groups

Reporting group title	Cohort A – Subjects with SVR
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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
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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