Clinical trial results:
A Single Country, Multicenter, Open-Label and Non-Randomised Clinical Trial With Moroctocog Alfa (AF-CC) Prophylaxis and Treatment of Bleeding Episodes in Previously Treated Patients With Moderate and Severe Hemophilia A for a Duration of 8 Weeks

Summary

EudraCT number	2020-004570-21
Trial protocol	Outside EU/EEA
Global end of trial date	24 September 2020

Results information

Result version number	v1 (current)
This version publication date	21 March 2021
First version publication date	21 March 2021

Trial information

Trial identification

Sponsor protocol code	B1831097

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04396639
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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	06 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the safety of moroctocog alfa (AF-CC) when administered for prophylaxis with respect to incidence of factor VIII (FVIII) inhibitor development.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 January 2020
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: 50
Worldwide total number of subjects	50
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)	4
Adults (18-64 years)	46
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this study, subjects aged greater than or equal to (>=) 12 years to less than or equal to (<=) 65 years, with moderate or severe hemophilia A (circulating factor VIII [FVIII: C] <=5 percent [%]), who previously had at least 50 exposure days to FVIII-containing products were enrolled.

Pre-assignment

Screening details:

This study was conducted in 4 sites in India from 25-Jan-2020 to 24-Sep-2020. This study used an Institutional Review Board/Ethics Committee.

Period 1

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

Arms

Arm title	Moroctocog Alfa (AF-CC)

Arm description:

Moroctocog alfa was administered prophylactically at a dose of 30 international unit per kilogram (IU/kg), 3 times weekly in accordance with local product document and with procedures provided by physicians. For on-demand treatment, the amount administered and the frequency of administration of moroctocog alfa was tailored to the clinical effectiveness in individual subjects by their physicians. Subjects continued participating in the study until 24 exposure days or until 8 weeks of treatment (whichever occurred first). Post treatment subjects were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Moroctocog Alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Moroctocog alfa was administered prophylactically at a dose of 30 IU/kg, 3 times weekly until 24 exposure days or until 8 weeks of treatment.

Number of subjects in period 1	Moroctocog Alfa (AF-CC)
Started	50
Completed Follow up	48
Completed	48
Not completed	2
Consent withdrawn by subject	1
Unspecified	1

Baseline characteristics

Reporting groups	
Reporting group title	Moroctocog Alfa (AF-CC)

Reporting group description:

Moroctocog alfa was administered prophylactically at a dose of 30 international unit per kilogram (IU/kg), 3 times weekly in accordance with local product document and with procedures provided by physicians. For on-demand treatment, the amount administered and the frequency of administration of moroctocog alfa was tailored to the clinical effectiveness in individual subjects by their physicians. Subjects continued participating in the study until 24 exposure days or until 8 weeks of treatment (whichever occurred first). Post treatment subjects were followed up to 28 days.

Reporting group values	Moroctocog Alfa (AF-CC)	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	46	46	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	29.58		
standard deviation	± 9.80	-	
Sex: Female, Male Units: subjects			
Female	0	0	
Male	50	50	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	50	50	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	50	50	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Moroctocog Alfa (AF-CC)

Reporting group description:

Moroctocog alfa was administered prophylactically at a dose of 30 international unit per kilogram (IU/kg), 3 times weekly in accordance with local product document and with procedures provided by physicians. For on-demand treatment, the amount administered and the frequency of administration of moroctocog alfa was tailored to the clinical effectiveness in individual subjects by their physicians. Subjects continued participating in the study until 24 exposure days or until 8 weeks of treatment (whichever occurred first). Post treatment subjects were followed up to 28 days.

Primary: Percentage of Subjects who Developed Factor VIII (FVIII) Inhibitors

End point title	Percentage of Subjects who Developed Factor VIII (FVIII) Inhibitors[1]

End point description:

FVIII inhibitor development was defined as an inhibitor titer of >=0.6 Bethesda units per milliliter (BU)/mL as confirmed by the central laboratory during the course of the study. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Primary

End point timeframe:

24 exposure days or 8 weeks of treatment during the study (whichever occurred first)

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 reported for this endpoint.

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: percentage of subjects				
number (confidence interval 90%)	0 (0.00 to 0.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Treatment emergent are events between first dose of study drug and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. In this endpoint all AEs are reported. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Secondary

End point timeframe:

Day 1 up to 28 days after last dose of study drug (approximately maximum up to 12 Weeks)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment Emergent Serious Adverse Events (SAEs)

End point description:

SAEs: an adverse event resulting in any of the following outcomes or deemed significant for any other reason: death; inpatient hospitalisation or prolongation of existing hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect. Treatment emergent are events between first dose of study drug and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Secondary

End point timeframe:

Day 1 up to 28 days after last dose of study drug (approximately maximum up to 12 Weeks)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualised Bleeding Rate (ABR) During Prophylaxis

End point title	Mean Annualised Bleeding Rate (ABR) During Prophylaxis

End point description:

Subjects who had bleeding episode, ABR was derived by the following formula: ABR = number of bleeds per treatment interval duration per 365.25. Subjects who did not have bleeding episodes for them ABR was 0. In this endpoint, mean ABR was reported considering all the subjects (with bleeding episodes and

without bleeding episodes). Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Secondary

End point timeframe:

24 exposure days or 8 weeks of treatment during the study (whichever occurred first)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: bleeds per year				
arithmetic mean (standard deviation)	0.79 (± 2.042)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualised Total Factor Consumption (TFC)

End point title	Mean Annualised Total Factor Consumption (TFC)

End point description:

The total amount in international units (IU) infused for each infusion recorded were summed to calculate the TFC for each subject during the treatment interval duration (up to 8 weeks of treatment, or sooner, once 24 exposure days are achieved). The annualised TFC of moroctocog alfa was derived for each subject by using the following formula: Annualised TFC = (TFC / treatment interval duration)*365.25. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Secondary

End point timeframe:

24 exposure days or 8 weeks of treatment during the study (whichever occurred first)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: international units				
arithmetic mean (standard deviation)	287432.26 (± 93866.233)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualised Total Factor Consumption (TFC) by Weight

End point title	Mean Annualised Total Factor Consumption (TFC) by Weight

End point description:

The total amount in IU infused for each infusion recorded was summed to calculate the TFC for each subjects during the treatment interval duration (up to 8 weeks of treatment, or sooner, once 24 exposure days are achieved). The annualised TFC of moroctocog alfa was derived for each subject by using the following formula: Annualised TFC = (TFC / treatment interval duration)*365.25. To calculate the annualised TFC per weight, the most recently recorded weight measurement was used. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

End point type	Secondary

End point timeframe:

24 exposure days or 8 weeks of treatment during the study (whichever occurred first)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: international units per kilogram				
arithmetic mean (standard deviation)	4175.67 (± 858.383)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of Number of Moroctocog Alfa (AF-CC) Infusions Used to Treat Each New Bleed

End point title	Mean of Number of Moroctocog Alfa (AF-CC) Infusions Used to Treat Each New Bleed

End point description:

Number of moroctocog alfa infusions used to treat each bleed was calculated by adding the initial (on-demand) infusion to any subsequent (on-demand) infusions for the same bleed (same bleed start date/time). If there was more than one bleed location (e.g., ankle and joint) with identical bleed start date and time, it was treated as one bleed occurrence. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa. Here, 'Number of Subjects Analysed' = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

24 exposure days or 8 weeks of treatment during the study (whichever occurred first)

End point values	Moroctocog Alfa (AF-CC)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: infusions per bleed				
arithmetic mean (standard deviation)	1.0 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to 28 days after last dose of study drug (approximately maximum up to 12 Weeks)

Adverse event reporting additional description:

Same event may appear as AE and SAEs, what is presented are distinct events. Event may be categorised as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis set included all subjects who received at least 1 dose of moroctocog alfa.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Moroctocog Alfa (AF-CC)

Reporting group description:

Moroctocog alfa was administered prophylactically at a dose of 30 IU/kg, 3 times weekly in accordance with local product document and with procedures provided by physicians. For on-demand treatment, the amount administered and the frequency of administration of moroctocog alfa was tailored to the clinical effectiveness in individual subjects by their physicians. Subjects continued participating in the study until 24 exposure days or until 8 weeks of treatment (whichever occurred first). Post treatment subjects were followed up to 28 days.

Serious adverse events	Moroctocog Alfa (AF-CC)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Moroctocog Alfa (AF-CC)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1 1 / 50 (2.00%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2019	In order to simplify dosing and minimizing potential waste a dosing variance of +/-5 IU/kg was permitted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported