Clinical trial results:
A Phase 2b, Dose-Ranging, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Rodatristat Ethyl in Patients with Pulmonary Arterial Hypertension

Summary

EudraCT number	2020-004971-42
Trial protocol	DE LV FR BE CZ PL IT BG ES AT
Global end of trial date	28 August 2023

Results information

Result version number	v1 (current)
This version publication date	01 February 2026
First version publication date	01 February 2026

Trial information

Trial identification

Sponsor protocol code	RVT-1201-2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04712669
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 126945

Notes:

Sponsors

Sponsor organisation name	Altavant Sciences GmbH
Sponsor organisation address	6501 Weston Parkway, Cary, United States,
Public contact	Information Desk, Altavant Sciences GmbH, clinicaltrials@altavant.com
Scientific contact	Information Desk, Altavant Sciences GmbH, clinicaltrials@altavant.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	26 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2023
Global end of trial reached?	Yes
Global end of trial date	28 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of rodatristat ethyl on the percent change from baseline of pulmonary vascular resistance (PVR), as measured by right heart catheterization (RHC) in patients with PAH.

Protection of trial subjects:

An external, multidisciplinary, Independent Data Monitoring Committee (IDMC) will review the progress of the study and perform interim reviews of unblinded safety and efficacy data at regular intervals and provide recommendations to the Sponsor whether the nature, frequency, and severity of AEs and AESIs associated with IP warrant the early termination of the study in the best interests of the subjects, whether the study should continue as planned, or whether the study should continue with modifications. The Clinical Endpoint Adjudication Committee (CEAC) including three Pulmonary Arterial Hypertension (PAH) expert physicians will adjudicate the clinical worsening events (CWEs) per Clinical Endpoint Adjudication Charter. The RHC data will be adjudicated by the blinded medical monitors per the RHC Adjudication Process Document.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	78 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Latvia: 12
Country: Number of subjects enrolled	United States: 44
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1

Country: Number of subjects enrolled	Moldova, Republic of: 12
Worldwide total number of subjects	108
EEA total number of subjects	47

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)	78
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately ninety (90) patients will be enrolled. Patients will be randomized 1:1:1 to placebo, 300 mg BID, or 600 mg BID of rodatristat ethyl. Patients who complete the Main Study will have the option to enroll into an OLE and continue to receive rodatristat ethyl.

Pre-assignment

Screening details:

The study will consist of a Screening Period (up to 28 days in duration)

Period 1

Period 1 title	Main Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

At the Baseline Visit, eligible patients will be randomly allocated (1:1:1) to one of the following 3 treatment groups. In order to maintain the study blind, patients will take 2 tablets in the morning and 2 tablets in the evening in one of the combinations.

Arms

Are arms mutually exclusive?	Yes
Arm title	Rodatristat Ethyl 300 mg BID

Arm description:

MAIN study: Rodatristat ethyl 300 mg and placebo tablet BID + standard of care medication(s) taken for 24 weeks

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

Dosage and administration details:

One 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Rodatristat Ethyl 600 mg BID

Arm description:

MAIN study:Rodatristat ethyl two 300 mg tablets BID + standard of care medication(s) taken for 24 weeks

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

Dosage and administration details:

Two 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Placebo

Arm description:

MAIN study: Matching two placebo tablets BID+ standard of care medication(s) taken for 24 weeks

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets of Placebo will be taken BID with food, approximately 12 hours apart.

Number of subjects in period 1	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo
Started	36	36	36
Completed	28	26	32
Not completed	8	10	4
Termination by Sponsor	-	-	1
Physician decision	1	-	-
Consent withdrawn by subject	3	6	-
Adverse event, non-fatal	4	4	3

Period 2

Period 2 title	Open Label Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo-Rodatristat Ethyl 300 mg

Arm description:

Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase

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

Dosage and administration details:

One 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Placebo-Rodatristat Ethyl 600 mg

Arm description:

Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase

Arm type	Experimental

Investigational medicinal product name	Rodatristat ethyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg

Arm description:

Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase

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

Dosage and administration details:

One 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg

Arm description:

Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase

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

Dosage and administration details:

Two 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Arm title	Rodatristat Ethyl 600 mg-Rodatristat Ethyl 600 mg

Arm description:

Subjects whose actual treatment group is Rodatristat ethyl two 600 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase

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

Dosage and administration details:

Two 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Investigational medicinal product name	Rodatristat ethyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two 300 mg tablet will be taken BID with food, approximately 12 hours apart.

Number of subjects in period 2[1]	Placebo-Rodatristat Ethyl 300 mg	Placebo-Rodatristat Ethyl 600 mg	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg
Started	15	16	22
Completed	0	0	0
Not completed	15	16	22
Termination by Sponsor	11	9	14
Adverse event, serious fatal	1	-	-
Physician decision	1	-	-
Consent withdrawn by subject	1	5	5
Adverse event, non-fatal	1	1	3
Lost to follow-up	-	-	-
Lack of efficacy	-	1	-

Number of subjects in period 2[1]	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg	Rodatristat Ethyl 600 mg-Rodatristat Ethyl 600 mg
Started	2	21
Completed	0	0
Not completed	2	21
Termination by Sponsor	-	14
Adverse event, serious fatal	-	-
Physician decision	-	-
Consent withdrawn by subject	-	4
Adverse event, non-fatal	1	2
Lost to follow-up	1	1
Lack of efficacy	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants completing Main Study are required to participate in Open Label Extension phase. Some participants choose not to participate in Open Label Extension Phase

Baseline characteristics

Reporting groups	
Reporting group title	Rodatristat Ethyl 300 mg BID
Reporting group description:	
MAIN study: Rodatristat ethyl 300 mg and placebo tablet BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Rodatristat Ethyl 600 mg BID
Reporting group description:	
MAIN study:Rodatristat ethyl two 300 mg tablets BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Placebo
Reporting group description:	
MAIN study: Matching two placebo tablets BID+ standard of care medication(s) taken for 24 weeks	

Reporting group values	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo
Number of subjects	36	36	36
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Between 18 and 65 years	32	29	27
>=65 years	4	7	9
Age continuous Units: years			
arithmetic mean	56.4	48.4	53.7
standard deviation	± 14.3	± 15.31	± 13.76
Gender categorical Units: Subjects			
Female	28	31	26
Male	8	5	10
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
White	29	29	25
More than one race	0	0	0
Unknown or Not Reported	5	5	7
Black or African American	0	1	2

Ethnicity Units: Subjects			
Hispanic or Latino	4	5	2
Not Hispanic or Latino	32	29	33
Unknown or Not Reported	0	2	1

Reporting group values	Total		
Number of subjects	108		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Between 18 and 65 years	88		
>=65 years	20		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	85		
Male	23		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	4		
Native Hawaiian or Other Pacific Islander	0		
White	83		
More than one race	0		
Unknown or Not Reported	17		
Black or African American	3		
Ethnicity Units: Subjects			
Hispanic or Latino	11		
Not Hispanic or Latino	94		
Unknown or Not Reported	3		

End points

End points reporting groups

Reporting group title	Rodatristat Ethyl 300 mg BID
Reporting group description:	
MAIN study: Rodatristat ethyl 300 mg and placebo tablet BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Rodatristat Ethyl 600 mg BID
Reporting group description:	
MAIN study:Rodatristat ethyl two 300 mg tablets BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Placebo
Reporting group description:	
MAIN study: Matching two placebo tablets BID+ standard of care medication(s) taken for 24 weeks	
Reporting group title	Placebo-Rodatristat Ethyl 300 mg
Reporting group description:	
Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase	
Reporting group title	Placebo-Rodatristat Ethyl 600 mg
Reporting group description:	
Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Reporting group title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg
Reporting group description:	
Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase	
Reporting group title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg
Reporting group description:	
Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Reporting group title	Rodatristat Ethyl 600 mg-Rodatristat Ethyl 600 mg
Reporting group description:	
Subjects whose actual treatment group is Rodatristat ethyl two 600 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who receive any amount of study drug.	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects randomized into any one of treatment groups.	

Primary: Percent change from baseline of pulmonary vascular resistance (PVR) at Week 24

End point title	Percent change from baseline of pulmonary vascular resistance (PVR) at Week 24
End point description:	
Pulmonary vascular resistance (PVR) was measured by right heart catheterization (RHC)	
End point type	Primary
End point timeframe:	
24 Weeks	

End point values	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo	ITT Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	36	36	36	72
Units: percent				
least squares mean (standard error)	63.083 (± 18.529)	64.219 (± 18.013)	5.813 (± 18.052)	63.651 (± 13.268)

Statistical analyses

Statistical analysis title	Percent change from baseline

Statistical analysis description:

Percent change from baseline of pulmonary vascular resistance (PVR) at Week 24. H0: The mean change from baseline in PVR at Week 24 is equal between placebo and rodatristat ethyl.

Comparison groups	Rodatristat Ethyl 300 mg BID v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0208 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	57.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.716
upper limit	105.824
Variability estimate	Standard error of the mean
Dispersion value	24.773

Notes:

[1] - LSM, SE, CIs for each treatment group; LSM Diff, SE, CIs, and p-value are estimated using an ANCOVA model incl. factors for treatment group and randomization strata with associated baseline value as a covariate.

Secondary: Change from baseline in World Health Organization (WHO) Functional Class (FC)

End point title	Change from baseline in World Health Organization (WHO) Functional Class (FC)

End point description:

PAH functional disease severity is classified according to World Health Organization (WHO) Functional Class (FC). Patients are classified into 1 of 4 functional classes on the basis of their degree of physical limitation and associated symptoms.

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo	ITT Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	36	36	36	72
Units: Count of Participants				
-II	0	0	0	0
-I	2	3	3	5
No Change	30	30	30	60
+I	4	3	3	7
+II	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels

End point title	Change from baseline in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels

End point description:

N-terminal prohormone of brain natriuretic peptide (NT-proBNP) is a strong predictor of disease progression and mortality in PAH patients. Current PAH treatment guidelines recommend measurement of NT-proBNP levels for both risk assessment and longitudinal follow up. NT-proBNP levels are also a good marker of response to treatment.

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo	ITT Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	36	36	36	72
Units: pg/mL				
least squares mean (standard error)	1145.7 (± 325.93)	886.1 (± 275.7)	19.8 (± 143.86)	1015.9 (± 215.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in six-minute walk distance (6MWD)

End point title	Change from baseline in six-minute walk distance (6MWD)

End point description:

The six-minute walk distance (6MWD) is a simple, commonly used, standardized measure of functional exercise capacity and endurance. It is a commonly used measure of efficacy in PAH clinical studies.

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Rodatristat Ethyl 300 mg BID	Rodatristat Ethyl 600 mg BID	Placebo	ITT Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	36	36	36	72
Units: six-minute walk distance (6MWD) (meters)				
median (inter-quartile range (Q1-Q3))	-14.5 (-31.5 to 28)	0 (-27.5 to 20)	2.5 (-13.5 to 23)	-4.25 (-31.0 to 25.0)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 48 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	Rodatristat Ethyl 300 mg BID
Reporting group description: MAIN study: Rodatristat ethyl 300 mg and placebo tablet BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Rodatristat Ethyl 600 mg BID
Reporting group description: MAIN study : Rodatristat ethyl two 300 mg tablets BID + standard of care medication(s) taken for 24 weeks	
Reporting group title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg
Reporting group description: Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Reporting group title	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg
Reporting group description: Subjects whose actual treatment group is Rodatristat ethyl two 300 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase	
Reporting group title	Placebo-Rodatristat Ethyl 600 mg
Reporting group description: Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Reporting group title	Rodatristat Ethyl 600 mg-Rodatristat Ethyl 600 mg
Reporting group description: Subjects whose actual treatment group is Rodatristat ethyl two 600 mg in the double-blind phase (Main Study) and received Rodatristat ethyl two 600 mg tablets BID in the open-label phase	
Reporting group title	Placebo-Rodatristat Ethyl 300 mg
Reporting group description: Subjects whose actual treatment group is Placebo in the double-blind phase (Main Study) and received Rodatristat ethyl two 300 mg tablets BID in the open-label phase	

Serious adverse events	Rodatristat Ethyl 300 mg BID	Placebo	Rodatristat Ethyl 600 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 36 (25.00%)	1 / 36 (2.78%)	6 / 36 (16.67%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant evaluation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device related thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sudden Death			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lung infiltration			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device extrusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device breakage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg	Placebo-Rodatristat Ethyl 600 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	6 / 22 (27.27%)	4 / 16 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant evaluation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device related thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Death			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acute respiratory failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device extrusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device breakage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Rodatristat Ethyl	Placebo-Rodatristat	

	600 mg-Rodatristat Ethyl 600 mg	Ethyl 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)	2 / 15 (13.33%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	2	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant evaluation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Angina pectoris			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Device related thrombosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 21 (4.76%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypoxia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device extrusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device breakage			

subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rodatristat Ethyl 300 mg BID	Placebo	Rodatristat Ethyl 600 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 36 (88.89%)	27 / 36 (75.00%)	34 / 36 (94.44%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Essential hypertension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	1 / 36 (2.78%)
occurrences (all)	0	4	1
Asthenia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Pyrexia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	6	1	3
Oedema peripheral			
subjects affected / exposed	4 / 36 (11.11%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	6	0	1
Non-cardiac chest pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	4	0	1
Fatigue			
subjects affected / exposed	5 / 36 (13.89%)	3 / 36 (8.33%)	2 / 36 (5.56%)
occurrences (all)	5	4	3

Pain			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	1 / 36 (2.78%)
occurrences (all)	3	2	2
Adverse drug reaction			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Device related thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Lithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	4 / 36 (11.11%)
occurrences (all)	1	4	4
Dysphonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 36 (2.78%)	3 / 36 (8.33%)	0 / 36 (0.00%)
occurrences (all)	1	3	0
Nasal congestion			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	1	2	0

Productive cough			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	1	2	0
Bronchospasm			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Epistaxis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Hiccups			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	5 / 36 (13.89%)	4 / 36 (11.11%)	2 / 36 (5.56%)
occurrences (all)	6	6	2
Upper-airway cough syndrome			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	4 / 36 (11.11%)
occurrences (all)	0	3	4
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	5	0	0
Anticoagulation drug level below therapeutic			

subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Alanine aminotransferase increased			
subjects affected / exposed	4 / 36 (11.11%)	0 / 36 (0.00%)	3 / 36 (8.33%)
occurrences (all)	4	0	4
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 36 (13.89%)	0 / 36 (0.00%)	4 / 36 (11.11%)
occurrences (all)	6	0	5
Gamma-glutamyltransferase increased			
subjects affected / exposed	14 / 36 (38.89%)	0 / 36 (0.00%)	11 / 36 (30.56%)
occurrences (all)	26	0	20
Platelet count decreased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Blood pH increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0
Palpitations			
subjects affected / exposed	1 / 36 (2.78%)	5 / 36 (13.89%)	0 / 36 (0.00%)
occurrences (all)	1	5	0
Right ventricular failure			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	2	1	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	3 / 36 (8.33%)
occurrences (all)	4	2	4
Syncope			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	4	0	0
Dizziness			

subjects affected / exposed	3 / 36 (8.33%)	5 / 36 (13.89%)	3 / 36 (8.33%)
occurrences (all)	3	5	3
Ageusia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Hypotonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	3	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	4 / 36 (11.11%)	0 / 36 (0.00%)	8 / 36 (22.22%)
occurrences (all)	5	0	9
Diarrhoea			
subjects affected / exposed	9 / 36 (25.00%)	4 / 36 (11.11%)	17 / 36 (47.22%)
occurrences (all)	11	5	24
Nausea			
subjects affected / exposed	11 / 36 (30.56%)	3 / 36 (8.33%)	13 / 36 (36.11%)
occurrences (all)	14	4	17
Abdominal distension			

subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	4 / 36 (11.11%)
occurrences (all)	3	0	5
Abdominal pain			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	4 / 36 (11.11%)
occurrences (all)	2	1	4
Dyspepsia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	2 / 36 (5.56%)
occurrences (all)	2	1	2
Abdominal pain lower			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	1 / 36 (2.78%)
occurrences (all)	2	3	1
Flatulence			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	5
Abdominal discomfort			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
Congestive hepatopathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	3	3	0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	2 / 36 (5.56%)
occurrences (all)	1	1	2
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	2 / 36 (5.56%)
occurrences (all)	1	1	2
Myalgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	5 / 36 (13.89%)	8 / 36 (22.22%)	3 / 36 (8.33%)
occurrences (all)	5	8	3
Influenza			

subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	1 / 36 (2.78%)
occurrences (all)	1	2	1
Nasopharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	3 / 36 (8.33%)	2 / 36 (5.56%)
occurrences (all)	1	4	2
Gastroenteritis viral			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection bacterial			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0
Abscess limb			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Helicobacter infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Infusion site infection			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	2 / 36 (5.56%)
occurrences (all)	3	1	2
Hypokalaemia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	1 / 36 (2.78%)
occurrences (all)	3	3	1
Fluid retention			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Hypoglycaemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0
Fluid overload			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 600 mg	Rodatristat Ethyl 300 mg-Rodatristat Ethyl 300 mg	Placebo-Rodatristat Ethyl 600 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	12 / 22 (54.55%)	15 / 16 (93.75%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Essential hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Adverse drug reaction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Peripheral swelling			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Device related thrombosis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Lithiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Pulmonary arterial hypertension			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 22 (13.64%)	7 / 16 (43.75%)
occurrences (all)	0	7	18
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pancreatic enzymes increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Blood pH increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Extrasystoles			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Palpitations			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Right ventricular failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Ventricular extrasystoles			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 2 (50.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 2 (50.00%)	2 / 22 (9.09%)	1 / 16 (6.25%)
occurrences (all)	2	2	1
Ageusia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Somnolence			

subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypotonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	1 / 2 (50.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	5 / 16 (31.25%)
occurrences (all)	0	3	7
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	6 / 16 (37.50%)
occurrences (all)	0	2	11
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	4 / 22 (18.18%)	3 / 16 (18.75%)
occurrences (all)	1	4	3
Abdominal distension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dyspepsia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pancreatitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 2 (50.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Flatulence			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eructation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	3
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Congestive hepatopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nocturia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 2 (50.00%)	5 / 22 (22.73%)	7 / 16 (43.75%)
occurrences (all)	1	5	8
Influenza			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Abscess limb			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infusion site infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)	3 / 22 (13.64%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Fluid retention			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Fluid overload			
subjects affected / exposed	0 / 2 (0.00%)	2 / 22 (9.09%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 22 (4.55%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 22 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	Rodatristat Ethyl 600 mg-Rodatristat Ethyl 600 mg	Placebo-Rodatristat Ethyl 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	12 / 15 (80.00%)	
Vascular disorders			

Hypotension			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Essential hypertension			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Adverse drug reaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Device related thrombosis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Lithiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 21 (14.29%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Dysphonia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Bronchospasm			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Epistaxis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hiccups			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	2 / 21 (9.52%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	3 / 21 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			

subjects affected / exposed	3 / 21 (14.29%)	4 / 15 (26.67%)	
occurrences (all)	6	10	
Platelet count decreased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Pancreatic enzymes increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Blood pH increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood potassium decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pericardial effusion			

subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Sinus tachycardia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Right ventricular failure			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 21 (14.29%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Syncope			
subjects affected / exposed	2 / 21 (9.52%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Ageusia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Hypotonia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Anosmia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 21 (23.81%)	2 / 15 (13.33%)	
occurrences (all)	5	3	
Diarrhoea			
subjects affected / exposed	3 / 21 (14.29%)	2 / 15 (13.33%)	
occurrences (all)	4	3	
Nausea			
subjects affected / exposed	2 / 21 (9.52%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Abdominal distension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Abdominal pain lower			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal sounds abnormal			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 15 (0.00%) 0	
Pancreatitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 15 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	1 / 15 (6.67%) 1	
Flatulence subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 15 (6.67%) 1	
Eructation subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 15 (6.67%) 1	
Toothache subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	1 / 15 (6.67%) 1	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	1 / 15 (6.67%) 1	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 15 (0.00%) 0	
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 15 (0.00%) 0	
Hepatobiliary disorders Congestive hepatopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 15 (6.67%) 1	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 15 (0.00%) 0	
Renal and urinary disorders			

Ureterolithiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Nocturia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hydronephrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 21 (28.57%)	3 / 15 (20.00%)	
occurrences (all)	6	5	
Influenza			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis viral			
subjects affected / exposed	1 / 21 (4.76%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			

subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 21 (9.52%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Abscess limb			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Helicobacter infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Infusion site infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vaginal infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 21 (4.76%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	2 / 21 (9.52%)	1 / 15 (6.67%)	
occurrences (all)	2	1	

Fluid retention			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypoglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Fluid overload			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Glucose tolerance impaired			
subjects affected / exposed	0 / 21 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 15 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2020	• Country Site list updated, Netherlands deleted & Czech Republic, Lativa were added • Updated wording for Inclusion Criteria on age of patient who can be enrolled • Deleted Inclusion Criteria on male patient eligibility that has a female partner who is or intends to become pregnant • Deleted Exclusion Criteria for elevated liver enzymes • Added Objective & Endpoint to evaluate the effect of Study Drug on Selexipag • Updated wording on stratification & capping of patients on Slexipag • Updates to Schedule of Assessments 1. Physical Exam removed at Follow-Up Visit 2. Optional Sample for Future Research & Pharmacogenetic Sample was added 3. Updated Footnote to clarify when weight will be collected, when Study Drug should be taken on clinic visit days, when ECGs should be collected, & clarify Right Heart Catheterization eligibility 4. Updated Footnote to clarify collection of Pharmacokinetics & Pharmacodynamic samples 5 .Updated Footnote to remove wording on amount of Study Drug received on Open-Label Extension • Updated wording on description of Study Drug to reflect new tablet appearance • Updated wording on clarification of dosing & timing of Study Drug in Main Study and Open-Label Extension • Updated wording on who can unblind a patient and how to unblind • Updated wording to clarify when C-SSRS to be collected • Updated Concomitant Medications to include Covid-19 vaccine • Updated Appendix 1 list of Concomitant & Prohibited medications • Added scoring & formula for REVEAL Lite 2.0 risk calculator

21 December 2021	• Updated Protocol wording to reflect Synopsis wording • Additional countries added (Serbia, Republica of Moldova, Austria & Bosnia) and number of Sites updated to approximately 68 Sites • Clarified ex-US Sites are not under US IND • Updated wording for Inclusion Criteria number 3, 5, 6 & 7 • Updated wording for Exclusion Criteria number 4, 15 & 26 • Added Exclusion Criteria number 27, 28 & 29 • Updates to Schedule of Assessments 1. Pulmonary Function Test added at Screening Visit and Pharmacogenetic sample collection added to Week 24 visit 2. Echocardiogram assessment moved from Day 1Visit to Screening Visit 3. Dispensing study drug removed from Week 8 and Week 18 Visit, Plasma NT-proBNP level was removed from Screening Visit & REVEAL Lite 2.0 assessment was removed 4 .Updated when & how Pregnancy Test, Coagulation Test & Urine Creatinine will be obtained during study • Updated Appendix 1 list of Concomitant & Prohibited medications • Updated wording on how Pulmonary Arterial Hypertension-Symptoms & Impact Questionnaire will be administered • Updated wording on procedures to be taken if patient exhibits suicidal ideation or behavior while on Study Drug • Updated wording to define stopping criteria for Study Drug non-compliance & clarification of reporting of Adverse Events of Special Interest • Updated wording on when to use contraception during study & methods of effective birth control • Updated wording on what assessments may be repeated at Screening Visit • Wording added to clarify unblinding procedure & process for randomization in Open-Label Extension and define end of study for patient participation in study • Wording added to Background & Pharmacokinetics section • Total time patient with be on Study Drug in Open-Label Extension was added • Deleted section on Right Heart Catheterization parameters measured during study
19 January 2022	• Updates to Schedule of Assessments 1. Week 8 of Main Study and Open-Label Extension changed from telephone/telemed visit to clinic visit 2. Wording added to clarify Unscheduled Visits. Safety and Laboratory assessments may be conducted at any time during the study if Investigator or Sponsor deems it necessary for the safety of the patient • Updated Objectives and Endpoints 1. Peptide (NT-proBNP) was deleted from additional objectives since it was already under Secondary Endpoint

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 July 2023	terminated during the Open-Label Extension phase based on Interim-Analysis results.	-

Notes:

Limitations and caveats

None reported