



Clinical trial results:

Phase IV Multi-Center, Prospective, Interventional, Post-Marketing Study in Hemophilia B Patients in India Receiving RIXUBIS as On-demand or Prophylaxis Under Standard Clinical Practice

Summary

EudraCT number	2022-002520-13
Trial protocol	Outside EU/EEA
Global end of trial date	11 August 2021

Results information

Result version number	v1 (current)
This version publication date	20 August 2022
First version publication date	20 August 2022

Trial information

Trial identification

Sponsor protocol code	251602
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03565237
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Baxalta Innovations GmbH
Sponsor organisation address	Industriestrasse 67, Vienna, Austria, 1220
Public contact	Study Director, Takeda, +1 866 842 5335, ClinicalTransparency@takeda.com
Scientific contact	Study Director, Baxalta Innovations GmbH, +1 866 842 5335, ClinicalTransparency@takeda.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 August 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the safety of RIXUBIS based on serious adverse events (SAEs) (including factor IX [FIX] inhibitors).

Protection of trial subjects:

This study was conducted in accordance with this protocol, the International Council for Harmonization Guideline for Good Clinical Practice E6 (ICH-GCP, April 1996), Title 21 of the US Code of Federal Regulations (US CFR), the EU Directives 2001/20/EC and 2005/28/EC, and applicable national and local regulatory requirements. In India, the study was registered with CTRI.nic.in (CTRI number: CTRI/2018/07/014754).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 December 2018
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	India: 25
Worldwide total number of subjects	25
EEA total number of subjects	0

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)	5
Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 8 study sites in India from 07 December 2018 to 11 August 2021.

Pre-assignment

Screening details:

A total 25 participants were enrolled and received RIXUBIS treatment regimen (either on-demand or prophylaxis) based on discretion of the physician choice under standard clinical practice. No participants were enrolled in the on-demand treatment of RIXUBIS. Hence, no data collection and analysis were done during on-demand treatment of this 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

Arm title	RIXUBIS: Prophylaxis Treatment
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Arm description:

Participants received intravenous bolus of RIXUBIS prophylaxis treatment at a maximum infusion rate of 10 milliliter (mL) per (/) minute based on discretion of the physician for up to 6 months as standard clinical practice.

Arm type	Experimental
Investigational medicinal product name	RIXUBIS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Participants were treated with RIXUBIS intravenously after reconstitution with Sterile Water for Injection (SWFI) under standard clinical practice.

Number of subjects in period 1	RIXUBIS: Prophylaxis Treatment
Started	25
Safety Analysis Set (SAS)	25
Effectiveness Full Analysis Set (EFAS)	25
Completed	23
Not completed	2
Physician decision	1
Non-compliance of Investigational Product	1

Baseline characteristics

Reporting groups

Reporting group title	RIXUBIS: Prophylaxis Treatment
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Reporting group description:

Participants received intravenous bolus of RIXUBIS prophylaxis treatment at a maximum infusion rate of 10 milliliter (mL) per (/) minute based on discretion of the physician for up to 6 months as standard clinical practice.

Reporting group values	RIXUBIS: Prophylaxis Treatment	Total	
Number of subjects	25	25	
Age Categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	24.6 ± 8.29	-	
Gender categorical Units: Subjects			
Male	25	25	
Female	0	0	
Race/Ethnicity, Customized Units: Subjects			
Asian: Indian	24	24	
More than one race	1	1	
Ethnicity Units: Subjects			
Not Hispanic or Latino	25	25	
Hispanic Or Latino	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	RIXUBIS: Prophylaxis Treatment
Reporting group description: Participants received intravenous bolus of RIXUBIS prophylaxis treatment at a maximum infusion rate of 10 milliliter (mL) per (/) minute based on discretion of the physician for up to 6 months as standard clinical practice.	

Primary: Number of Participants With Serious Treatment-emergent Adverse Events (TEAEs) Related to RIXUBIS

End point title	Number of Participants With Serious Treatment-emergent Adverse Events (TEAEs) Related to RIXUBIS ^[1]
End point description: TEAE was defined as any event not presented prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. A SAE was defined as any untoward medical occurrence that at any dose met one or more of the following criteria: outcome was fatal/resulted in death, life-threatening, required in-patient hospitalization or resulted in prolongation of an existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event that was not immediately life-threatening or resulted in death or required hospitalization but jeopardize the participant or required medical or surgical intervention to prevent any of the above outcomes. Relatedness to study drug was based on physician discretion. SAS included all enrolled participants having received RIXUBIS at any time during the study.	
End point type	Primary
End point timeframe: From start of study drug administration up to end of treatment (EOT) (up to 6 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: Only descriptive data was planned to be analysed for this endpoint.

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Related to RIXUBIS

End point title	Number of Participants With TEAEs Related to RIXUBIS
End point description: TEAE was defined as any event not presented prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. Relatedness to study drug was based on physician discretion. Number of participants with TEAEs related to RIXUBIS were reported. SAS included all enrolled participants having received RIXUBIS at any time during the study.	

End point type	Secondary
End point timeframe:	
From start of study drug administration up to EOT (up to 6 months)	

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Laboratory Abnormalities

End point title	Number of Participants With Clinically Significant Laboratory Abnormalities
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End point description:

Clinical laboratory evaluations included clinical chemistry (biochemistry and endocrinology), hematology and urinalysis. Any change in clinical laboratory abnormalities which were deemed clinically significant by the investigator were recorded as TEAEs (defined as any event not presented prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments). SAS included all enrolled participants having received RIXUBIS at any time during the study.

End point type	Secondary
End point timeframe:	
From start of study drug administration up to EOT (up to 6 months)	

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants				
Hematology	0			
Clinical chemistry	0			
Urinalysis	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Binding Antibodies (Immunoglobulin G [IgG] and Immunoglobulin M [IgM]) to Factor IX (FIX)

End point title	Number of Participants Who Developed Binding Antibodies (Immunoglobulin G [IgG] and Immunoglobulin M [IgM]) to Factor IX (FIX)
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End point description:

Binding antibodies (IgG and IgM) to FIX was determined using validated enzyme-linked immunosorbent assays (ELISAs) employing polyclonal anti-human IgG and IgM antibodies. Number of participants who developed binding antibodies (IgG and IgM) combined data to FIX were reported. SAS included all enrolled participants having received RIXUBIS at any time during the study.

End point type	Secondary
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End point timeframe:

From start of study drug administration up to EOT (up to 6 months)

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Binding Antibodies to Chinese Hamster Ovary (CHO) Proteins and rFurin

End point title	Number of Participants Who Developed Binding Antibodies to Chinese Hamster Ovary (CHO) Proteins and rFurin
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End point description:

Citrated plasma was assayed for the presence of antibodies to CHO protein and rFurin, derived from cultures of un-transfected cells. Testing for binding anti-CHO protein and rFurin antibodies was done on citrate-anti-coagulated plasma using an ELISA employing polyclonal anti-human IgG antibodies. Number of participants who developed binding antibodies to CHO proteins and rFurin were reported. SAS included all enrolled participants having received RIXUBIS at any time during the study.

End point type	Secondary
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End point timeframe:

From start of study drug administration up to EOT (up to 6 months)

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants				
CHO Proteins	0			
rFurin	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Bleeding Rate (ABR) With Prophylactic Use of RIXUBIS

End point title	Annualized Bleeding Rate (ABR) With Prophylactic Use of RIXUBIS
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End point description:

The ABR was defined as the total number of unique bleeding episodes by participants reported during RIXUBIS treatment for prophylaxis, divided by the RIXUBIS treatment duration for prophylaxis and multiplied by 365.25. A bleeding episode was defined as subjective (pain consistent with a joint bleed) or objective evidence of bleeding which may or may not be associated to a trauma event (spontaneous bleeding). Bleeding occurring at multiple locations related to the same injury (e.g., knee and ankle bleed following a fall) was counted as a single bleeding episode. The EFAS comprised of all participants for whom all inclusion and none of the exclusion criteria were met. Here, "number of participants analysed" refer to the participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

From start of study drug administration up to EOT (up to 6 months)

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Episodes per participant per year				
arithmetic mean (standard deviation)	0.914 ($\pm$ 1.6896)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Success of RIXUBIS for Treatment of Bleeding Episodes

End point title	Rate of Success of RIXUBIS for Treatment of Bleeding Episodes
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End point description:

The success of RIXUBIS for treatment of bleeding episodes was defined by grouping the categories of "Excellent"/"Good" of the corresponding hemostatic effectiveness ratings of a 4 point Likert scale ("Excellent", "Good", "Moderate" and "None") by the participants/legally authorized representative (LAR) (participants less than (<) 12 years: LAR, participants greater than or equal to [$\geq$] 12 years: self-assessment) for treatments given at home, or by the investigator for treatments given in the hospital/clinic. The rate of success of RIXUBIS for treatment of bleeding episodes was defined as: The number of successful bleeding episodes/total number of bleeding episodes where the treatment of the bleeding was rated *100. The EFAS comprised of all participants for whom all inclusion and none of the exclusion criteria were met. Here, "number of participants analysed" refer to the participants evaluable

for this endpoint.

End point type	Secondary
End point timeframe:	
From screening up to EOT (up to 6 months)	

End point values	RIXUBIS: Prophylaxis Treatment			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of bleeding episodes				
number (confidence interval 95%)	100 (54.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to EOT (up to 6 months)

Adverse event reporting additional description:

SAS included all enrolled participants having received RIXUBIS at any time during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	RIXUBIS: Prophylaxis Treatment
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Reporting group description:

Participants received intravenous bolus of RIXUBIS prophylaxis treatment at a maximum infusion rate of 10 mL/minute based on discretion of the physician for up to 6 months as standard clinical practice.

Serious adverse events	RIXUBIS: Prophylaxis Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	RIXUBIS: Prophylaxis Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)		
Musculoskeletal and connective tissue disorders			
Joint swelling			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Arthropathy			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Infections and infestations Dengue fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No participants were enrolled in the on-demand treatment of RIXUBIS. Hence, no data collection and analysis was done during on-demand treatment of this study.
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Notes: