Clinical trial results:
A Local, Single-Centre, Extension, Open Label Access Study, to Provide Sildenafil Therapy for Subjects who Completed A1481156 Study and are Judged by the Investigator to Derive Clinical Benefit From Continued Treatment With Sildenafil, Prior to Reimbursement and Availability for Subjects in Russian Federation

Summary

EudraCT number	2019-001552-18
Trial protocol	Outside EU/EEA
Global end of trial date	01 March 2019

Results information

Result version number	v1 (current)
This version publication date	24 August 2019
First version publication date	24 August 2019

Trial information

Trial identification

Sponsor protocol code	A1481307

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 8007181021, 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	01 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide sildenafil citrate therapy to the subjects who completed study A1481156 for the treatment of pulmonary arterial hypertension (PAH) in Russian Federation where Revatio has not been approved by the Ministry of Healthcare and Social Development for subjects with PAH, is not commercially available, is not reimbursed through drug reimbursement program and are judged by the Investigator to derive clinical benefit from continued treatment with sildenafil citrate.

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 Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2012
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	Russian Federation: 7
Worldwide total number of subjects	7
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)	1
Adolescents (12-17 years)	3
Adults (18-64 years)	3
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted between 19 November 2012 and 01 March 2019 in Russian Federation. Total of 7 subjects were enrolled, who had completed A1481156 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	Sildenafil Citrate

Arm description:

Subjects who completed Study A1481156 received sildenafil citrate as assigned by the investigator for the treatment of PAH until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation (approximately up to 76 months)

Arm type	Experimental
Investigational medicinal product name	Sildenafil Citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects aged greater than or equals to (>=) 18 years and pediatric subjects (aged 1-17 years) with body weight greater than (>) 20 kilogram (kg) received 20 milligram (mg) sildenafil tablet orally three times a day (TID) and pediatric subjects with body weight less than or equals to (<=) 20 kg received 10 mg sildenafil tablet orally TID until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation.

Number of subjects in period 1	Sildenafil Citrate
Started	7
Completed	5
Not completed	2
Consent withdrawn by subject	1
Noncompliance	1

Baseline characteristics

Reporting groups	
Reporting group title	Sildenafil Citrate

Reporting group description:

Subjects who completed Study A1481156 received sildenafil citrate as assigned by the investigator for the treatment of PAH until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation (approximately up to 76 months)

Reporting group values	Sildenafil Citrate	Total	
Number of subjects	7	7	
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)	1	1	
Adolescents (12-17 years)	3	3	
Adults (18-64 years)	3	3	
From 65-84 years	0	0	
85 years and over	0	0	
Gender Categorical Units: Subjects			
Female	6	6	
Male	1	1	

End points

End points reporting groups

Reporting group title	Sildenafil Citrate

Reporting group description:

Subjects who completed Study A1481156 received sildenafil citrate as assigned by the investigator for the treatment of PAH until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation (approximately up to 76 months)

Primary: Subjects With Clinical Benefit on Usage of Continued Sildenafil Citrate

End point title	Subjects With Clinical Benefit on Usage of Continued Sildenafil Citrate[1]

End point description:

Sildenafil citrate therapy was provided to subjects for the treatment of PAH and were judged by the investigator to derive clinical benefit from continued treatment with the study drug. It was planned to be supplied until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation.

End point type	Primary

End point timeframe:

Up to 76 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	Sildenafil Citrate			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: subjects				

Notes:

[2] - No efficacy analysis was performed for this study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 76 months

Adverse event reporting additional description:

Same event may appear as both an adverse event and a serious adverse event. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both the events. Version was not captured, here 0.0 is mentioned for dictionary version.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	0.0

Reporting groups

Reporting group title	Sildenafil Citrate

Reporting group description:

Subjects who completed Study A1481156 received sildenafil citrate as assigned by the investigator for the treatment of PAH until the subjects gained access to reimbursed sildenafil citrate through drug reimbursement program of the Ministry of Healthcare and Social Development of Russian Federation (approximately up to 76 months)

Serious adverse events	Sildenafil Citrate		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sildenafil Citrate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
Pregnancy, puerperium and perinatal conditions			

MATERNAL EXPOSURE DURING PREGNANCY subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2011	Changes in sildenafil dose were made based on the data monitoring committee (DMC) recommendations following the DMC meeting on 04 August 2011.
14 March 2013	Changes to the safety language were made based on February 2013 updates to the CT02 protocol template.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported