



Clinical trial results:

A Multicenter, Open-label, Phase III Study to Assess the Efficacy, Safety, and Pharmacokinetics of Macitentan in Japanese Pediatric Patients (≥ 3 months to <15 years) with Pulmonary Arterial Hypertension

Summary

EudraCT number	2023-000984-30
Trial protocol	Outside EU/EEA
Global end of trial date	04 March 2025

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	67896062PAH3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05167825
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Pharmaceutical K.K.
Sponsor organisation address	Nishi-kanda, Chiyoda-ku, Tokyo, Japan, 3-5-2
Public contact	Clinical Registry Group, Janssen Pharmaceutical K.K., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Pharmaceutical K.K., ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 March 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the effect of macitentan on hemodynamic measures at Week 24.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 7
Worldwide total number of subjects	7
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2
Children (2-11 years)	4
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 7 participants were enrolled and treated in the study.

Pre-assignment

Screening details:

A total of 7 participants were enrolled and treated in the study.

Period 1

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

Blinding implementation details:

Not blinded

Arms

Arm title	Macitentan
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Arm description:

Participants received macitentan 1 milligram (mg) or 2.5 mg tablets orally once daily based on age and body weight. Participants aged greater than or equal to ($\geq$) 3 months to less than ($<$) 6 months received daily dose of macitentan 1 mg, $\geq$ 6 months to $<$ 2 years received daily dose of macitentan 2.5 mg. For participants above 2 years (inclusive) of age, daily doses of macitentan were 3.5 mg ($<$ 15 kilograms [kg] body weight [BW]), 5 mg ($\geq$ 15 kg to $<$ 25 kg BW), 7.5 mg ($\geq$ 25 kg to $<$ 50 kg BW), and 10 mg ($\geq$ 50 kg BW). Treatment was administered from Day 1 to Week 52.

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

Dosage and administration details:

Participants aged between 3 months and 14 years, inclusive with PAH received macitentan 1 mg or 2.5 mg tablets orally once daily based on age and body weight. Participants aged $\geq$ 3 months to $<$ 6 months received daily dose of macitentan 1 mg, $\geq$ 6 months to $<$ 2 years received daily dose of macitentan 2.5 mg. For participants above 2 years (inclusive) of age, daily doses of macitentan were 3.5 mg ($<$ 15 kg BW), 5 mg ($\geq$ 15 kg to $<$ 25 kg BW), 7.5 mg ($\geq$ 25 kg to $<$ 50 kg BW), and 10 mg ($\geq$ 50 kg BW). Treatment was administered from Day 1 to Week 52 followed by 30 days follow up after end of treatment.

Number of subjects in period 1	Macitentan
Started	7
Completed	7

Baseline characteristics

Reporting groups

Reporting group title	Macitentan
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Reporting group description:

Participants received macitentan 1 milligram (mg) or 2.5 mg tablets orally once daily based on age and body weight. Participants aged greater than or equal to ($\geq$) 3 months to less than ($<$) 6 months received daily dose of macitentan 1 mg, $\geq$ 6 months to $<$ 2 years received daily dose of macitentan 2.5 mg. For participants above 2 years (inclusive) of age, daily doses of macitentan were 3.5 mg ($<$ 15 kilograms [kg] body weight [BW]), 5 mg ($\geq$ 15 kg to $<$ 25 kg BW), 7.5 mg ($\geq$ 25 kg to $<$ 50 kg BW), and 10 mg ($\geq$ 50 kg BW). Treatment was administered from Day 1 to Week 52.

Reporting group values	Macitentan	Total	
Number of subjects	7	7	
Age categorical			
Units: Subjects			
In Utero	0	0	
Preterm newborn infants (gestational age $<$ 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days - 23 months)	2	2	
Children (2 - 11 years)	4	4	
12 - 17 years	1	1	
Adults (18 - 64 years)	0	0	
From 65 - 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous			
Units: years			
arithmetic mean	5.7		
standard deviation	$\pm$ 5.12	-	
Title for Gender			
Units: subjects			
Female	3	3	
Male	4	4	

End points

End points reporting groups

Reporting group title	Macitentan
Reporting group description:	
Participants received macitentan 1 milligram (mg) or 2.5 mg tablets orally once daily based on age and body weight. Participants aged greater than or equal to ($\geq$) 3 months to less than ($<$) 6 months received daily dose of macitentan 1 mg, $\geq$ 6 months to $<$ 2 years received daily dose of macitentan 2.5 mg. For participants above 2 years (inclusive) of age, daily doses of macitentan were 3.5 mg ($<$ 15 kilograms [kg] body weight [BW]), 5 mg ($\geq$ 15 kg to $<$ 25 kg BW), 7.5 mg ($\geq$ 25 kg to $<$ 50 kg BW), and 10 mg ($\geq$ 50 kg BW). Treatment was administered from Day 1 to Week 52.	

Primary: Fold Change from Baseline at Week 24 in Pulmonary Vascular Resistance Index (PVRI)

End point title	Fold Change from Baseline at Week 24 in Pulmonary Vascular Resistance Index (PVRI) ^[1]
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End point description:

PVRI fold change at Week 24 was calculated as: $100 \times (\text{PVRI at Week 24} / \text{PVRI at baseline})$. PVR was determined by right heart catheterization. Efficacy analysis set included all participants who took at least 1 dose of study intervention.

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics was planned for this endpoint. No inferential statistics was planned.

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percent change				
geometric mean (geometric coefficient of variation)	59.43 ($\pm$ 75.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Pulmonary Vascular Resistance (PVR)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Pulmonary Vascular Resistance (PVR)
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End point description:

Change from baseline to Week 24 in hemodynamic variable: PVR was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Week 24

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: wood units (WU)				
arithmetic mean (standard deviation)	-3.734 ($\pm$ 4.4971)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Mean Right Atrial Pressure (mRAP)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Mean Right Atrial Pressure (mRAP)
End point description:	Change from baseline to Week 24 in hemodynamic variable: mRAP was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.
End point type	Secondary
End point timeframe:	From baseline (Day 1) up to Week 24

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)	-2.9 ($\pm$ 8.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Mean Pulmonary Atrial Pressure (mPAP)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Mean Pulmonary Atrial Pressure (mPAP)
End point description:	Change from baseline to Week 24 in hemodynamic variable: mPAP was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.
End point type	Secondary

End point timeframe:

From baseline (Day 1) up to Week 24

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)	-8.0 ($\pm$ 12.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Cardiac Index (CI)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Cardiac Index (CI)
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End point description:

Change from baseline to Week 24 in hemodynamic variable: CI was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Week 24

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: liters/minute/meter square (L/min/m ²)				
arithmetic mean (standard deviation)	-0.03 ($\pm$ 1.019)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline at Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52 in World Health Organization (WHO) Functional Class (FC)

End point title	Number of Participants With Change from Baseline at Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52 in World Health Organization (WHO) Functional Class (FC)
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End point description:

WHO-FC for participants with pulmonary arterial hypertension (PAH) ranges: Class I (no limitation in

physical activity, ordinary physical activity did not cause undue dyspnea or fatigue, chest pain or near syncope), Class II (slight limitation of physical activity, comfortable at rest, ordinary physical activity caused undue dyspnea or fatigue, chest pain, or near syncope), Class III (marked limitation of physical activity, comfortable at rest, less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope) and Class IV (cannot perform a physical activity without any symptoms, signs of right heart failure, dyspnea and/or fatigue may be present even at rest, discomfort is increased by any physical activity). Participants who improve in WHO FC are reported below. Improvement was defined as reduction in FC. Analysis population included all participants greater than (>) 4 years of age.

End point type	Secondary
End point timeframe:	
Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants				
Baseline	0			
Week 4	0			
Week 8	0			
Week 12	0			
Week 16	0			
Week 20	0			
Week 24	0			
Week 28	0			
Week 40	0			
Week 52	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 24 in Hemodynamic Variable: Mixed Venous Oxygen Saturation (SvO[2])

End point title	Percent Change from Baseline to Week 24 in Hemodynamic Variable: Mixed Venous Oxygen Saturation (SvO[2])
End point description:	
Change from baseline to Week 24 in hemodynamic variable: SvO(2) was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.	
End point type	Secondary
End point timeframe:	
From baseline (Day 1) up to Week 24	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percent change				
arithmetic mean (standard deviation)	-2.9 ($\pm$ 9.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Cardiac Output (CO)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Cardiac Output (CO)
End point description: Change from baseline to Week 24 in hemodynamic variable: CO was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention.	
End point type	Secondary
End point timeframe: From baseline (Day 1) up to Week 24	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: liters per minute (L/min)				
arithmetic mean (standard deviation)	0.07 ($\pm$ 0.743)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Hemodynamic Variable: Total Pulmonary Resistance (TPR)

End point title	Change from Baseline to Week 24 in Hemodynamic Variable: Total Pulmonary Resistance (TPR)
End point description: Change from baseline to Week 24 in hemodynamic variable: TPR was reported. TPR was calculated as: (mPAP/CO)*80. Efficacy analysis set included all participants who took at least 1 dose of study intervention.	
End point type	Secondary
End point timeframe: From baseline (Day 1) up to Week 24	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: dynes second/centimeter^5				
arithmetic mean (standard deviation)	-243.0 (± 410.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change from Baseline at Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52 in Panama Functional Class (FC)

End point title	Number of Participants With Change from Baseline at Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52 in Panama Functional Class (FC)
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End point description:

Panama FC for PAH ranges: Class I (asymptomatic, growing normally, attending nursery/school regularly, no limitation of physical activity, playing sports with his/her classmates), Class II (slight limitation of physical activity, unduly dyspnoeic and fatigued when playing with his/her classmates, comfortable at rest, grow along own centiles, nursery/school attendance 75% normal, no chest pain), Class IIIa (marked limitation of physical activity, no attempt at sports, comfortable at rest, less than ordinary activity (eg: dressing) causes undue dyspnea, fatigue, syncope and/or presyncope or chest pain, nursery/schooling compromised <50% normal attendance), Class IIIb (growth compromised, poor appetite, supplemental feeding, same as class IIIa) and Class IV (cannot perform a physical activity without any symptoms, dyspnea at rest). Participants improved in were classified into Improved (reduction in FC), No change (no change in FC) and Worsened (increase in FC). Efficacy analysis set was used.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Baseline	0			
Week 4	0			
Week 8	0			
Week 12	0			
Week 16	0			
Week 20	0			
Week 24	0			
Week 28	0			
Week 40	0			
Week 52	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 24 and 52 in 6-minute Walk Distance (6MWD) as Measured by the 6-minute Walk Test (6MWT)

End point title	Change from Baseline to Weeks 24 and 52 in 6-minute Walk Distance (6MWD) as Measured by the 6-minute Walk Test (6MWT)
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End point description:

Change from baseline to Weeks 24 and 52 in 6MWD as measured by 6MWT was reported. 6MWD was the distance that a participant could walk in 6 minutes. Rest periods were allowed if the participant could no longer continue. If the participant need to rest, he/she may pause, lean against the wall and continue walking whenever he/she feels able. The timer continued to run even if the participant stopped to rest. Analysis population included all participants greater than equal to ($\geq$) 6 years of age. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 24 and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: meters				
arithmetic mean (standard deviation)				
Week 24 (n=3)	4.897 ($\pm$ 43.6657)			
Week 52 (n=2)	24.710 ($\pm$ 105.6559)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, 28, 40, and 52 in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP)

End point title	Change from Baseline to Weeks 12, 24, 28, 40, and 52 in N-terminal Pro-brain Natriuretic Peptide (NT-proBNP)
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End point description:

Change from baseline to Weeks 12, 24, 28, 40, and 52 in NT-proBNP was reported. Efficacy analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, 28, 40, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: picograms per milliliter (pg/mL)				
arithmetic mean (standard deviation)				
Week 12 (n=7)	6.5911 (± 18.85065)			
Week 24 (n=7)	-3.7423 (± 7.79983)			
Week 28 (n=6)	-3.1663 (± 20.38136)			
Week 40 (n=7)	-5.7146 (± 14.23745)			
Week 52 (n=6)	-0.2360 (± 10.15074)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Tricuspid Annular Plane Systolic Excursion (TAPSE)

End point title	Change from Baseline to Weeks 12, 24, and 52 in Tricuspid Annular Plane Systolic Excursion (TAPSE)
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End point description:

Change from baseline to Weeks 12, 24, and 52 in TAPSE was reported. It is calculated as: original TAPSE value/body surface area (BSA). TAPSE was a dimension used to evaluate Right Ventricle (RV) longitudinal systolic function; it measured the extent of systolic motion of the lateral portion of the tricuspid ring towards the apex. Efficacy analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: millimeters per meter square (mm/m ²)				
arithmetic mean (standard deviation)				
Week 12 (n=7)	2.766 (± 1.6763)			

Week 24 (n=7)	1.873 (± 1.0379)			
Week 52 (n=6)	2.412 (± 1.3666)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Left Ventricular Eccentricity Index (LVEI)

End point title	Change from Baseline to Weeks 12, 24, and 52 in Left Ventricular Eccentricity Index (LVEI)
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End point description:

Change from baseline to Weeks 12, 24, and 52 in LVEI was reported. It included diastolic (D) LVEI and systolic (S) LVEI. LV internal diameters were measured using the parasternal short axis view at the level of the papillary muscles: D1: LV internal diameter perpendicular to interventricular septum at end-diastole; D2: LV internal diameter parallel to interventricular septum, and at right angle from D1, at end-diastole; S1: LV internal diameter perpendicular to interventricular septum at end-systole; S2: LV internal diameter parallel to interventricular septum, and at a right angle from S1, at end-systole. The LVEI was a ratio that was calculated by sponsor as: LVEI diastole = D2/D1; LVEI systole = S2/S1. Efficacy analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Ratio				
arithmetic mean (standard deviation)				
Diastolic: Week 12	0.116 (± 0.1241)			
Diastolic: Week 24	0.125 (± 0.1491)			
Diastolic: Week 52	0.128 (± 0.0762)			
Systolic: Week 12	0.237 (± 0.1519)			
Systolic: Week 24	0.229 (± 0.2396)			
Systolic: Week 52	0.237 (± 0.1225)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Quality of Life (QoL) as Assessed by Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scales Short Form (SF-15)

End point title	Change from Baseline to Weeks 12, 24, and 52 in Quality of Life (QoL) as Assessed by Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scales Short Form (SF-15)
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End point description:

Change from baseline to Weeks 12, 24, and 52 in QoL as assessed by PedsQL 4.0 generic core scales SF-15 was reported. The PedsQL 4.0 questionnaire generic core scales score SF-15 assessed general physical, emotional, social and school functioning on a 5-point Likert scale from 0 to 4 with 0= if it is never a problem, 1= if it is almost never a problem, 2= if it is sometime a problem, 3= if it is often a problem, 4 if it is almost always a problem. Scores were transformed on a scale from 0 to 100. Higher scores indicated better health related QoL. The QoL questionnaire was completed by parent(s)/caregiver(s) and by participants. Analysis population included all participants ≥ 2 years of age. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Total score parents/caregiver report: Week 12 (n=5)	8.905 ($\pm$ 6.1274)			
Total score parents/caregiver report: Week 24 (n=5)	8.190 ($\pm$ 11.3259)			
Total score parents/caregiver report: Week 52 (n=5)	15.810 ($\pm$ 7.8366)			
Total score - participant report: Week 12 (n=3)	8.889 ($\pm$ 3.4694)			
Total score - participant report: Week 24 (n=3)	-2.222 ($\pm$ 17.8211)			
Total score - participant report: Week 52 (n=3)	16.667 ($\pm$ 20.2759)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Number of Hours of Daytime Activity

End point title	Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Number of Hours of Daytime Activity
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End point description:

Change from baseline to Weeks 12, 24, and 52 in physical activity as measured by accelerometry: number of hours of daytime activity was reported. Analysis population included all participants ≥ 2 years of age.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hours				
arithmetic mean (standard deviation)				
Week 12	-0.929 ($\pm$ 0.9741)			
Week 24	-0.280 ($\pm$ 1.3553)			
Week 52	0.144 ($\pm$ 0.4985)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Count Per Minute of Daily Activity

End point title	Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Count Per Minute of Daily Activity
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End point description:

Change from baseline to Weeks 12, 24, and 52 in physical activity as measured by accelerometry: mean count per minute of daily activity was reported. Analysis population included all participants ≥ 2 years of age.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: counts per minute				
arithmetic mean (standard deviation)				
Week 12	73.946 ($\pm$ 205.4249)			
Week 24	112.733 ($\pm$ 219.3168)			
Week 52	125.427 ($\pm$ 157.5824)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Daily Time Spent in Light Physical Activity

End point title	Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Daily Time Spent in Light Physical Activity
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End point description:

Change from baseline to Weeks 12, 24, and 52 in physical activity as measured by accelerometry: mean daily time spent in light physical activity was reported. Analysis population included all participants ≥ 2 years of age.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: minutes				
arithmetic mean (standard deviation)				
Week 12	1.600 ($\pm$ 46.5857)			
Week 24	35.159 ($\pm$ 92.2011)			
Week 52	38.852 ($\pm$ 57.1818)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Daily Time Spent in Moderate to Vigorous Physical Activity

End point title	Change from Baseline to Weeks 12, 24, and 52 in Physical Activity as Measured by Accelerometry: Mean Daily Time Spent in Moderate to Vigorous Physical Activity
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End point description:

Change from baseline to Weeks 12, 24, and 52 in physical activity as measured by accelerometry: mean daily time spent in moderate to vigorous physical activity was reported. Analysis population included all participants ≥ 2 years of age.

End point type	Secondary
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End point timeframe:

From baseline (Day 1) up to Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: minutes				
arithmetic mean (standard deviation)				
Week 12	0.032 (± 0.4424)			
Week 24	0.169 (± 0.6058)			
Week 52	0.493 (± 1.5023)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Macitentan: Participants ≥ 2 Years Old

End point title	Plasma Concentration of Macitentan: Participants ≥ 2 Years Old
End point description: Plasma concentration of macitentan was reported. Analysis population included all participants ≥ 2 years of age. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.	
End point type	Secondary
End point timeframe: Day 11 (0, 1, 2, 4, 8, 12, 24 hours post-dose), Week 12	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 11: 0 hour (n=5)	94.4 (± 28.9)			
Day 11: 1 hour (n=5)	93.4 (± 27.7)			
Day 11: 2 hours (n=5)	121 (± 55.1)			
Day 11: 4 hours (n=5)	227 (± 38.5)			
Day 11: 8 hours (n=5)	192 (± 93.2)			
Day 11: 12 hours (n=5)	166 (± 75.5)			
Day 11: 24 hours (n=5)	93.3 (± 26.9)			
Week 12 (n=4)	85.6 (± 37.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Aprocitentan: Participants ≥ 2 Years Old

End point title	Plasma Concentration of Aprocitentan: Participants ≥ 2 Years Old
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End point description:

Plasma concentration of aprocitentan was reported. Analysis population included all participants ≥ 2 years of age. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Day 11 (0, 1, 2, 4, 8, 12, 24 hours post-dose), Week 12

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 11: 0 hour (n=5)	993 ($\pm$ 285)			
Day 11: 1 hour (n=5)	789 ($\pm$ 228)			
Day 11: 2 hours (n=5)	763 ($\pm$ 309)			
Day 11: 4 hours (n=5)	944 ($\pm$ 211)			
Day 11: 8 hours (n=5)	773 ($\pm$ 308)			
Day 11: 12 hours (n=5)	789 ($\pm$ 255)			
Day 11: 24 hours (n=5)	929 ($\pm$ 251)			
Week 12 (n=4)	917 ($\pm$ 266)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Macitentan: Participants < 2 Years Old

End point title	Plasma Concentration of Macitentan: Participants < 2 Years Old
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End point description:

Plasma concentration of macitentan was reported. The data was not summarized since N=2, hence participants wise data was reported. Analysis population included all participants < 2 years of age. Here, "99999" refers to standard deviation not evaluable for single participant.

End point type	Secondary
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End point timeframe:

Day 1 (2, 5, 24 hours post-dose), Weeks 4 and 8

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Participant 1: Day 1 (2 hours)	33.6 (± 99999)			
Participant 1: Day 1 (5 hours)	120 (± 99999)			
Participant 1: Day 1 (24 hours)	24.2 (± 99999)			
Participant 1: Week 4	55.1 (± 99999)			
Participant 1: Week 8	59.4 (± 99999)			
Participant 2: Day 1 (2 hours)	81.4 (± 99999)			
Participant 2: Day 1 (5 hours)	155 (± 99999)			
Participant 2: Day 1 (24 hours)	61.1 (± 99999)			
Participant 2: Week 4	143 (± 99999)			
Participant 2: Week 8	83.5 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Aprocitentan: Participants <2 Years Old

End point title	Plasma Concentration of Aprocitentan: Participants <2 Years Old
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End point description:

Plasma concentration of aprocitentan was reported. The data was not summarized since N=2, hence participants wise data was reported. Analysis population included all participants <2 years of age. Here, "99999" refers to standard deviation not evaluable for single participant.

End point type	Secondary
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End point timeframe:

Day 1 (2, 5, 24 hours post-dose), Weeks 4 and 8

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Participant 1: Day 1 (2 hours)	7.98 (± 99999)			
Participant 1: Day 1 (5 hours)	65.9 (± 99999)			
Participant 1: Day 1 (24 hours)	162 (± 99999)			
Participant 1: Week 4	864 (± 99999)			
Participant 1: Week 8	982 (± 99999)			
Participant 2: Day 1 (2 hours)	7.62 (± 99999)			
Participant 2: Day 1 (5 hours)	29.2 (± 99999)			
Participant 2: Day 1 (24 hours)	119 (± 99999)			
Participant 2: Week 4	662 (± 99999)			
Participant 2: Week 8	648 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 24 and Week 52 in Borg Dyspnea Index

End point title	Change From Baseline to Week 24 and Week 52 in Borg Dyspnea Index
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End point description:

Change from baseline to Weeks 24 and 52 in Borg dyspnea index was reported. BDI was a 10-point scale rating the maximum level of dyspnea experienced during the 6MWT. Scores ranged from 0 (no shortness of breath) to 10 (worst shortness of breath you have ever had). Higher score indicated worse outcome. Analysis population included all participants greater than equal to ($\geq$) 6 years of age. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 24 and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Before 6MWT: Week 24 (n=3)	0.00 ($\pm$ 0.000)			
Before 6MWT: Week 52 (n=2)	0.00 ($\pm$ 0.000)			
After 6MWT: Week 24 (n=3)	-1.17 ($\pm$ 0.764)			
After 6MWT: Week 52 (n=2)	-1.00 ($\pm$ 0.707)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs)
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End point description:

Number of participants with TEAEs was reported. An adverse event (AE) was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. TEAEs are defined as any AE occurring at or after the initial administration of study intervention through the day of last dose plus 30 days. Safety analysis set included all participants who took at least 1 dose

of study intervention.

End point type	Secondary
End point timeframe:	
From Baseline (Day 1) up to Week 56	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Postbaseline Markedly Abnormal Hematology Laboratory Values

End point title	Number of Participants With Postbaseline Markedly Abnormal Hematology Laboratory Values
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End point description:

Number of participants with postbaseline markedly abnormal hematology laboratory values was reported. Abnormality was judged at the discretion of investigator. Data is reported for categories where atleast one participant had abnormality. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
End point timeframe:	
Weeks 20, 40, and 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Hematocrit: <0.28% of blood cells(<0.32M): Week 20	1			
Hemoglobin: < 100 grams per liter (g/L): Week 20	1			
Leukocytes: <3.0 10 ⁹ cells/L: Week 40	1			
Leukocytes: <3.0 10 ⁹ cells/L: Week 52	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs of Special Interest

End point title	Number of Participants With TEAEs of Special Interest
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End point description:

Number of participants with TEAEs of special interest was reported. It included anemia/decreased hemoglobin level, oedema/fluid retention, hepatic impairment and hypotension. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From Baseline (Day 1) up to Week 56

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Serious Adverse Events (TESAEs)
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End point description:

Number of participants with TESAEs was reported. An AE is any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. A SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TESAEs are defined as any SAE occurring at or after the initial administration of study intervention through the day of last dose plus 30 days. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From Baseline (Day 1) up to Week 56

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs Leading to Premature Discontinuation of Study Drug

End point title	Number of Participants With AEs Leading to Premature Discontinuation of Study Drug
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End point description:

Number of participants with AEs leading to premature discontinuation of study drug was reported. An AE is any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From Baseline (Day 1) up to Week 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Postbaseline Markedly Abnormal Clinical Chemistry Laboratory Values

End point title	Number of Participants With Postbaseline Markedly Abnormal Clinical Chemistry Laboratory Values
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End point description:

Number of participants with postbaseline markedly abnormal clinical chemistry laboratory values was reported. Abnormality was judged at the discretion of investigator. Data is reported for categories where atleast one participant had abnormality. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Weeks 4 and 28

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants				
Potassium: >6.0 mmol/L: Week 4 (n=7)	1			
Calcium: <1.75 mmol/L: Week 4 (n=7)	1			
ALP: > 2.5 * ULN: Week 28 (n=6)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Pulse Rate

End point title	Change from Baseline in Vital Signs: Pulse Rate
End point description: Change from baseline in vital signs: pulse rate was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.	
End point type	Secondary
End point timeframe: Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 4 (n=7)	-4.4 (± 7.87)			
Week 8 (n=7)	-1.7 (± 15.24)			
Week 12 (n=7)	-12.1 (± 7.45)			
Week 16 (n=7)	-13.4 (± 17.06)			
Week 20 (n=7)	-7.4 (± 17.50)			
Week 24 (n=7)	-2.4 (± 30.72)			
Week 28 (n=6)	-7.2 (± 12.42)			
Week 40 (n=7)	-10.3 (± 9.30)			
Week 52 (n=7)	-14.7 (± 9.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Blood Pressure

End point title	Change from Baseline in Vital Signs: Blood Pressure
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End point description:

Change from baseline in vital signs: blood pressure was reported. It included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP: Week 4 (n=7)	-5.3 (± 12.61)			
SBP: Week 8 (n=7)	-5.3 (± 14.86)			
SBP: Week 12 (n=7)	0.4 (± 4.79)			
SBP: Week 16 (n=7)	-1.7 (± 10.29)			
SBP: Week 20 (n=7)	-1.1 (± 13.35)			
SBP: Week 24 (n=7)	-5.3 (± 9.79)			
SBP: Week 28 (n=6)	-5.5 (± 6.09)			
SBP: Week 40 (n=7)	-3.3 (± 9.05)			
SBP: Week 52 (n=7)	-9.3 (± 12.00)			
DBP: Week 4 (n=6)	-9.0 (± 9.06)			
DBP: Week 8 (n=6)	-4.5 (± 6.41)			
DBP: Week 12 (n=7)	-3.7 (± 11.83)			
DBP: Week 16 (n=7)	-6.1 (± 11.78)			
DBP: Week 20 (n=7)	0.9 (± 19.04)			
DBP: Week 24 (n=7)	-7.1 (± 7.06)			
DBP: Week 28 (n=6)	-8.0 (± 8.32)			
DBP: Week 40 (n=7)	-0.7 (± 10.13)			
DBP: Week 52 (n=7)	-4.0 (± 16.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Electrocardiogram (ECG) Parameter: Heart Rate

End point title	Change from Baseline in Electrocardiogram (ECG) Parameter: Heart Rate
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End point description:

Change from baseline in ECG: heart rate was reported. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 12	-4.0 ($\pm$ 19.04)			
Week 24	-3.6 ($\pm$ 25.48)			
Week 52	-12.0 ($\pm$ 8.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Electrocardiogram (ECG) Parameter: PR, QRS, QT, Corrected QT interval-Bazett's Formula (QTcB), and Corrected QT Interval-Fridericia's Formula (QTcF) Intervals

End point title	Change from Baseline in Electrocardiogram (ECG) Parameter: PR, QRS, QT, Corrected QT interval-Bazett's Formula (QTcB), and Corrected QT Interval-Fridericia's Formula (QTcF) Intervals
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End point description:

Change from baseline in ECG: PR, QRS, QT, QTcB, and QTcF intervals was reported. Safety analysis set included all participants who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 12, 24, and 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: milliseconds (msec)				
arithmetic mean (standard deviation)				
PR Interval: Week 12	3.4 ($\pm$ 10.94)			
PR Interval: Week 24	14.6 ($\pm$ 15.10)			
PR Interval: Week 52	4.0 ($\pm$ 7.57)			
QRS Interval: Week 12	-0.3 ($\pm$ 4.96)			
QRS Interval: Week 24	0.3 ($\pm$ 4.19)			
QRS Interval: Week 52	0.3 ($\pm$ 3.15)			
QT Interval: Week 12	16.1 ($\pm$ 29.61)			
QT Interval: Week 24	12.4 ($\pm$ 34.52)			
QT Interval: Week 52	32.1 ($\pm$ 16.69)			
QTcB Interval: Week 12	10.6 ($\pm$ 13.59)			
QTcB Interval: Week 24	4.0 ($\pm$ 24.53)			
QTcB Interval: Week 52	11.4 ($\pm$ 13.89)			

QTcf Interval: Week 12	12.6 (± 14.29)			
QTcf Interval: Week 24	6.7 (± 21.16)			
QTcf Interval: Week 52	19.0 (± 11.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameters: Platelets, Leukocytes, Neutrophils Band Form (NBF), Lymphocytes, Monocytes, Eosinophils, and Basophils

End point title	Change from Baseline in Hematology Parameters: Platelets, Leukocytes, Neutrophils Band Form (NBF), Lymphocytes, Monocytes, Eosinophils, and Basophils
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End point description:

Change from baseline in hematology parameters: platelets, leukocytes, NBF, lymphocytes, monocytes, eosinophils, and basophils was reported. Data for each parameters was planned to be reported at specified timepoints only. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints. Here, "99999" refers to standard deviation data was not calculated for single participant

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: 10 ⁹ cells per liter (10 ⁹ /L)				
arithmetic mean (standard deviation)				
Platelets: Week 4 (n=7)	-20.4 (± 31.90)			
Platelets: Week 8 (n=7)	-47.9 (± 42.32)			
Platelets: Week 12 (n=7)	-23.3 (± 70.86)			
Platelets: Week 16 (n=7)	-41.3 (± 53.21)			
Platelets: Week 20 (n=7)	-42.4 (± 86.32)			
Platelets: Week 24 (n=7)	-42.6 (± 77.72)			
Platelets: Week 28 (n=6)	-22.0 (± 59.29)			
Platelets: Week 40 (n=7)	-40.3 (± 106.10)			
Platelets: Week 52 (n=7)	-56.7 (± 92.37)			
Leukocytes: Week 4 (n=7)	0.031 (± 3.7398)			
Leukocytes: Week 8 (n=7)	0.549 (± 3.4816)			
Leukocytes: Week 12 (n=7)	-0.131 (± 2.3574)			

Leukocytes: Week 16 (n=7)	-0.321 (± 1.5230)			
Leukocytes: Week 20 (n=7)	-1.256 (± 3.7745)			
Leukocytes: Week 24 (n=7)	0.214 (± 3.6431)			
Leukocytes: Week 28 (n=6)	-0.347 (± 2.8012)			
Leukocytes: Week 40 (n=7)	-1.660 (± 3.0486)			
Leukocytes: Week 52 (n=7)	-0.541 (± 2.7583)			
NBF: Week 8 (n=1)	0.120 (± 99999)			
NBF: Week 16 (n=1)	0.480 (± 99999)			
NBF: Week 20 (n=2)	0.055 (± 0.1485)			
NBF: Week 40 (n=1)	-0.050 (± 99999)			
NBF: Week 52 (n=1)	-0.030 (± 99999)			
Lymphocytes: Week 4 (n=7)	-0.144 (± 0.4446)			
Lymphocytes: Week 8 (n=7)	-0.240 (± 0.5289)			
Lymphocytes: Week 12 (n=7)	-0.451 (± 0.3151)			
Lymphocytes: Week 16 (n=7)	-0.294 (± 0.1784)			
Lymphocytes: Week 20 (n=7)	-0.286 (± 0.8204)			
Lymphocytes: Week 24 (n=7)	-0.224 (± 0.5638)			
Lymphocytes: Week 28 (n=6)	-0.255 (± 0.5392)			
Lymphocytes: Week 40 (n=7)	-0.649 (± 0.5258)			
Lymphocytes: Week 52 (n=7)	-0.411 (± 0.5227)			
Monocytes: Week 4 (n=7)	-0.029 (± 0.0807)			
Monocytes: Week 8 (n=7)	0.070 (± 0.2063)			
Monocytes: Week 12 (n=7)	0.033 (± 0.0925)			
Monocytes: Week 16 (n=7)	-0.046 (± 0.0382)			
Monocytes: Week 20 (n=7)	-0.081 (± 0.0928)			
Monocytes: Week 24 (n=7)	0.017 (± 0.1042)			
Monocytes: Week 28 (n=6)	-0.052 (± 0.0884)			
Monocytes: Week 40 (n=7)	-0.103 (± 0.0911)			
Monocytes: Week 52 (n=7)	-0.086 (± 0.0988)			
Eosinophils: Week 4 (n=7)	-0.011 (± 0.0811)			
Eosinophils: Week 8 (n=7)	-0.009 (± 0.0795)			

Eosinophils: Week 12 (n=7)	0.066 (± 0.1153)			
Eosinophils: Week 16 (n=7)	0.030 (± 0.1606)			
Eosinophils: Week 20 (n=7)	0.086 (± 0.1752)			
Eosinophils: Week 24 (n=7)	-0.016 (± 0.1066)			
Eosinophils: Week 28 (n=6)	-0.040 (± 0.1119)			
Eosinophils: Week 40 (n=7)	0.000 (± 0.0693)			
Eosinophils: Week 52 (n=7)	0.220 (± 0.6577)			
Basophils: Week 4 (n=7)	0.016 (± 0.0162)			
Basophils: Week 8 (n=7)	0.009 (± 0.0273)			
Basophils: Week 12 (n=7)	0.016 (± 0.0270)			
Basophils: Week 16 (n=7)	0.016 (± 0.0465)			
Basophils: Week 20 (n=7)	0.000 (± 0.0183)			
Basophils: Week 24 (n=7)	0.016 (± 0.0257)			
Basophils: Week 28 (n=6)	0.008 (± 0.0256)			
Basophils: Week 40 (n=7)	-0.004 (± 0.0276)			
Basophils: Week 52 (n=7)	0.053 (± 0.1073)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Hematocrit

End point title	Change from Baseline in Hematology Parameter: Hematocrit
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End point description:

Change from baseline in hematology parameter: hematocrit was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of blood cells				
arithmetic mean (standard deviation)				
Week 4 (n=7)	0.009 (± 0.0204)			
Week 8 (n=7)	0.016 (± 0.0223)			
Week 12 (n=7)	0.004 (± 0.0230)			
Week 16 (n=7)	-0.006 (± 0.0299)			
Week 20 (n=7)	-0.004 (± 0.0282)			
Week 24 (n=7)	0.006 (± 0.0355)			
Week 28 (n=6)	0.010 (± 0.0237)			
Week 40 (n=7)	0.010 (± 0.0216)			
Week 52 (n=7)	0.010 (± 0.0404)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Hemoglobin

End point title	Change from Baseline in Hematology Parameter: Hemoglobin
End point description:	
Change from baseline in hematology parameter: hemoglobin was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
Week 4 (n=7)	1.9 (± 9.12)			
Week 8 (n=7)	2.3 (± 8.28)			
Week 12 (n=7)	-0.1 (± 9.60)			
Week 16 (n=7)	-3.0 (± 9.35)			
Week 20 (n=7)	-4.1 (± 5.84)			
Week 24 (n=7)	-0.3 (± 9.81)			

Week 28 (n=6)	-2.7 (± 8.71)			
Week 40 (n=7)	0.1 (± 8.91)			
Week 52 (n=7)	0.7 (± 11.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Erythrocytes

End point title	Change from Baseline in Hematology Parameter: Erythrocytes
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End point description:

Change from baseline in hematology parameter: erythrocytes was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: 10 ¹² cells per liter (10 ¹² /L)				
arithmetic mean (standard deviation)				
Week 4 (n=7)	0.03 (± 0.236)			
Week 8 (n=7)	0.13 (± 0.309)			
Week 12 (n=7)	0.04 (± 0.336)			
Week 16 (n=7)	-0.07 (± 0.269)			
Week 20 (n=7)	-0.06 (± 0.230)			
Week 24 (n=7)	0.04 (± 0.299)			
Week 28 (n=6)	0.07 (± 0.266)			
Week 40 (n=7)	0.07 (± 0.335)			
Week 52 (n=7)	0.04 (± 0.412)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Chemistry Parameters: Sodium, Potassium, Urea Nitrogen, Glucose, and Calcium

End point title	Change from Baseline in Chemistry Parameters: Sodium, Potassium, Urea Nitrogen, Glucose, and Calcium
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End point description:

Change from baseline in chemistry parameters: sodium, potassium, urea nitrogen, glucose, and calcium

was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
End point timeframe:	
Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: 10 ¹² cells per liter (10 ¹² /L)				
arithmetic mean (standard deviation)				
Sodium: Week 4 (n=7)	-0.1 (± 3.85)			
Sodium: Week 8 (n=7)	0.1 (± 1.57)			
Sodium: Week 12 (n=6)	0.2 (± 1.17)			
Sodium: Week 16 (n=7)	-0.7 (± 1.98)			
Sodium: Week 20 (n=7)	-0.1 (± 2.34)			
Sodium: Week 24 (n=7)	0.3 (± 2.98)			
Sodium: Week 28 (n=6)	1.5 (± 1.87)			
Sodium: Week 40 (n=7)	-0.1 (± 2.04)			
Sodium: Week 52 (n=7)	-0.7 (± 2.43)			
Potassium: Week 4 (n=7)	0.46 (± 1.137)			
Potassium: Week 8 (n=7)	0.03 (± 0.330)			
Potassium: Week 12 (n=6)	0.10 (± 0.494)			
Potassium: Week 16 (n=7)	-0.09 (± 0.234)			
Potassium: Week 20 (n=7)	0.03 (± 0.315)			
Potassium: Week 24 (n=7)	-0.09 (± 0.261)			
Potassium: Week 28 (n=6)	-0.07 (± 0.186)			
Potassium: Week 40 (n=7)	0.07 (± 0.298)			
Potassium: Week 52 (n=7)	0.04 (± 0.336)			
Urea Nitrogen: Week 4 (n=7)	-0.0510 (± 1.32665)			
Urea Nitrogen: Week 8 (n=7)	-0.3060 (± 1.32665)			
Urea Nitrogen: Week 12 (n=6)	0.0000 (± 1.39184)			
Urea Nitrogen: Week 16 (n=7)	0.3060 (± 1.19170)			
Urea Nitrogen: Week 20 (n=7)	-0.8160 (± 1.10448)			
Urea Nitrogen: Week 24 (n=7)	-0.1020 (± 1.14229)			
Urea Nitrogen: Week 28 (n=6)	-0.3570 (± 0.98418)			
Urea Nitrogen: Week 40 (n=7)	-0.8160 (± 1.40875)			
Urea Nitrogen: Week 52 (n=7)	-0.3060 (± 1.84847)			
Glucose: Week 4 (n=7)	0.34099 (± 0.601656)			

Glucose: Week 8 (n=7)	0.22204 (± 0.652101)			
Glucose: Week 12 (n=6)	0.05548 (± 0.641615)			
Glucose: Week 16 (n=7)	0.35684 (± 0.503536)			
Glucose: Week 20 (n=7)	0.47580 (± 0.527417)			
Glucose: Week 24 (n=7)	0.60266 (± 0.730401)			
Glucose: Week 28 (n=6)	0.60133 (± 0.933768)			
Glucose: Week 40 (n=7)	0.39649 (± 0.628362)			
Glucose: Week 52 (n=7)	0.00791 (± 0.554573)			
Calcium: Week 4 (n=7)	-0.09980 (± 0.293456)			
Calcium: Week 8 (n=7)	-0.00357 (± 0.098172)			
Calcium: Week 12 (n=6)	-0.04158 (± 0.068184)			
Calcium: Week 16 (n=7)	-0.04634 (± 0.124293)			
Calcium: Week 20 (n=7)	-0.07486 (± 0.097716)			
Calcium: Week 24 (n=7)	-0.03564 (± 0.097564)			
Calcium: Week 28 (n=6)	-0.02495 (± 0.130142)			
Calcium: Week 40 (n=7)	-0.06416 (± 0.145380)			
Calcium: Week 52 (n=7)	-0.03563 (± 0.108627)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Chemistry Parameters: Creatinine (Jaffe Reaction), Bilirubin, and Direct Bilirubin,

End point title	Change from Baseline in Chemistry Parameters: Creatinine (Jaffe Reaction), Bilirubin, and Direct Bilirubin,
End point description: Change from baseline in chemistry parameters: creatinine, bilirubin, and direct bilirubin was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.	
End point type	Secondary
End point timeframe: Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: micromoles per liter (mcmol/L)				
arithmetic mean (standard deviation)				
Creatinine: Week 4 (n=6)	-0.2947 (± 4.92719)			
Creatinine: Week 8 (n=7)	-4.0411 (± 7.82156)			
Creatinine: Week 12 (n=6)	-1.9153 (± 11.69311)			
Creatinine: Week 16 (n=7)	-2.5257 (± 8.69784)			
Creatinine: Week 20 (n=7)	-2.5257 (± 10.36492)			
Creatinine: Week 24 (n=7)	0.1263 (± 9.20703)			
Creatinine: Week 28 (n=6)	-3.5360 (± 8.69741)			
Creatinine: Week 40 (n=7)	-1.1366 (± 8.82104)			
Creatinine: Week 52 (n=7)	-1.2629 (± 11.22665)			
Bilirubin: Week 4 (n=7)	-0.733 (± 1.6688)			
Bilirubin: Week 8 (n=7)	0.733 (± 2.9382)			
Bilirubin: Week 12 (n=6)	-0.570 (± 0.8830)			
Bilirubin: Week 16 (n=7)	-0.489 (± 0.8344)			
Bilirubin: Week 20 (n=7)	0.489 (± 1.2926)			
Bilirubin: Week 24 (n=7)	0.733 (± 1.6688)			
Bilirubin: Week 28 (n=6)	0.285 (± 0.6981)			
Bilirubin: Week 40 (n=7)	0.244 (± 1.1800)			
Bilirubin: Week 52 (n=7)	0.733 (± 0.9140)			
Direct Bilirubin: Week 4 (n=5)	0.000 (± 0.0000)			
Direct Bilirubin: Week 8 (n=6)	0.285 (± 0.6981)			
Direct Bilirubin: Week 12 (n=6)	0.000 (± 0.0000)			
Direct Bilirubin: Week 16 (n=6)	0.000 (± 0.0000)			
Direct Bilirubin: Week 20 (n=7)	0.000 (± 0.0000)			
Direct Bilirubin: Week 24 (n=6)	0.000 (± 0.0000)			
Direct Bilirubin: Week 28 (n=6)	0.000 (± 0.0000)			
Direct Bilirubin: Week 40 (n=7)	0.000 (± 0.0000)			
Direct Bilirubin: Week 52 (n=5)	0.000 (± 0.0000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Chemistry Parameters: Creatinine Clearance

End point title	Change from Baseline in Chemistry Parameters: Creatinine Clearance
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End point description:

Change from baseline in chemistry parameter: creatinine clearance was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: milliliters per second (mL/s)				
arithmetic mean (standard deviation)				
Week 4 (n=6)	0.08337 (± 0.227335)			
Week 8 (n=7)	0.19291 (± 0.280068)			
Week 12 (n=6)	0.13057 (± 0.353525)			
Week 16 (n=7)	0.16670 (± 0.296181)			
Week 20 (n=7)	0.23817 (± 0.382532)			
Week 24 (n=7)	0.07384 (± 0.285638)			
Week 28 (n=6)	0.23615 (± 0.307994)			
Week 40 (n=7)	0.12623 (± 0.344860)			
Week 52 (n=7)	0.21671 (± 0.540583)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Chemistry Parameters: Glomerular Filtration Rate (GFR) from Cystatin C Adjusted for Body Surface Area (BSA)

End point title	Change from Baseline in Chemistry Parameters: Glomerular Filtration Rate (GFR) from Cystatin C Adjusted for Body Surface Area (BSA)
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End point description:

Change from baseline in chemistry parameter: GFR from Cystatin C Adjusted for BSA was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: mL/second/meter square(mL/s/m^2)				
arithmetic mean (standard deviation)				
Week 4 (n=7)	0.05670 (± 0.193047)			
Week 8 (n=7)	0.11014 (± 0.233865)			
Week 12 (n=6)	0.12838 (± 0.262144)			
Week 16 (n=7)	0.05853 (± 0.181786)			
Week 20 (n=7)	0.07144 (± 0.264242)			
Week 24 (n=7)	0.04350 (± 0.180046)			
Week 28 (n=6)	0.03373 (± 0.182168)			
Week 40 (n=7)	0.06939 (± 0.205418)			
Week 52 (n=7)	0.03863 (± 0.203820)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Chemistry Parameters: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP)

End point title	Change from Baseline in Chemistry Parameters: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP)
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End point description:

Change from baseline in chemistry parameters: AST, ALT, and ALP was reported. Safety analysis set included all participants who took at least 1 dose of study intervention. Here, "n" (number analyzed) refer to the number of participants evaluable at specified timepoints.

End point type	Secondary
End point timeframe:	
Baseline (Day 1), Weeks 4, 8, 12, 16, 20, 24, 28, 40, 52	

End point values	Macitentan			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Enzyme units per liter (Enzyme U/L)				
arithmetic mean (standard deviation)				
AST: Week 4 (n=6)	4.2 (± 5.60)			
AST: Week 8 (n=6)	4.5 (± 10.33)			
AST: Week 12 (n=6)	-0.8 (± 1.94)			
AST: Week 16 (n=7)	-2.0 (± 4.97)			
AST: Week 20 (n=7)	0.1 (± 4.78)			
AST: Week 24 (n=6)	0.8 (± 1.47)			
AST: Week 28 (n=6)	-2.2 (± 4.49)			
AST: Week 40 (n=7)	0.1 (± 9.75)			
AST: Week 52 (n=7)	-2.9 (± 4.22)			
ALT: Week 4 (n=7)	3.3 (± 4.57)			
ALT: Week 8 (n=7)	1.6 (± 3.69)			
ALT: Week 12 (n=6)	1.2 (± 3.19)			
ALT: Week 16 (n=7)	-1.6 (± 3.31)			
ALT: Week 20 (n=7)	0.0 (± 1.41)			
ALT: Week 24 (n=7)	2.6 (± 5.74)			
ALT: Week 28 (n=6)	-1.2 (± 2.40)			
ALT: Week 40 (n=7)	1.3 (± 6.21)			
ALT: Week 52 (n=7)	0.4 (± 4.12)			
ALP: Week 4 (n=7)	-15.4 (± 47.60)			
ALP: Week 8 (n=7)	-12.3 (± 35.45)			
ALP: Week 12 (n=6)	-37.2 (± 27.75)			
ALP: Week 16 (n=7)	-12.0 (± 48.25)			
ALP: Week 20 (n=7)	-21.1 (± 39.81)			
ALP: Week 24 (n=7)	20.7 (± 120.53)			
ALP: Week 28 (n=6)	153.8 (± 436.62)			
ALP: Week 40 (n=7)	-37.0 (± 44.79)			
ALP: Week 52 (n=7)	-6.4 (± 29.79)			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: From screening (Day -30) up to Week 56; Serious and Non-serious AEs: From baseline (Day 1) up to Week 56

Adverse event reporting additional description:

Safety analysis set included all participants who took at least 1 dose of study intervention.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Macitentan
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Reporting group description:

Participants received macitentan 1 milligram (mg) or 2.5 mg tablets orally once daily based on age and body weight. Participants aged greater than or equal to ($\geq$) 3 months to less than ($<$) 6 months received daily dose of macitentan 1 mg, $\geq$ 6 months to $<$ 2 years received daily dose of macitentan 2.5 mg. For participants above 2 years (inclusive) of age, daily doses of macitentan were 3.5 mg ($<$ 15 kilograms [kg] body weight [BW]), 5 mg ($\geq$ 15 kg to $<$ 25 kg BW), 7.5 mg ($\geq$ 25 kg to $<$ 50 kg BW), and 10 mg ($\geq$ 50 kg BW). Treatment was administered from Day 1 to Week 52.

Serious adverse events	Macitentan		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Bacterial			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metapneumovirus Infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Macitentan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter Site Dermatitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Obstructive Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nasal Obstruction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Investigations			
Crystal Urine Present			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Post-Traumatic Neck Syndrome subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Head Injury subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Fall subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Arthropod Bite subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Congenital, familial and genetic disorders Ichthyosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Nervous system disorders Tongue Biting subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Blood and lymphatic system disorders Iron Deficiency Anaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Neutropenia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Eye disorders Conjunctivitis Allergic subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Ocular Hyperaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Strabismus			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Gastrointestinal disorders			
Abdominal Pain subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 4		
Faeces Soft subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders			
Haemorrhage Subcutaneous subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Dermatitis Allergic subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Acne subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Urticaria subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Rash subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Miliaria subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Infections and infestations			
Viral Infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Streptococcal Infection			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Pneumonia Viral			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Paronychia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Otitis Media			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	6 / 7 (85.71%)		
occurrences (all)	24		
Adenovirus Infection			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Conjunctivitis Bacterial			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Herpes Virus Infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2021	The reason for this protocol amendment was to clarify that the treatment of pulmonary arterial hypertension (PAH) worsening is not limited to a specific drug, but within the scope of routine clinical practice.
25 November 2021	The reason for this protocol amendment was to modify the amount of blood collected and to add time points for blood collection in pediatric participants < 2 years. Minor corrections and editorial revisions were also implemented.
09 March 2022	The reason for this protocol amendment was to change the inclusion/exclusion criteria, to update the method of administration and to modify the definition prohibited concomitant therapy. Minor corrections and editorial revisions were also implemented.
09 March 2023	The reason for this protocol amendment was to add allowance for Day 1 and to add interpretation of exclusion criteria, and to also allow for the use of local laboratory data for eligibility assessment. Minor corrections and editorial revisions were also implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The interpretation of study results was limited by small sample size of only 7 participants. Study was not controlled, hence no comparison to Standard of Care (or placebo) was possible.

Notes: