EU Clinical Trials Register

Clinical trial results:
A Long Term Follow-up Registry of Subjects Treated in A Gilead-Sponsored Trial in Subjects with Chronic Hepatitis B Infection

Summary

EudraCT number	2015-001050-16
Trial protocol	IT
Global end of trial date	14 August 2017

Results information

Result version number	v1 (current)
This version publication date	29 August 2018
First version publication date	29 August 2018

Trial information

Trial identification

Sponsor protocol code	GS-US-330-1508

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02258581
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive , Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	14 August 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the long term effects of hepatitis B virus (HBV) treatment of the parental study on the HBV serologic changes through Week 144.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 December 2014
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	United States: 147
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 18
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	India: 5
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Italy: 26
Worldwide total number of subjects	240
EEA total number of subjects	32

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)	230
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Asia-Pacific. The first participant was screened on 09 December 2014. The last study visit occurred on 14 August 2017.

Pre-assignment

Screening details:

245 participants were screened.

Period 1

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

Arms

Arm title	Registry Study

Arm description:

Participants who had been treated in selected Gilead-sponsored studies (GS-US-330-0101, GS-US-330-1401, GS-US-283-1059, and
GS-US-174-0149) for chronic hepatitis B.

Arm type	No Intervention
Investigational medicinal product name	HBV treatment in the parental study
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No investigational treatment was administered in this study. Routes of administration and pharmaceutical forms are entered because these are required data elements in the system.

Number of subjects in period 1	Registry Study
Started	240
Completed	1
Not completed	239
Withdrawal By Subject	19
Study Terminated By Sponsor	218
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Registry Study
Reporting group description:	
Participants who had been treated in selected Gilead-sponsored studies (GS-US-330-0101, GS-US-330-1401, GS-US-283-1059, and GS-US-174-0149) for chronic hepatitis B.	

Reporting group values	Registry Study	Total	
Number of subjects	240	240	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 49 ± 10.4	 -	
Gender categorical Units: Subjects			
Female	69	69	
Male	171	171	
Race Units: Subjects			
Asian	179	179	
Black or African American	8	8	
Native Hawaiian or Pacific Islander	5	5	
White	47	47	
Other	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	232	232	
Not Permitted	5	5	
HBsAg Status Units: Subjects			
Negative	11	11	
Positive	229	229	
HBeAg Status Units: Subjects			
Negative	190	190	
Positive	49	49	
Missing	1	1	
HBsAg Units: log10 IU/mL arithmetic mean standard deviation	 2.8 ± 1.16	 -	
HBV DNA Units: log10 IU/mL			

arithmetic mean	1.4		
standard deviation	± 0.73	-	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with serum HBsAg decline ≥ 0.5 log10 IU/ml from baseline at Week 144

End point title	Percentage of participants with serum HBsAg decline ≥ 0.5 log10 IU/ml from baseline at Week 144

End point description:

Participants in the Full Analysis Set (who were HBsAg positive at baseline) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 144

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage of participants				
number (not applicable)	9.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve HBsAg loss at Week 48

End point title	Percentage of participants who achieve HBsAg loss at Week 48

End point description:

Participants in the Full Analysis Set (who were HBsAg positive at baseline) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	178			
Units: Percentage of Participants				
number (not applicable)	0.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who achieve HBsAg loss at Week 144

End point title	Percentage of participants who achieve HBsAg loss at Week 144
End point description:	
Participants in the Full Analysis Set (who were HBsAg positive at baseline) with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Week 144	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hepatitis B e antigen (HBeAg) loss and seroconversion at Week 48

End point title	Percentage of participants with hepatitis B e antigen (HBeAg) loss and seroconversion at Week 48
End point description:	
Participants in the Full Analysis Set (who were HBeAg positive at baseline) with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Percentage of participants				
number (not applicable)	2.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HBeAg loss and seroconversion at Week 144

End point title	Percentage of participants with HBeAg loss and seroconversion at Week 144
End point description:	
Participants in the Full Analysis Set (who were HBeAg positive at baseline) with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Week 144	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of participants				
number (not applicable)	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who remain HBeAg negative and HBeAb positive at Week 48

End point title	Percentage of participants who remain HBeAg negative and HBeAb positive at Week 48
End point description:	
Participants in the Full Analysis Set who achieved HBeAg seroconversion during the parental study were analyzed.	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HBV DNA < the lower limit of quantitation (LLOQ < 20 IU/mL) at Week 48

End point title	Percentage of participants with HBV DNA < the lower limit of quantitation (LLOQ < 20 IU/mL) at Week 48
End point description:	
Participants in the Full Analysis Set (who were on treatment with oral antiviral (OAV) for HBV) with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	161			
Units: Percentage of participants				
number (not applicable)	93.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HBV DNA < LLOQ at Week 96

End point title	Percentage of participants with HBV DNA < LLOQ at Week 96
End point description:	
Participants in the Full Analysis Set (who were on treatment with OAV for HBV) with available data were analyzed.	
End point type	Secondary
End point timeframe:	
Week 96	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Percentage of participants				
number (not applicable)	96.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HBV DNA < LLOQ at Week 144

End point title	Percentage of participants with HBV DNA < LLOQ at Week 144

End point description:

Participants (who were on treatment with OAV for HBV) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 144

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage of participants				
number (not applicable)	90.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HBV DNA at Week 48

End point title	Change from Baseline in HBV DNA at Week 48

End point description:

Participants in the Full Analysis Set (all enrolled participants with at least one dose if one of the parental protocol defined treatment regimens and one visit during the registry) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.01 (± 0.403)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HBV DNA at Week 96

End point title	Change from Baseline in HBV DNA at Week 96
End point description: Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Week 96	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	0.01 (± 0.202)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HBV DNA at Week 144

End point title	Change from Baseline in HBV DNA at Week 144
End point description: Participants in the Full Analysis Set with available data were analyzed.	
End point type	Secondary
End point timeframe: Week 144	

End point values	Registry Study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: log10 IU/mL				
arithmetic mean (standard deviation)	0.09 (± 0.310)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Up to Week 144	
Adverse event reporting additional description:	
Safety Analysis Set: participants with at least one dose of one of the parental protocol defined treatment regimens	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

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

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: No participants experienced any adverse events during this registry.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2015	1. Added language specifying study inclusion criteria for subjects who participated in Gilead-sponsored study number GS-US-174-0149 2. Revised study design and inclusion criteria so that Baseline visit may occur up to 120 days since the last study visit of Gilead-sponsored study for CHB 3. Updated analysis objectives and endpoints 4. Added language to specify distinction between symptom-directed physical exam and vital signs collection 5. Addition of quality of life assessments 6. Added language to clarify collection of adverse events deemed by investigator to be related to treatment from previous Gilead-sponsored CHB treatment protocol
05 October 2016	1. Added language to clarify how Adverse Events, Serious Adverse Events, and Special Situations are collected and reported based on association with registry protocol mandated procedures, initial Gilead-sponsored study, or commercially approved Gilead product as part of CHB standard of care treatment 2. Removed references throughout to the observational nature of the study 3. Clarified that no formal sample size statistical analysis will be performed

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 August 2017	The registry was meant to evaluate the long-term effects of anti-HBV compounds. These compounds are either no longer in development or have not, to date, met the primary efficacy endpoint, and therefore the registry was terminated early. Consequently, although up to 500 participants were planned for the registry only 240 subjects were enrolled.	-

Notes:

Limitations and caveats

None reported