



Clinical trial results:

A Multicenter, Single-arm, Open-label, Long-term Follow-up Safety Study of Selexipag in Participants who Participated in a Previous Selexipag Study

Summary

EudraCT number	2020-000475-21
Trial protocol	RO
Global end of trial date	10 November 2023

Results information

Result version number	v1 (current)
This version publication date	24 October 2024
First version publication date	24 October 2024

Trial information

Trial identification

Sponsor protocol code	67896049PUH3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04565990
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Actelion Pharmaceuticals Ltd
Sponsor organisation address	16 Gewerbestrasse, Allschwil, Switzerland, 4123
Public contact	Clinical Registry Group, Actelion Pharmaceuticals Ltd, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Actelion Pharmaceuticals Ltd, ClinicalTrialsEU@its.jnj.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	10 November 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the long-term safety of selexipag while providing continued selexipag treatment for subjects who were previously enrolled in an Actelion-sponsored study with selexipag and who derived benefit from selexipag in indications for which a positive benefit-risk has been established.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2021
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	Belarus: 21
Country: Number of subjects enrolled	India: 4
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Ukraine: 9
Worldwide total number of subjects	43
EEA total number of subjects	2

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)	37
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 43 subjects were rolled over from GRIPHON OL (originating study) and entered in this open label (OL) (SOMBRERO) study of which 36 subjects completed the 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	Selexipag
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Arm description:

Subjects with pulmonary arterial hypertension (PAH) who completed the parent study AC-065A302 continued treatment with selexipag in this study (200 to 1600 micrograms [mcg] selexipag tablet orally twice daily [bid]) from Day 1 up to 28 months with the same individual maximum tolerated dose (iMTD) that they were taking at the end of their parent study. Subjects were then followed for safety up to 30 days after the last dose of selexipag. Eligible subjects were then followed up for safety for up to 30 days after the last dose of selexipag.

Arm type	Experimental
Investigational medicinal product name	Selexipag
Investigational medicinal product code	JNJ-67896049
Other name	ACT-293987
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects with pulmonary arterial hypertension (PAH) who completed the parent study AC-065A302 continued treatment with selexipag in this study (200 to 1600 micrograms [mcg] selexipag tablet orally twice daily [bid]) from Day 1 up to 28 months with the same individual maximum tolerated dose (iMTD) that they were taking at the end of their parent study.

Number of subjects in period 1	Selexipag
Started	43
Completed	36
Not completed	7
Consent withdrawn by subject	1
Death	5
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Selexipag
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Reporting group description:

Subjects with pulmonary arterial hypertension (PAH) who completed the parent study AC-065A302 continued treatment with selexipag in this study (200 to 1600 micrograms [mcg] selexipag tablet orally twice daily [bid]) from Day 1 up to 28 months with the same individual maximum tolerated dose (iMTD) that they were taking at the end of their parent study. Subjects were then followed for safety up to 30 days after the last dose of selexipag. Eligible subjects were then followed up for safety for up to 30 days after the last dose of selexipag.

Reporting group values	Selexipag	Total	
Number of subjects	43	43	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	37	37	
From 65 to 84 years	6	6	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	50.6		
standard deviation	± 13.25	-	
Title for Gender Units: subjects			
Female	36	36	
Male	7	7	

End points

End points reporting groups

Reporting group title	Selexipag
Reporting group description:	
Subjects with pulmonary arterial hypertension (PAH) who completed the parent study AC-065A302 continued treatment with selexipag in this study (200 to 1600 micrograms [mcg] selexipag tablet orally twice daily [bid]) from Day 1 up to 28 months with the same individual maximum tolerated dose (iMTD) that they were taking at the end of their parent study. Subjects were then followed for safety up to 30 days after the last dose of selexipag. Eligible subjects were then followed up for safety for up to 30 days after the last dose of selexipag.	

Primary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) ^[1]
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End point description:

Number of Subjects with TEAEs were reported. Adverse event (AE) was defined as any untoward medical occurrence in a clinical study subject administered a pharmaceutical (investigational or non investigational) product. An AE did not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAEs were defined as AEs occurring at or after the initial administration of study intervention through the day of last dose plus 3 days. Data includes all TEAEs irrespective of whether they were serious or non-serious. Safety analysis set included all subjects who received at least 1 dose of study intervention in this study.

End point type	Primary
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End point timeframe:

From Day 1 up to 3 days after last dose of drug (up to 28 months 3 days)

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: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	Selexipag			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Subjects	22			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With TEAEs Leading to Premature Discontinuation of Selexipag

End point title	Number of Subjects With TEAEs Leading to Premature Discontinuation of Selexipag ^[2]
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End point description:

Number of subjects with TEAEs leading to premature discontinuation of selexipag were reported. AE was defined as any untoward medical occurrence in a clinical study subject administered a pharmaceutical (investigational or non investigational) product. An AE did not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAEs were defined as AEs occurring at or after the initial administration of study intervention through the day of last dose plus 3 days. Safety analysis set included all subjects who received at least 1 dose of study intervention in this study.

End point type	Primary
End point timeframe:	
From Day 1 up to 3 days after last dose of drug (up to 28 months 3 days)	
Notes:	
[2] - 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: Descriptive statistics was done, no inferential statistical analysis was performed.	

End point values	Selexipag			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Pregnant Females With Maternal Exposure to Selexipag

End point title	Number of Pregnant Females With Maternal Exposure to Selexipag ^[3]
End point description:	
Number of pregnant females with maternal exposure to selexipag were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention in this study. Here, 'N' (number of subjects analysed) signifies subjects evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
From Day 1 up to 30 days after last dose of drug (up to 29 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: Descriptive statistics was done, no inferential statistical analysis was performed.	

End point values	Selexipag			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With TEAE Deaths

End point title	Number of Subjects With TEAE Deaths ^[4]
End point description:	
Number of subjects with TEAE deaths during the study were reported. Safety analysis set included all subjects who received at least 1 dose of study intervention in this study.	
End point type	Primary

End point timeframe:

From Day 1 up to 3 days after last dose of drug (up to 28 months 3 days)

Notes:

[4] - 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: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	Selexipag			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Subjects	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Serious Adverse Events (TESAEs) ^[5]
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End point description:

Number of subjects with TESAEs were reported. AE was defined as any untoward medical occurrence in a clinical study subject administered a pharmaceutical (investigational or non investigational) product. An AE did not necessarily have a causal relationship with the pharmaceutical/biological agent under study. A SAE was any untoward medical occurrence at any dose that: resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or resulted in congenital anomaly/birth defect. TESAEs were defined as TSAEs occurring at or after the initial administration of study intervention through the day of last dose plus 3 days. Safety analysis set included all subjects who received at least 1 dose of study intervention in this study.

End point type	Primary
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End point timeframe:

From Day 1 up to 3 days after last dose of drug (up to 28 months 3 days)

Notes:

[5] - 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: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	Selexipag			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Subjects	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality: From Day 1 up to 30 days after last dose of drug (up to 29 months), Other AEs and SAEs: From Day 1 up to 3 days after last dose of drug (up to 28 months 3 days)

Adverse event reporting additional description:

Safety analysis set included all enrolled subjects who received at least 1 dose of study intervention in this study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Selexipag
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Reporting group description:

Subjects with pulmonary arterial hypertension (PAH) who completed the parent study AC-065A303 (NCT01112306) continued treatment with selexipag in this study (200 to 1600 micrograms [mcg] selexipag tablet orally twice daily [bid]) from Day 1 up to 28 months with the same individual maximum tolerated dose (iMTD) that they were taking at the end of their parent study. Eligible subjects were then followed for safety up to 30 days after the last dose of selexipag.

Serious adverse events	Selexipag		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 43 (16.28%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Cardiac Failure Acute			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary Arterial Hypertension			

subjects affected / exposed	3 / 43 (6.98%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Musculoskeletal and connective tissue disorders			
Systemic Scleroderma			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19 Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subacute Endocarditis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Syphilis			
subjects affected / exposed	1 / 43 (2.33%)		
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	Selexipag		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 43 (46.51%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Haemangioma of liver subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Benign biliary neoplasm subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2 1 / 43 (2.33%) 1		
Reproductive system and breast disorders Heavy menstrual bleeding subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Respiratory, thoracic and mediastinal disorders Respiratory disorder subjects affected / exposed occurrences (all) Pulmonary arterial hypertension subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Investigations			

Double stranded DNA antibody positive subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Complement factor C4 decreased subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Complement factor C3 decreased subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Injury, poisoning and procedural complications Vaccination complication subjects affected / exposed occurrences (all) Rib fracture subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Cardiac disorders Pericardial effusion subjects affected / exposed occurrences (all) Sinus tachycardia subjects affected / exposed occurrences (all) Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Gastrointestinal disorders Gastric mucosa erythema			

subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Chronic gastritis			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Steatohepatitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Non-alcoholic fatty liver			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Cholecystitis chronic			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Infections and infestations			
Covid-19			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Otitis media acute			

subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2020	The purpose of this amendment was to adapt safety reporting processes as part of the full transition of Actelion into Janssen, to align with transCelerate protocol template, coronavirus disease-2019 (COVID-19).
26 October 2021	The purpose of this amendment was to clarify the definition of end-of-study (EOS) and safety reporting requirements for subjects who completed treatment in the study and who continued with selexipag treatment by rolling over into a post-trial access (PTA) program or Study NOPRODPAPUH3001 (PLATYPUS).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported