Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single Ascending Doses of REGN5381, an NPR1 Agonist, in Heart Failure Patients with Elevated Pulmonary Capillary Wedge Pressure

Summary

EudraCT number	2021-006337-19
Trial protocol	BE HU
Global end of trial date	02 June 2025

Results information

Result version number	v1 (current)
This version publication date	18 June 2026
First version publication date	18 June 2026

Trial information

Trial identification

Sponsor protocol code	R5381-HF-2159

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05353166
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.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	22 July 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 June 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the safety and tolerability of single doses of REGN5381 in patients with heart failure with evidence of congestion.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	30 June 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	Moldova, Republic of: 59
Worldwide total number of subjects	59
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	34
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

101 participants were screened. A total of 59 participants were randomized and received study treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A: Placebo

Arm description:

Participants with heart failure with reduced ejection fraction (HFrEF) not taking sacubitril/valsartan received a single intravenous (IV) infusion of matching placebo for REGN5381.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 matching placebo as a single dose administered via intravenous (IV) infusion.

Arm title	Group A: REGN5381 10 mg

Arm description:

Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 10 milligrams (mg).

Arm type	Experimental
Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group A: REGN5381 30 mg

Arm description:

Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.

Arm type	Experimental

Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group A: REGN5381 100 mg

Arm description:

Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.

Arm type	Experimental
Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group A: REGN5381 300 mg

Arm description:

Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.

Arm type	Experimental
Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group C: Placebo

Arm description:

Participants with heart failure with preserved ejection fraction (HFpEF) not taking sacubitril/valsartan received a single IV infusion of matching placebo for REGN5381.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 matching placebo as a single dose administered via IV infusion.

Arm title	Group C: REGN5381 30 mg

Arm description:

Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.

Arm type	Experimental

Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group C: REGN5381 100 mg

Arm description:

Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.

Arm type	Experimental
Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Arm title	Group C: REGN5381 300 mg

Arm description:

Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.

Arm type	Experimental
Investigational medicinal product name	REGN5381
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received REGN5381 as a single dose administered via IV infusion.

Number of subjects in period 1	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg
Started	7	3	3
Received study treatment	7	3	3
Completed	7	3	3
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	Group A: REGN5381 100 mg	Group A: REGN5381 300 mg	Group C: Placebo
Started	6	4	18
Received study treatment	6	4	18
Completed	6	3	18
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

Number of subjects in period 1	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg	Group C: REGN5381 300 mg
Started	3	3	12
Received study treatment	3	3	12
Completed	3	3	12
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Group A: Placebo
Reporting group description:	
Participants with heart failure with reduced ejection fraction (HFrEF) not taking sacubitril/valsartan received a single intravenous (IV) infusion of matching placebo for REGN5381.	
Reporting group title	Group A: REGN5381 10 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 10 milligrams (mg).	
Reporting group title	Group A: REGN5381 30 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.	
Reporting group title	Group A: REGN5381 100 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.	
Reporting group title	Group A: REGN5381 300 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.	
Reporting group title	Group C: Placebo
Reporting group description:	
Participants with heart failure with preserved ejection fraction (HFpEF) not taking sacubitril/valsartan received a single IV infusion of matching placebo for REGN5381.	
Reporting group title	Group C: REGN5381 30 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.	
Reporting group title	Group C: REGN5381 100 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.	
Reporting group title	Group C: REGN5381 300 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.	

Reporting group values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg
Number of subjects	7	3	3
Age Categorical			
Age Group at screening			
Units: participants			
< 18 years	0	0	0
≥ 18 to < 45 years	0	0	0
≥ 45 to < 65 years	5	3	3
≥ 65 to < 75 years	2	0	0
≥ 75 years	0	0	0

Sex: Female, Male Units: participants			
Female	1	0	1
Male	6	3	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	3	3
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	3	3
Unknown or Not Reported	0	0	0

Reporting group values	Group A: REGN5381 100 mg	Group A: REGN5381 300 mg	Group C: Placebo
Number of subjects	6	4	18
Age Categorical			
Age Group at screening			
Units: participants			
< 18 years	0	0	0
≥ 18 to < 45 years	2	0	0
≥ 45 to < 65 years	3	4	7
≥ 65 to < 75 years	1	0	11
≥ 75 years	0	0	0
Sex: Female, Male Units: participants			
Female	1	1	5
Male	5	3	13
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	4	18
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	4	18
Unknown or Not Reported	0	0	0

Reporting group values	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg	Group C: REGN5381 300 mg

Number of subjects	3	3	12
Age Categorical			
Age Group at screening			
Units: participants			
< 18 years	0	0	0
≥ 18 to < 45 years	0	0	0
≥ 45 to < 65 years	0	2	5
≥ 65 to < 75 years	3	1	6
≥ 75 years	0	0	1
Sex: Female, Male Units: participants			
Female	0	0	4
Male	3	3	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	12
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	12
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	59		
Age Categorical			
Age Group at screening			
Units: participants			
< 18 years	0		
≥ 18 to < 45 years	2		
≥ 45 to < 65 years	32		
≥ 65 to < 75 years	24		
≥ 75 years	1		
Sex: Female, Male Units: participants			
Female	13		
Male	46		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	59		
Unknown or Not Reported	0		
Race/Ethnicity, Customized			
Race			
Units: Subjects			

American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	59		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Group A: Placebo
Reporting group description:	
Participants with heart failure with reduced ejection fraction (HFrEF) not taking sacubitril/valsartan received a single intravenous (IV) infusion of matching placebo for REGN5381.	
Reporting group title	Group A: REGN5381 10 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 10 milligrams (mg).	
Reporting group title	Group A: REGN5381 30 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.	
Reporting group title	Group A: REGN5381 100 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.	
Reporting group title	Group A: REGN5381 300 mg
Reporting group description:	
Participants with HFrEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.	
Reporting group title	Group C: Placebo
Reporting group description:	
Participants with heart failure with preserved ejection fraction (HFpEF) not taking sacubitril/valsartan received a single IV infusion of matching placebo for REGN5381.	
Reporting group title	Group C: REGN5381 30 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 30 mg.	
Reporting group title	Group C: REGN5381 100 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 100 mg.	
Reporting group title	Group C: REGN5381 300 mg
Reporting group description:	
Participants with HFpEF not taking sacubitril/valsartan received a single IV infusion of REGN5381 at a dose of 300 mg.	
Subject analysis set title	Groups A and B: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with HFrEF or HFpEF not taking sacubitril/valsartan received a single IV infusion of matching placebo for REGN5381.	

Primary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs)[1]
End point description:	
An adverse event (AE) was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. TEAEs were defined as those adverse events with either initial onset after study drug dose or that represented an exacerbation of a pre-existing condition after the study drug dose. The safety analysis set (SAF) included all randomized participants who received any study drug.	
End point type	Primary

End point timeframe:

From first dose (Day 1) up to end of study (Day 126)

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: Statistical analysis not conducted.

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: participants	1	1	1	1

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: participants	3	3	1	2

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulmonary Capillary Wedge Pressure (PCWP)

End point title	Change from Baseline in Pulmonary Capillary Wedge Pressure (PCWP)

End point description:

PCWP was collected during the right heart catheterization on Day 1. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (2 hours, 4 hours, and 6 hours post end of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
2 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-4.7 (± 3.34)	-5.9 (± 6.00)	-4.6 (± 1.67)	-7.1 (± 3.12)
4 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-5.4 (± 2.49)	-4.7 (± 6.24)	-4.7 (± 2.91)	-6.3 (± 2.09)
6 hours post end of infusion n=6,3,3,4,4,18,3,2,11	-3.8 (± 2.67)	-4.6 (± 5.48)	-3.3 (± 3.93)	-8.0 (± 1.59)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
2 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-5.8 (± 3.80)	-2.7 (± 1.66)	-5.9 (± 5.67)	-7.6 (± 1.50)
4 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-7.4 (± 4.56)	-3.2 (± 1.95)	-5.8 (± 4.88)	-7.0 (± 0.88)
6 hours post end of infusion n=6,3,3,4,4,18,3,2,11	-6.7 (± 6.65)	-3.3 (± 2.32)	-4.8 (± 4.17)	-9.3 (± 1.41)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
2 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-4.8 (± 1.51)			
4 hours post end of infusion n=6,3,3,4,4,18,3,3,11	-5.4 (± 2.14)			
6 hours post end of infusion n=6,3,3,4,4,18,3,2,11	-7.2 (± 2.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Central Venous Pressure (CVP)

End point title	Change from Baseline in Central Venous Pressure (CVP)

End point description:

CVP was collected during the right heart catheterization on day 1. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0-1 hour, 1-2 hours, 2-3 hours, 3-4 hours, 4-5 hours, 5-6 hours, and 6-7 hours post start of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=4,0,3,4,4,18,3,3,11	1.7 (± 1.62)	99999 (± 99999)	-4.6 (± 7.71)	-0.2 (± 0.43)
1-2hrs post start infusion n=4,0,3,4,4,18,3,3,11	1.2 (± 2.07)	99999 (± 99999)	-4.1 (± 7.96)	0.0 (± 1.08)
2-3hrs post start infusion n=4,0,3,4,4,18,3,3,11	-0.7 (± 3.73)	99999 (± 99999)	-6.0 (± 8.37)	-0.3 (± 3.26)
3-4hrs post start infusion n=4,0,3,4,4,18,3,3,11	-0.3 (± 2.76)	99999 (± 99999)	-5.5 (± 7.95)	-1.3 (± 1.03)
4-5hrs post start infusion n=4,0,3,4,4,18,3,3,11	-0.5 (± 3.39)	99999 (± 99999)	-6.7 (± 8.67)	-1.5 (± 1.40)
5-6hrs post start infusion n=4,0,3,4,4,18,3,3,11	-0.7 (± 1.95)	99999 (± 99999)	-5.7 (± 8.61)	-2.3 (± 1.57)
6-7hrs post start infusion n=4,0,3,4,4,18,3,2,11	0.2 (± 2.23)	99999 (± 99999)	-5.6 (± 8.92)	-3.2 (± 2.42)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=4,0,3,4,4,18,3,3,11	-0.3 (± 0.44)	-0.3 (± 1.56)	-0.3 (± 1.82)	-0.2 (± 0.15)
1-2hrs post start infusion n=4,0,3,4,4,18,3,3,11	-1.6 (± 1.09)	-0.9 (± 2.04)	-1.1 (± 2.58)	-1.7 (± 1.18)
2-3hrs post start infusion n=4,0,3,4,4,18,3,3,11	-2.9 (± 1.97)	-1.8 (± 1.44)	-1.3 (± 1.41)	-2.1 (± 1.15)
3-4hrs post start infusion n=4,0,3,4,4,18,3,3,11	-2.8 (± 1.98)	-1.4 (± 2.78)	-3.2 (± 2.15)	-2.3 (± 2.13)
4-5hrs post start infusion n=4,0,3,4,4,18,3,3,11	-4.1 (± 3.26)	-2.2 (± 2.54)	-4.1 (± 2.80)	-2.9 (± 1.84)
5-6hrs post start infusion n=4,0,3,4,4,18,3,3,11	-4.7 (± 3.80)	-2.7 (± 2.73)	-3.5 (± 1.24)	-3.6 (± 1.52)
6-7hrs post start infusion n=4,0,3,4,4,18,3,2,11	-4.6 (± 3.07)	-3.0 (± 2.48)	-4.1 (± 2.32)	-3.3 (± 0.55)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=4,0,3,4,4,18,3,3,11	-0.6 (± 2.52)			
1-2hrs post start infusion n=4,0,3,4,4,18,3,3,11	-1.6 (± 2.64)			
2-3hrs post start infusion n=4,0,3,4,4,18,3,3,11	-1.7 (± 2.35)			
3-4hrs post start infusion n=4,0,3,4,4,18,3,3,11	-3.3 (± 2.79)			
4-5hrs post start infusion n=4,0,3,4,4,18,3,3,11	-4.3 (± 2.29)			
5-6hrs post start infusion n=4,0,3,4,4,18,3,3,11	-4.4 (± 2.39)			
6-7hrs post start infusion n=4,0,3,4,4,18,3,2,11	-5.0 (± 2.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Invasive Cardiac Output (CO)

End point title	Change from Baseline in Invasive Cardiac Output (CO)

End point description:

CO was collected during the right heart catheterization on day 1. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0-1 hour, 1-2 hours, 2-3 hours, 3-4 hours, 4-5 hours, 5-6 hours, and 6-7 hours post start of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: Liters per minute (L/min)				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=5,0,3,4,4,18,3,3,11	0.16 (± 0.953)	99999 (± 99999)	-0.44 (± 1.258)	0.17 (± 0.674)

1-2hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.29 (± 0.811)	99999 (± 99999)	-0.57 (± 1.555)	0.03 (± 0.942)
2-3hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.00 (± 1.005)	99999 (± 99999)	-0.64 (± 1.337)	-0.08 (± 0.894)
3-4hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.39 (± 0.705)	99999 (± 99999)	-0.91 (± 1.409)	-0.53 (± 0.946)
4-5hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.61 (± 1.120)	99999 (± 99999)	-1.31 (± 0.444)	-0.12 (± 1.214)
5-6hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.18 (± 1.128)	99999 (± 99999)	-1.06 (± 0.912)	0.27 (± 1.550)
6-7hrs post start infusion n=5,0,3,4,4,18,3,2,11	0.06 (± 1.186)	99999 (± 99999)	-1.22 (± 0.530)	0.06 (± 1.140)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: Liters per minute (L/min)				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=5,0,3,4,4,18,3,3,11	0.27 (± 0.157)	-0.14 (± 0.547)	-0.01 (± 0.394)	0.12 (± 0.260)
1-2hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.48 (± 0.829)	0.05 (± 0.622)	0.02 (± 0.552)	0.26 (± 0.255)
2-3hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.31 (± 0.866)	0.25 (± 0.404)	0.39 (± 0.713)	0.09 (± 0.381)
3-4hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.36 (± 1.111)	0.46 (± 0.807)	0.84 (± 0.846)	0.21 (± 0.386)
4-5hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.48 (± 1.271)	0.75 (± 0.856)	0.00 (± 1.257)	0.12 (± 0.482)
5-6hrs post start infusion n=5,0,3,4,4,18,3,3,11	0.18 (± 0.926)	0.55 (± 0.663)	-0.40 (± 0.993)	0.01 (± 0.339)
6-7hrs post start infusion n=5,0,3,4,4,18,3,2,11	-0.01 (± 1.182)	0.42 (± 0.788)	0.14 (± 0.914)	-0.45 (± 0.575)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Liters per minute (L/min)				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=5,0,3,4,4,18,3,3,11	-0.36 (± 0.598)			
1-2hrs post start infusion n=5,0,3,4,4,18,3,3,11	-0.37 (± 0.658)			
2-3hrs post start infusion n=5,0,3,4,4,18,3,3,11	-0.23 (± 0.849)			
3-4hrs post start infusion n=5,0,3,4,4,18,3,3,11	-0.08 (± 1.020)			
4-5hrs post start infusion n=5,0,3,4,4,18,3,3,11	-0.39 (± 1.055)			
5-6hrs post start infusion n=5,0,3,4,4,18,3,3,11	-0.31 (± 0.970)			

6-7hrs post start infusion n=5,0,3,4,4,18,3,2,11	-0.63 (± 1.173)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Systemic Vascular Resistance (SVR)

End point title	Change from Baseline in Systemic Vascular Resistance (SVR)

End point description:

SVR was derived as follows: [(Mean Arterial Pressure-Central Venous Pressure)*80]/ Invasive Cardiac Output. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0 hours, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, and 6 hours post end of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: dynes*second/centimeter^5 (dynes*s/cm^5)				
arithmetic mean (standard deviation)				
0 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	-532.3 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
1 hr post end of infusion n=2,0,0,0,4,18,3,3,11	-177.8 (± 57.33)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
2 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	-200.2 (± 393.80)	99999 (± 99999)	144.4 (± 410.20)	-111.1 (± 161.60)
3 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	-783.1 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
4 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	-286.9 (± 426.15)	99999 (± 99999)	337.1 (± 212.36)	-92.5 (± 343.89)
5 hrs post end of infusion n=1,0,0,0,4,18,3,2, 11	-931.1 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
6 hrs post end of infusion n=4,0,3,4,4,15,3,2,7	-26.1 (± 514.13)	99999 (± 99999)	207.5 (± 35.47)	-273.2 (± 399.00)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: dynes*second/centimeter^5				

(dynes*s/cm^5)				
arithmetic mean (standard deviation)				
0 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	-140.4 (± 376.06)	-47.0 (± 249.47)	8.8 (± 341.15)	-134.2 (± 37.16)
1 hr post end of infusion n=2,0,0,0,4,18,3,3,11	-135.8 (± 621.85)	22.8 (± 281.92)	-111.9 (± 349.44)	-98.8 (± 42.21)
2 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	72.2 (± 530.78)	-48.4 (± 248.87)	-417.6 (± 436.76)	-87.6 (± 130.03)
3 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	-8.1 (± 369.55)	-187.5 (± 320.75)	-279.4 (± 584.68)	-176.0 (± 157.69)
4 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	67.0 (± 499.98)	-204.9 (± 303.79)	315.9 (± 432.37)	-175.3 (± 233.77)
5 hrs post end of infusion n=1,0,0,0,4,18,3,2, 11	56.9 (± 199.05)	-74.1 (± 263.81)	-44.3 (± 323.25)	-89.4 (± 270.01)
6 hrs post end of infusion n=4,0,3,4,4,15,3,2,7	243.2 (± 583.73)	-58.5 (± 262.84)	-53.2 (± 211.54)	-26.3 (± 234.13)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: dynes*second/centimeter^5 (dynes*s/cm^5)				
arithmetic mean (standard deviation)				
0 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	110.1 (± 350.02)			
1 hr post end of infusion n=2,0,0,0,4,18,3,3,11	195.3 (± 316.23)			
2 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	-31.1 (± 266.34)			
3 hrs post end of infusion n=1,0,0,0,4,18,3,3,11	22.2 (± 380.63)			
4 hrs post end of infusion n=4,0,3,4,4,18,3,3,11	166.1 (± 348.38)			
5 hrs post end of infusion n=1,0,0,0,4,18,3,2, 11	103.2 (± 316.66)			
6 hrs post end of infusion n=4,0,3,4,4,15,3,2,7	196.8 (± 369.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Mean Pulmonary Artery Pressure (mPAP)

End point title	Change from Baseline in Mean Pulmonary Artery Pressure (mPAP)

End point description:

mPAP was collected during the right heart catheterization on day 1. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0-1 hour, 1-2 hours, 2-3 hours, 3-4 hours, 4-5 hours, 5-6 hours, and 6-7 hours post start of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=6,3,3,4,4,18,3,3,11	0.5 (± 1.39)	-0.3 (± 5.15)	0.3 (± 0.84)	-2.2 (± 2.52)
1-2hr post start of infusion n=6,3,3,4,4,18,3,3,11	1.1 (± 2.05)	4.2 (± 0.92)	0.6 (± 1.70)	-2.1 (± 2.09)
2-3hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.6 (± 1.62)	0.4 (± 4.16)	-4.0 (± 4.61)	-2.3 (± 1.76)
3-4hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.4 (± 0.90)	-4.1 (± 1.27)	-1.4 (± 1.82)	-4.5 (± 1.58)
4-5hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.6 (± 2.40)	-2.1 (± 3.05)	-7.2 (± 9.51)	-2.4 (± 4.13)
5-6hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.9 (± 1.55)	-0.8 (± 2.33)	-3.0 (± 4.22)	-5.5 (± 2.08)
6-7hr post start of infusion n=6,3,3,4,4,18,3,2,11	-0.4 (± 1.33)	-0.1 (± 2.66)	-4.6 (± 8.28)	-5.5 (± 3.15)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=6,3,3,4,4,18,3,3,11	-0.2 (± 1.52)	0.2 (± 1.46)	-1.4 (± 2.78)	-0.8 (± 0.04)
1-2hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.7 (± 2.48)	0.2 (± 2.05)	-1.9 (± 2.13)	-2.9 (± 2.04)
2-3hr post start of infusion n=6,3,3,4,4,18,3,3,11	-2.3 (± 1.57)	-0.4 (± 1.61)	-2.1 (± 3.94)	-3.6 (± 3.17)
3-4hr post start of infusion n=6,3,3,4,4,18,3,3,11	-2.9 (± 1.49)	-0.2 (± 2.56)	-4.3 (± 5.98)	-5.8 (± 4.69)
4-5hr post start of infusion n=6,3,3,4,4,18,3,3,11	-3.9 (± 3.89)	-1.6 (± 1.56)	-6.0 (± 5.73)	-6.4 (± 3.42)
5-6hr post start of infusion n=6,3,3,4,4,18,3,3,11	-4.6 (± 5.69)	-2.3 (± 2.45)	-5.0 (± 4.53)	-7.6 (± 6.64)
6-7hr post start of infusion n=6,3,3,4,4,18,3,2,11	-4.5 (± 4.40)	-2.2 (± 2.38)	-5.7 (± 6.79)	-3.8 (± 1.45)

End point values	Group C: REGN5381 300			

	mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmHg				
arithmetic mean (standard deviation)				
0-1hr post start of infusion n=6,3,3,4,4,18,3,3,11	-0.8 (± 1.50)			
1-2hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.0 (± 1.89)			
2-3hr post start of infusion n=6,3,3,4,4,18,3,3,11	-1.8 (± 2.08)			
3-4hr post start of infusion n=6,3,3,4,4,18,3,3,11	-2.9 (± 2.95)			
4-5hr post start of infusion n=6,3,3,4,4,18,3,3,11	-4.2 (± 2.10)			
5-6hr post start of infusion n=6,3,3,4,4,18,3,3,11	-4.6 (± 1.80)			
6-7hr post start of infusion n=6,3,3,4,4,18,3,2,11	-5.2 (± 2.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulmonary Vascular Resistance (PVR)

End point title	Change from Baseline in Pulmonary Vascular Resistance (PVR)

End point description:

Pulmonary Vascular Resistance was derived as follows: [(Mean Pulmonary Artery Pressure-Pulmonary Capillary Wedge Pressure)*80]/ Invasive Cardiac Output. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (2 hours, 4 hours, and 6 hours post end of infusion)

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: dynes*s/cm^5				
arithmetic mean (standard deviation)				
2 hrs post end of infusion n=5,0,3,3,4,18,3,3,11	11.5 (± 45.44)	99999 (± 99999)	72.1 (± 55.44)	78.2 (± 37.28)
4 hrs post end of infusion n=5,0,3,4,4,18,3,3,11	15.3 (± 74.84)	99999 (± 99999)	84.8 (± 53.05)	64.1 (± 74.11)
6 hrs post end of infusion n=5,0,3,4,4,18,3,2,11	7.7 (± 95.34)	99999 (± 99999)	37.7 (± 38.82)	55.2 (± 70.42)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: dynes*s/cm^5				
arithmetic mean (standard deviation)				
2 hrs post end of infusion n=5,0,3,3,4,18,3,3,11	89.9 (± 96.89)	31.5 (± 52.14)	13.5 (± 13.55)	30.0 (± 68.26)
4 hrs post end of infusion n=5,0,3,4,4,18,3,3,11	114.4 (± 172.35)	-2.1 (± 49.65)	69.1 (± 42.29)	7.5 (± 66.87)
6 hrs post end of infusion n=5,0,3,4,4,18,3,2,11	147.8 (± 164.45)	-1.1 (± 51.76)	-21.4 (± 73.65)	51.2 (± 35.76)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: dynes*s/cm^5				
arithmetic mean (standard deviation)				
2 hrs post end of infusion n=5,0,3,3,4,18,3,3,11	59.1 (± 82.64)			
4 hrs post end of infusion n=5,0,3,4,4,18,3,3,11	37.6 (± 46.72)			
6 hrs post end of infusion n=5,0,3,4,4,18,3,2,11	68.6 (± 76.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Systolic Blood Pressure (SBP)

End point title	Change from Baseline in Systolic Blood Pressure (SBP)

End point description:

The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0, 1, 2, 3, 4, 5, 6, 7, 8 hours post end of infusion [EOI]), Day 2 to Day 5 every 8 hours, Day 6 first 8 hours, Day 8, Day 15, Day 22, Day 36, Day 57, Day 78, Day 99, Day 126

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	3.7 (± 11.59)	99999 (± 99999)	99999 (± 99999)	2.0 (± 8.49)
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	4.0 (± 5.29)	99999 (± 99999)	99999 (± 99999)	3.0 (± 1.41)
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	3.0 (± 11.02)	-10.3 (± 12.01)	-7.7 (± 5.51)	-7.5 (± 5.32)
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-5.0 (± 3.46)	99999 (± 99999)	99999 (± 99999)	-5.5 (± 6.36)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-2.3 (± 4.03)	-9.0 (± 9.64)	-9.0 (± 13.45)	-2.3 (± 7.66)
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	3.0 (± 12.17)	99999 (± 99999)	99999 (± 99999)	-4.0 (± 8.49)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.3 (± 2.56)	-7.3 (± 15.04)	-2.0 (± 6.93)	-5.7 (± 7.26)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-6.7 (± 16.33)	-13.3 (± 2.08)	7.0 (± 20.66)	-7.2 (± 9.75)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-20.7 (± 15.40)	-17.7 (± 8.62)	-7.0 (± 18.33)	-11.0 (± 11.78)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-10.9 (± 11.81)	-21.7 (± 11.37)	-4.0 (± 24.27)	-9.2 (± 11.36)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-16.1 (± 16.75)	-18.0 (± 6.24)	-8.7 (± 9.50)	-4.8 (± 10.01)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-11.0 (± 7.26)	99999 (± 99999)	99999 (± 99999)	-3.3 (± 9.29)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	-6.8 (± 21.25)	99999 (± 99999)	99999 (± 99999)	-5.3 (± 11.06)
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-7.8 (± 14.31)	99999 (± 99999)	99999 (± 99999)	-2.0 (± 17.58)
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	2.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.0 (± 8.49)
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	-9.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	-4.5 (± 10.61)
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	-8.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.0 (± 21.21)
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-7.0 (± 99999)
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-2.0 (± 99999)
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-6.0 (± 99999)
Day 8 n=7,3,3,6,3,18,3,3,12	-4.1 (± 15.23)	-12.0 (± 13.75)	8.3 (± 4.51)	2.8 (± 12.73)
Day 15 n=7,3,3,6,3,18,3,3,12	-7.3 (± 10.48)	-8.7 (± 17.47)	9.3 (± 6.66)	-4.8 (± 9.99)
Day 22 n=7,3,3,6,3,18,3,3,12	-9.1 (± 12.08)	-15.7 (± 17.90)	4.3 (± 7.09)	1.3 (± 16.02)
Day 36 n=6,0,3,6,3,18,3,3,12	-14.5 (± 13.84)	99999 (± 99999)	2.3 (± 11.93)	1.5 (± 13.77)
Day 57 n=5,0,0,6,3,15,0,3,12	-4.2 (± 8.98)	99999 (± 99999)	99999 (± 99999)	1.8 (± 17.79)
Day 78 n=5,0,0,6,3,15,0,3,12	-9.8 (± 11.90)	99999 (± 99999)	99999 (± 99999)	-0.5 (± 15.50)
Day 99 n=2,0,0,0,3,12,0,0,12	-4.0 (± 14.14)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Day 126 n=2,0,0,0,3,12,0,0,12	-8.0 (± 15.56)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	1.5 (± 5.57)	-0.8 (± 8.83)	1.7 (± 13.61)	-1.7 (± 4.51)
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	3.8 (± 9.00)	-0.5 (± 10.89)	-1.7 (± 13.65)	-4.3 (± 5.77)
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	1.3 (± 8.50)	-0.6 (± 10.31)	-13.0 (± 11.79)	-5.0 (± 6.56)
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	2.5 (± 8.50)	-4.7 (± 8.92)	-12.7 (± 10.50)	-12.7 (± 4.16)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-0.5 (± 8.35)	-4.6 (± 10.59)	2.7 (± 2.31)	-10.3 (± 9.24)
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-6.5 (± 16.42)	-1.9 (± 10.75)	-7.7 (± 15.01)	-6.3 (± 14.05)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-7.5 (± 15.61)	-1.5 (± 11.52)	-1.7 (± 10.69)	-5.7 (± 6.43)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-8.5 (± 21.19)	-12.9 (± 15.22)	-14.7 (± 15.53)	-8.0 (± 6.93)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-8.3 (± 25.05)	-21.8 (± 14.63)	-15.7 (± 14.05)	-7.3 (± 5.03)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.5 (± 16.84)	-13.4 (± 15.27)	-14.7 (± 9.81)	-14.3 (± 11.24)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.5 (± 13.23)	-20.4 (± 14.21)	-22.3 (± 16.29)	-18.3 (± 11.55)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-15.8 (± 16.88)	-12.0 (± 13.23)	-8.7 (± 7.37)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-12.1 (± 15.69)	-6.7 (± 16.04)	-6.0 (± 3.46)
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-39.0 (± 99999)	-18.9 (± 15.94)	-15.7 (± 15.57)	-12.3 (± 2.08)
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	99999 (± 99999)	-16.3 (± 19.67)	-9.3 (± 18.23)	-17.5 (± 2.12)
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	99999 (± 99999)	-12.7 (± 16.84)	-9.3 (± 13.65)	-15.0 (± 5.66)
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	99999 (± 99999)	-16.6 (± 16.98)	-22.3 (± 22.37)	-20.0 (± 13.00)
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	-6.5 (± 19.09)	99999 (± 99999)	99999 (± 99999)
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	-13.0 (± 18.38)	99999 (± 99999)	99999 (± 99999)
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 8 n=7,3,3,6,3,18,3,3,12	-13.3 (± 19.86)	-16.6 (± 17.39)	-21.7 (± 8.74)	-16.3 (± 6.43)
Day 15 n=7,3,3,6,3,18,3,3,12	-8.0 (± 14.11)	-9.7 (± 15.86)	-15.7 (± 13.01)	-12.7 (± 6.81)
Day 22 n=7,3,3,6,3,18,3,3,12	0.3 (± 26.39)	-8.8 (± 16.37)	-9.0 (± 14.11)	-17.7 (± 10.97)
Day 36 n=6,0,3,6,3,18,3,3,12	-1.0 (± 24.76)	-12.4 (± 13.88)	-7.3 (± 13.20)	-11.3 (± 9.29)

Day 57 n=5,0,0,6,3,15,0,3,12	-3.7 (± 25.38)	-10.4 (± 11.83)	99999 (± 99999)	-14.0 (± 11.53)
Day 78 n=5,0,0,6,3,15,0,3,12	-10.7 (± 17.56)	-9.5 (± 12.28)	99999 (± 99999)	-18.7 (± 7.64)
Day 99 n=2,0,0,0,3,12,0,0,12	-13.7 (± 29.70)	-4.0 (± 13.21)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	-1.7 (± 10.60)	-9.8 (± 16.01)	99999 (± 99999)	99999 (± 99999)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	1.6 (± 9.22)			
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	-0.6 (± 12.70)			
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-6.7 (± 14.00)			
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-8.3 (± 16.09)			
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-7.5 (± 13.91)			
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-7.7 (± 13.98)			
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-7.9 (± 13.21)			
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-15.2 (± 14.55)			
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-22.3 (± 8.52)			
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-11.8 (± 11.09)			
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-11.3 (± 11.24)			
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-19.7 (± 13.45)			
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	-5.6 (± 17.47)			
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-8.5 (± 13.85)			
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	-9.7 (± 12.49)			
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	-9.1 (± 9.17)			
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	-10.0 (± 11.10)			
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	-17.0 (± 12.73)			
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	-5.0 (± 9.90)			
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)			
Day 8 n=7,3,3,6,3,18,3,3,12	-3.9 (± 12.71)			
Day 15 n=7,3,3,6,3,18,3,3,12	-3.8 (± 10.94)			

Day 22 n=7,3,3,6,3,18,3,3,12	0.0 (± 12.95)			
Day 36 n=6,0,3,6,3,18,3,3,12	-4.1 (± 12.84)			
Day 57 n=5,0,0,6,3,15,0,3,12	-1.4 (± 13.69)			
Day 78 n=5,0,0,6,3,15,0,3,12	-3.5 (± 8.95)			
Day 99 n=2,0,0,0,3,12,0,0,12	-4.3 (± 16.69)			
Day 126 n=2,0,0,0,3,12,0,0,12	-6.0 (± 14.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Diastolic Blood Pressure (DBP)

End point title	Change from Baseline in Diastolic Blood Pressure (DBP)

End point description:

The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (0, 1, 2, 3, 4, 5, 6, 7, 8 hours post end of infusion [EOI]), Day 2 to Day 5 every 8 hours, Day 6 first 8 hours, Day 8, Day 15, Day 22, Day 36, Day 57, Day 78, Day 99, Day 126

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	0.3 (± 8.08)	99999 (± 99999)	9999 (± 99999)	6.0 (± 5.66)
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	1.7 (± 2.89)	99999 (± 99999)	99999 (± 99999)	4.0 (± 2.83)
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	0.9 (± 7.90)	-3.3 (± 6.03)	-7.7 (± 4.51)	-8.3 (± 5.28)
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-4.7 (± 5.69)	99999 (± 99999)	99999 (± 99999)	-4.0 (± 8.49)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-3.9 (± 5.21)	-8.3 (± 5.77)	-8.0 (± 11.36)	-2.3 (± 6.56)
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	0.0 (± 5.00)	99999 (± 99999)	99999 (± 99999)	-2.0 (± 4.24)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.3 (± 6.32)	-7.7 (± 7.51)	-6.7 (± 13.43)	-4.8 (± 7.70)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.3 (± 7.99)	-10.7 (± 1.53)	-0.3 (± 13.58)	-8.2 (± 6.82)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-15.3 (± 7.52)	-18.3 (± 6.35)	-9.0 (± 13.08)	-10.7 (± 7.94)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-9.7 (± 10.89)	-16.3 (± 7.77)	-9.0 (± 16.82)	-8.7 (± 10.27)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-11.9 (± 11.98)	-13.7 (± 6.11)	-13.0 (± 8.54)	-8.5 (± 4.72)

Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-8.3 (± 6.34)	99999 (± 99999)	99999 (± 99999)	-5.3 (± 7.51)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	-5.3 (± 12.97)	99999 (± 99999)	99999 (± 99999)	-4.3 (± 11.02)
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-6.3 (± 12.53)	99999 (± 99999)	99999 (± 99999)	-6.3 (± 15.63)
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	-3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	-1.0 (± 5.66)
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	-15.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	-4.5 (± 9.19)
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	2.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	-0.5 (± 19.09)
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-8.0 (± 99999)
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-8.0 (± 99999)
Day 8 n=7,3,3,6,3,18,3,3,12	-5.6 (± 13.25)	-7.0 (± 15.72)	-4.3 (± 2.89)	-2.7 (± 8.80)
Day 15 n=7,3,3,6,3,18,3,3,12	-7.7 (± 5.68)	-6.3 (± 13.65)	-1.3 (± 3.06)	-5.5 (± 11.15)
Day 22 n=7,3,3,6,3,18,3,3,12	-8.0 (± 7.26)	-16.3 (± 9.50)	-2.0 (± 5.29)	-2.7 (± 7.12)
Day 36 n=6,0,3,6,3,18,3,3,12	-12.3 (± 8.85)	99999 (± 99999)	-6.7 (± 12.42)	-1.5 (± 14.29)
Day 57 n=5,0,0,6,3,15,0,3,12	-5.8 (± 7.36)	99999 (± 99999)	99999 (± 99999)	-2.5 (± 15.88)
Day 78 n=5,0,0,6,3,15,0,3,12	-5.6 (± 5.77)	99999 (± 99999)	99999 (± 99999)	-6.5 (± 14.24)
Day 99 n=2,0,0,0,3,12,0,0,12	-2.0 (± 2.83)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	-6.0 (± 12.73)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-3.3 (± 5.62)	-1.0 (± 5.78)	0.0 (± 5.20)	-2.7 (± 4.51)
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	-1.8 (± 6.50)	0.8 (± 8.14)	-1.3 (± 2.31)	-4.7 (± 4.73)
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-0.5 (± 5.45)	-0.8 (± 7.96)	-9.3 (± 10.50)	-7.3 (± 6.66)
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-1.3 (± 6.85)	-3.1 (± 6.77)	-6.3 (± 9.61)	-8.3 (± 1.53)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-3.0 (± 4.69)	-2.7 (± 7.69)	0.0 (± 4.00)	-7.3 (± 4.04)
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-4.3 (± 6.80)	-0.6 (± 7.24)	0.0 (± 8.54)	-5.7 (± 7.02)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-5.8 (± 6.50)	1.9 (± 9.10)	1.3 (± 2.89)	-6.7 (± 4.73)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-12.8 (± 12.58)	-7.2 (± 9.85)	-9.0 (± 9.00)	-3.3 (± 3.21)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-13.3 (± 10.84)	-10.3 (± 10.03)	-9.7 (± 5.51)	-5.7 (± 7.02)

Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-8.5 (± 8.50)	-9.3 (± 9.87)	-11.0 (± 8.19)	-8.0 (± 6.24)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-9.8 (± 6.24)	-11.3 (± 8.78)	-15.0 (± 15.10)	-8.7 (± 5.03)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-8.6 (± 11.12)	-14.3 (± 9.07)	-6.7 (± 4.93)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-7.1 (± 8.37)	-16.3 (± 14.22)	-5.3 (± 3.06)
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-31.0 (± 99999)	-8.8 (± 9.01)	-14.7 (± 4.62)	-8.3 (± 4.04)
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	99999 (± 99999)	-8.2 (± 12.28)	-15.3 (± 14.64)	-12.0 (± 8.49)
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	99999 (± 99999)	-6.4 (± 11.54)	-15.7 (± 9.24)	-8.0 (± 5.66)
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	99999 (± 99999)	-8.1 (± 10.10)	-16.0 (± 15.13)	-11.7 (± 7.51)
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	-6.5 (± 12.02)	99999 (± 99999)	99999 (± 99999)
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	99999 (± 99999)	-9.0 (± 8.49)	99999 (± 99999)	99999 (± 99999)
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 8 n=7,3,3,6,3,18,3,3,12	-12.7 (± 13.87)	-9.3 (± 10.46)	-15.7 (± 11.93)	-9.3 (± 3.51)
Day 15 n=7,3,3,6,3,18,3,3,12	-12.7 (± 6.51)	-5.2 (± 8.77)	-10.0 (± 9.64)	-7.0 (± 6.00)
Day 22 n=7,3,3,6,3,18,3,3,12	-10.7 (± 16.62)	-3.1 (± 9.29)	-12.0 (± 9.54)	-9.7 (± 3.06)
Day 36 n=6,0,3,6,3,18,3,3,12	-15.7 (± 20.74)	-5.3 (± 6.82)	-10.7 (± 7.37)	-6.7 (± 5.86)
Day 57 n=5,0,0,6,3,15,0,3,12	-17.0 (± 22.61)	-4.5 (± 7.02)	99999 (± 99999)	-6.3 (± 6.43)
Day 78 n=5,0,0,6,3,15,0,3,12	-16.0 (± 13.89)	-3.3 (± 6.69)	99999 (± 99999)	-8.3 (± 3.06)
Day 99 n=2,0,0,0,3,12,0,0,12	-18.0 (± 18.25)	-0.3 (± 6.20)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	-11.7 (± 14.01)	-3.8 (± 10.82)	99999 (± 99999)	99999 (± 99999)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (0 hrs post EOI) n=3,0,0,2,4,18,3,3,12	0.7 (± 6.80)			
Day 1 (1 hr post EOI) n=3,0,0,2,4,18,3,3,12	0.8 (± 4.73)			
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.2 (± 8.08)			
Day 1 (3 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-3.8 (± 8.94)			
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-4.4 (± 8.20)			
Day 1 (5 hrs post EOI) n=3,0,0,2,4,18,3,3,12	-4.1 (± 9.17)			

Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-3.3 (± 8.15)			
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-9.1 (± 8.02)			
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-13.6 (± 8.62)			
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-8.2 (± 7.47)			
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-5.7 (± 7.40)			
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-10.9 (± 8.77)			
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	-5.2 (± 11.61)			
Day 4 (first 8 hrs) n=4,0,0,3,1,18,3,3,12	-6.5 (± 8.15)			
Day 4 (second 8 hrs) n=1,0,0,2,0,18,3,2,12	-6.8 (± 7.29)			
Day 4 (third 8 hrs) n=1,0,0,2,0,18,3,2,12	-7.2 (± 6.94)			
Day 5 (first 8 hrs) n=1,0,0,2,0,18,3,3,12	-8.2 (± 7.93)			
Day 5 (second 8 hrs) n=0,0,0,1,0,2,0,0,2	-11.5 (± 3.54)			
Day 5 (third 8 hrs) n=0,0,0,1,0,2,0,0,2	-7.0 (± 2.83)			
Day 6 (first 8 hrs) n=0,0,0,1,0,0,0,0,0	99999 (± 99999)			
Day 8 n=7,3,3,6,3,18,3,3,12	-2.8 (± 7.03)			
Day 15 n=7,3,3,6,3,18,3,3,12	-4.8 (± 5.47)			
Day 22 n=7,3,3,6,3,18,3,3,12	-3.8 (± 7.59)			
Day 36 n=6,0,3,6,3,18,3,3,12	-5.1 (± 12.91)			
Day 57 n=5,0,0,6,3,15,0,3,12	-2.7 (± 5.63)			
Day 78 n=5,0,0,6,3,15,0,3,12	-5.8 (± 6.94)			
Day 99 n=2,0,0,0,3,12,0,0,12	-3.8 (± 8.50)			
Day 126 n=2,0,0,0,3,12,0,0,12	-4.2 (± 10.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Mean Arterial Pressure (MAP)

End point title	Change from Baseline in Mean Arterial Pressure (MAP)

End point description:

MAP was derived as follows: (1/3*SBP + 2/3*DBP). The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (2 hours, 4 hours, and 6 hours post end of infusion [EOI]), Day 2 (first 8 hours, second 8 hours, third 8 hours), Day 3 (first 8 hours, second 8 hours, third 8 hours), Day 8, Day 15, Day 22, Day 36, Day 57, Day 78, Day 99, Day 126

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	1.5 (± 9.10)	-5.6 (± 7.13)	-7.3 (± 2.91)	-8.4 (± 5.03)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-3.4 (± 4.30)	-8.8 (± 4.17)	-8.1 (± 12.08)	-2.7 (± 6.84)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.0 (± 5.04)	-7.7 (± 11.02)	-5.0 (± 11.67)	-5.6 (± 7.96)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.4 (± 10.44)	-12.3 (± 1.20)	1.9 (± 15.60)	-8.3 (± 6.80)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-17.0 (± 8.84)	-18.8 (± 7.24)	-8.2 (± 15.00)	-10.8 (± 8.72)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-10.2 (± 10.90)	-18.1 (± 7.43)	-7.7 (± 19.22)	-8.7 (± 10.39)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-13.0 (± 12.70)	-15.6 (± 4.17)	-11.7 (± 7.62)	-8.1 (± 5.98)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-9.6 (± 6.56)	99999 (± 99999)	99999 (± 99999)	-5.1 (± 6.47)
Day 3 (third 8hrs) n=4,0,0,3,0,18,3,3,12	-5.6 (± 15.57)	99999 (± 99999)	99999 (± 99999)	-4.3 (± 10.49)
Day 8 n=7,3,3,6,3,18,3,3,12	-4.3 (± 12.43)	-9.1 (± 14.83)	-0.2 (± 3.56)	-0.9 (± 10.06)
Day 15 n=7,3,3,6,3,18,3,3,12	-7.4 (± 7.15)	-8.0 (± 14.71)	1.9 (± 3.91)	-4.9 (± 10.56)
Day 22 n=7,3,3,6,3,18,3,3,12	-8.1 (± 7.78)	-17.3 (± 10.68)	0.2 (± 5.82)	-1.4 (± 10.23)
Day 36 n=6,0,3,6,3,18,3,3,12	-13.6 (± 9.41)	99999 (± 99999)	-3.6 (± 12.73)	-1.1 (± 12.99)
Day 57 n=5,0,0,6,3,15,0,3,12	-4.7 (± 3.89)	99999 (± 99999)	99999 (± 99999)	-1.4 (± 16.42)
Day 78 n=5,0,0,6,3,15,0,3,12	-6.7 (± 6.97)	99999 (± 99999)	99999 (± 99999)	-3.9 (± 13.83)
Day 99 n=2,0,0,0,3,12,0,0,12	-3.0 (± 2.36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	-5.7 (± 4.71)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	0.0 (± 2.33)	-0.5 (± 8.64)	-9.4 (± 11.75)	-7.8 (± 4.81)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.9 (± 0.96)	-3.3 (± 8.27)	2.2 (± 2.34)	-8.3 (± 5.70)

Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-7.2 (± 7.83)	0.8 (± 9.75)	1.6 (± 5.48)	-6.7 (± 4.41)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-11.6 (± 14.23)	-8.9 (± 10.93)	-10.2 (± 10.03)	-5.4 (± 3.83)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-10.8 (± 16.01)	-14.1 (± 9.68)	-11.4 (± 8.50)	-6.9 (± 5.83)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.2 (± 10.93)	-10.5 (± 10.10)	-10.3 (± 8.41)	-10.1 (± 7.90)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	9.2 (± 8.57)	-14.0 (± 8.91)	-16.9 (± 14.54)	-12.2 (± 6.99)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-10.6 (± 12.17)	-12.3 (± 8.19)	-7.6 (± 5.54)
Day 3 (third 8hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	-8.8 (± 9.95)	-12.2 (± 13.49)	-5.8 (± 3.27)
Day 8 n=7,3,3,6,3,18,3,3,12	-12.9 (± 14.00)	-11.5 (± 12.01)	-16.9 (± 9.73)	-12.0 (± 4.26)
Day 15 n=7,3,3,6,3,18,3,3,12	-11.2 (± 7.38)	-6.2 (± 10.02)	-12.9 (± 8.66)	-9.2 (± 6.74)
Day 22 n=7,3,3,6,3,18,3,3,12	-7.0 (± 19.01)	-5.2 (± 10.63)	-8.7 (± 9.17)	-12.7 (± 5.46)
Day 36 n=6,0,3,6,3,18,3,3,12	-11.7 (± 21.23)	-7.5 (± 7.78)	-8.6 (± 7.58)	-8.0 (± 7.06)
Day 57 n=5,0,0,6,3,15,0,3,12	-12.3 (± 23.69)	-6.5 (± 7.86)	99999 (± 99999)	-9.4 (± 7.90)
Day 78 n=5,0,0,6,3,15,0,3,12	-14.0 (± 15.77)	-5.7 (± 7.66)	99999 (± 99999)	-11.3 (± 2.03)
Day 99 n=2,0,0,0,3,12,0,0,12	-17.1 (± 21.27)	-1.9 (± 7.61)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	-8.7 (± 12.00)	-5.9 (± 11.81)	99999 (± 99999)	99999 (± 99999)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-3.4 (± 8.69)			
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-5.4 (± 8.87)			
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-5.1 (± 9.01)			
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-11.7 (± 9.31)			
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-16.8 (± 8.04)			
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-9.8 (± 8.33)			
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-7.7 (± 7.66)			
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	-13.9 (± 9.23)			
Day 3 (third 8hrs) n=4,0,0,3,0,18,3,3,12	-4.6 (± 13.09)			
Day 8 n=7,3,3,6,3,18,3,3,12	-2.4 (± 7.82)			
Day 15 n=7,3,3,6,3,18,3,3,12	-4.2 (± 5.43)			
Day 22 n=7,3,3,6,3,18,3,3,12	-2.9 (± 7.51)			

Day 36 n=6,0,3,6,3,18,3,3,12	-5.2 (± 12.01)			
Day 57 n=5,0,0,6,3,15,0,3,12	-2.0 (± 6.75)			
Day 78 n=5,0,0,6,3,15,0,3,12	-5.1 (± 6.94)			
Day 99 n=2,0,0,0,3,12,0,0,12	-3.9 (± 10.42)			
Day 126 n=2,0,0,0,3,12,0,0,12	-4.6 (± 11.30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate (PR)

End point title	Change from Baseline in Pulse Rate (PR)

End point description:

The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point and "99999 " = not applicable.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (2 hours, 4 hours, and 6 hours post end of infusion [EOI]), Day 2 (first 8 hours, second 8 hours, third 8 hours), Day 3 (first 8 hours, second 8 hours, third 8 hours), Day 8, Day 15, Day 22, Day 36, Day 57, Day 78, Day 99, Day 126

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	1.3 (± 5.85)	-5.3 (± 7.57)	7.7 (± 8.33)	-3.5 (± 6.38)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-5.4 (± 6.00)	-1.3 (± 4.93)	4.7 (± 2.89)	-0.7 (± 4.46)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	-1.7 (± 5.31)	-3.0 (± 8.19)	4.3 (± 1.15)	-2.0 (± 3.85)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-4.4 (± 10.03)	-5.3 (± 11.02)	11.7 (± 6.66)	-4.5 (± 7.12)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	-2.3 (± 13.57)	-11.0 (± 1.00)	6.3 (± 4.93)	-2.2 (± 6.37)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	-0.9 (± 17.33)	-8.3 (± 4.51)	4.0 (± 6.08)	-4.2 (± 5.56)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	0.9 (± 14.65)	-7.0 (± 10.44)	1.0 (± 3.61)	-5.0 (± 7.32)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	10.5 (± 10.28)	99999 (± 99999)	99999 (± 99999)	2.0 (± 8.19)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	8.8 (± 6.95)	99999 (± 99999)	99999 (± 99999)	-1.0 (± 7.55)
Day 8 n=7,3,3,6,3,18,3,3,12	2.4 (± 10.42)	0.0 (± 12.77)	-6.0 (± 10.82)	-2.5 (± 5.32)
Day 15 n=7,3,3,6,3,18,3,3,12	-2.1 (± 16.71)	-1.7 (± 7.02)	0.7 (± 7.51)	-4.7 (± 8.85)
Day 22 n=7,3,3,6,3,18,3,3,12	0.3 (± 16.78)	-3.0 (± 9.64)	0.7 (± 8.33)	-4.7 (± 8.80)

Day 36 n=6,0,3,6,3,18,3,3,12	-3.2 (± 14.69)	99999 (± 99999)	-5.3 (± 5.13)	-1.3 (± 9.87)
Day 57 n=5,0,0,6,3,15,0,3,12	-2.0 (± 11.87)	99999 (± 99999)	99999 (± 99999)	2.2 (± 12.75)
Day 78 n=5,0,0,6,3,15,0,3,12	-2.8 (± 10.13)	99999 (± 99999)	99999 (± 99999)	-1.5 (± 11.79)
Day 99 n=2,0,0,0,3,12,0,0,12	4.0 (± 18.38)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	8.5 (± 17.68)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	11.8 (± 9.64)	2.4 (± 5.09)	8.0 (± 13.89)	3.7 (± 0.58)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	7.5 (± 8.81)	2.7 (± 6.50)	0.0 (± 5.57)	4.7 (± 4.04)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	16.5 (± 10.28)	2.9 (± 5.63)	9.0 (± 14.73)	5.3 (± 6.66)
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	17.0 (± 20.12)	4.2 (± 9.80)	1.3 (± 3.51)	4.7 (± 6.51)
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	6.8 (± 25.55)	4.1 (± 7.09)	-0.3 (± 3.51)	3.3 (± 5.51)
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	9.3 (± 22.23)	1.8 (± 6.39)	-1.3 (± 4.16)	1.7 (± 7.51)
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	2.3 (± 18.25)	1.1 (± 8.05)	-1.3 (± 10.21)	2.3 (± 8.74)
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	1.9 (± 5.99)	-1.0 (± 6.24)	-0.3 (± 6.51)
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	99999 (± 99999)	0.2 (± 6.90)	-3.0 (± 4.58)	0.3 (± 10.69)
Day 8 n=7,3,3,6,3,18,3,3,12	3.7 (± 6.43)	1.9 (± 8.52)	3.3 (± 2.52)	-0.3 (± 8.08)
Day 15 n=7,3,3,6,3,18,3,3,12	2.0 (± 8.89)	3.5 (± 7.75)	0.3 (± 3.51)	-2.3 (± 5.51)
Day 22 n=7,3,3,6,3,18,3,3,12	5.0 (± 16.09)	4.1 (± 9.05)	2.0 (± 12.00)	-0.7 (± 11.55)
Day 36 n=6,0,3,6,3,18,3,3,12	7.0 (± 23.64)	4.7 (± 12.38)	6.3 (± 11.06)	-1.0 (± 10.58)
Day 57 n=5,0,0,6,3,15,0,3,12	12.0 (± 18.25)	2.9 (± 12.09)	99999 (± 99999)	3.3 (± 7.37)
Day 78 n=5,0,0,6,3,15,0,3,12	4.7 (± 16.86)	4.3 (± 12.47)	99999 (± 99999)	0.7 (± 11.85)
Day 99 n=2,0,0,0,3,12,0,0,12	6.7 (± 20.23)	4.2 (± 11.40)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,12,0,0,12	13.3 (± 10.50)	5.0 (± 15.16)	99999 (± 99999)	99999 (± 99999)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			

Units: beats per minute (bpm)				
arithmetic mean (standard deviation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,18,3,3,12	6.5 (± 16.19)			
Day 1 (4 hrs post EOI) n=7,3,3,6,4,18,3,3,12	5.0 (± 9.94)			
Day 1 (6 hrs post EOI) n=7,3,3,6,4,18,3,3,12	4.3 (± 9.24)			
Day 2 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	1.4 (± 11.22)			
Day 2 (second 8 hrs) n=7,3,3,6,4,18,3,3,12	4.5 (± 8.17)			
Day 2 (third 8 hrs) n=7,3,3,6,4,18,3,3,12	1.3 (± 9.06)			
Day 3 (first 8 hrs) n=7,3,3,6,4,18,3,3,12	-1.7 (± 9.61)			
Day 3 (second 8 hrs) n=4,0,0,3,0,18,3,3,12	0.9 (± 9.04)			
Day 3 (third 8 hrs) n=4,0,0,3,0,18,3,3,12	0.8 (± 6.21)			
Day 8 n=7,3,3,6,3,18,3,3,12	4.2 (± 10.15)			
Day 15 n=7,3,3,6,3,18,3,3,12	1.7 (± 11.81)			
Day 22 n=7,3,3,6,3,18,3,3,12	1.3 (± 5.68)			
Day 36 n=6,0,3,6,3,18,3,3,12	2.6 (± 13.71)			
Day 57 n=5,0,0,6,3,15,0,3,12	4.1 (± 12.87)			
Day 78 n=5,0,0,6,3,15,0,3,12	4.3 (± 9.85)			
Day 99 n=2,0,0,0,3,12,0,0,12	7.2 (± 10.12)			
Day 126 n=2,0,0,0,3,12,0,0,12	7.3 (± 11.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Fold Change from Baseline in N-terminal Pro-Brain Natriuretic Peptide (NT-proBNP)

End point title	Fold Change from Baseline in N-terminal Pro-Brain Natriuretic Peptide (NT-proBNP)

End point description:

NTproBNP is a clinical biomarker of heart failure. Coefficient of Variation for Fold Change from Baseline was computed as (standard deviation of the natural log-scale of the respective variable) *100. Fold Change from Baseline is the ratio of Post-Baseline to Baseline, and it is assumed to follow a lognormal distribution. The pharmacodynamic analysis set included all randomized participants who received any study drug and had at least 1 post-dose pharmacodynamic measurement. Here, "n" is the number of participants evaluable for this outcome measure at the specified time point, "99999 " = not applicable, and the "±" is representing the Geometric Coefficient of Variation, expressed as a percentage.

End point type	Secondary

End point timeframe:

Baseline, Day 1 (2 hours, 4 hours, and 6 hours post end of infusion [EOI]), Day 2 (24 hours post EOI), Day 3, Day 4, Day 5, Day 8, Day 15, Day 22, Day 36, Day 57, Day 78, Day 99, Day 126

End point values	Group A: Placebo	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	3	6
Units: picograms per milliliter (pg/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,17,3,3,12	1.09 (± 26.9)	1.26 (± 30.8)	1.30 (± 26.9)	0.97 (± 14.8)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,17,3,3,12	1.13 (± 25.2)	1.23 (± 28.4)	1.36 (± 20.9)	0.96 (± 12.7)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,17,3,3,12	1.19 (± 28.7)	1.35 (± 32.6)	1.39 (± 20.3)	1.01 (± 14.4)
Day 2 (24 hrs post EOI) n=7,3,3,6,4,17,3,3,12	1.12 (± 32.7)	0.96 (± 18.3)	1.12 (± 22.5)	0.64 (± 39.2)
Day 3 n=7,3,3,6,4,17,3,3,12	0.66 (± 25.8)	1.00 (± 18.6)	1.09 (± 48.2)	0.75 (± 48.6)
Day 4 n=1,0,0,2,0,17,3,3,12	0.98 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.76 (± 80.2)
Day 5 n=1,0,0,2,0,17,3,3,12	0.73 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.81 (± 49.0)
Day 8 n=7,3,3,6,3,17,3,3,12	1.06 (± 32.3)	1.45 (± 36.7)	3.01 (± 20.1)	1.57 (± 44.7)
Day 15 n=7,3,3,6,3,17,3,3,12	0.96 (± 51.8)	1.41 (± 50.6)	2.92 (± 19.0)	1.07 (± 62.3)
Day 22 n=7,3,3,6,3,17,3,3,12	1.00 (± 62.2)	1.20 (± 55.0)	1.92 (± 21.3)	1.17 (± 56.5)
Day 36 n=6,0,3,6,3,17,3,3,12	0.80 (± 47.3)	99999 (± 99999)	1.41 (± 68.0)	0.98 (± 41.5)
Day 57 n=5,0,0,6,3,14,0,3,12	1.04 (± 93.2)	99999 (± 99999)	99999 (± 99999)	0.76 (± 58.2)
Day 78 n=5,0,0,6,3,14,0,3,12	0.63 (± 56.6)	99999 (± 99999)	99999 (± 99999)	0.79 (± 44.2)
Day 99 n=2,0,0,0,3,11,0,0,12	0.91 (± 37.2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,11,0,0,12	0.92 (± 52.2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Group A: REGN5381 300 mg	Group C: Placebo	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	3	3
Units: picograms per milliliter (pg/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.91 (± 11.2)	1.01 (± 12.4)	1.05 (± 6.6)	1.04 (± 18.2)
Day 1 (4 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.95 (± 7.0)	0.99 (± 18.3)	0.97 (± 11.1)	1.03 (± 19.0)
Day 1 (6 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.98 (± 10.0)	1.05 (± 19.8)	1.04 (± 12.2)	1.19 (± 23.7)
Day 2 (24 hrs post EOI) n=7,3,3,6,4,17,3,3,12	1.13 (± 102.5)	0.99 (± 23.8)	0.79 (± 12.2)	0.74 (± 37.7)
Day 3 n=7,3,3,6,4,17,3,3,12	1.32 (± 126.1)	0.77 (± 35.6)	0.66 (± 1.7)	0.69 (± 11.9)
Day 4 n=1,0,0,2,0,17,3,3,12	99999 (± 99999)	0.80 (± 37.2)	0.72 (± 11.8)	0.71 (± 15.7)
Day 5 n=1,0,0,2,0,17,3,3,12	99999 (± 99999)	0.72 (± 67.5)	0.97 (± 13.2)	0.89 (± 21.5)
Day 8 n=7,3,3,6,3,17,3,3,12	1.23 (± 77.6)	1.11 (± 38.3)	1.02 (± 70.1)	1.53 (± 39.8)

Day 15 n=7,3,3,6,3,17,3,3,12	1.42 (± 28.4)	1.18 (± 43.3)	2.19 (± 17.2)	1.47 (± 51.0)
Day 22 n=7,3,3,6,3,17,3,3,12	0.80 (± 56.2)	1.30 (± 43.5)	1.90 (± 40.6)	3.34 (± 150.2)
Day 36 n=6,0,3,6,3,17,3,3,12	0.59 (± 23.3)	1.13 (± 38.7)	1.41 (± 32.2)	2.66 (± 109.5)
Day 57 n=5,0,0,6,3,14,0,3,12	1.47 (± 54.3)	1.13 (± 36.6)	99999 (± 99999)	1.86 (± 86.3)
Day 78 n=5,0,0,6,3,14,0,3,12	0.46 (± 24.4)	1.09 (± 40.3)	99999 (± 99999)	1.75 (± 81.5)
Day 99 n=2,0,0,0,3,11,0,0,12	0.42 (± 20.5)	1.21 (± 42.5)	99999 (± 99999)	99999 (± 99999)
Day 126 n=2,0,0,0,3,11,0,0,12	0.63 (± 57.0)	0.97 (± 37.7)	99999 (± 99999)	99999 (± 99999)

End point values	Group C: REGN5381 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: picograms per milliliter (pg/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (2 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.94 (± 13.2)			
Day 1 (4 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.89 (± 14.8)			
Day 1 (6 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.91 (± 20.8)			
Day 2 (24 hrs post EOI) n=7,3,3,6,4,17,3,3,12	0.63 (± 51.0)			
Day 3 n=7,3,3,6,4,17,3,3,12	0.68 (± 32.6)			
Day 4 n=1,0,0,2,0,17,3,3,12	0.89 (± 51.2)			
Day 5 n=1,0,0,2,0,17,3,3,12	0.99 (± 45.6)			
Day 8 n=7,3,3,6,3,17,3,3,12	1.40 (± 26.0)			
Day 15 n=7,3,3,6,3,17,3,3,12	1.43 (± 50.8)			
Day 22 n=7,3,3,6,3,17,3,3,12	1.29 (± 49.4)			
Day 36 n=6,0,3,6,3,17,3,3,12	1.24 (± 58.0)			
Day 57 n=5,0,0,6,3,14,0,3,12	1.19 (± 48.8)			
Day 78 n=5,0,0,6,3,14,0,3,12	0.99 (± 38.4)			
Day 99 n=2,0,0,0,3,11,0,0,12	0.90 (± 42.8)			
Day 126 n=2,0,0,0,3,11,0,0,12	1.03 (± 49.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Concentration (Cmax) of REGN5381 in Serum

End point title	Peak Concentration (Cmax) of REGN5381 in Serum[2]

End point description:

The pharmacokinetic analysis set (PKAS) included all participants who received any study drug and who had at least 1 non-missing result following the first dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 126

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo arms not included in this endpoint.

End point values	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg	Group A: REGN5381 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	4
Units: mg/L				
arithmetic mean (standard deviation)	2.17 (± 0.208)	6.38 (± 1.34)	26.5 (± 6.06)	61.9 (± 14.8)

End point values	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg	Group C: REGN5381 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: mg/L				
arithmetic mean (standard deviation)	7.37 (± 1.29)	22.7 (± 4.01)	68.3 (± 14.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve from Time Zero to the Time of Last Measurable Concentration (AUClast) of REGN5381 in Serum

End point title	Area Under the Concentration-time Curve from Time Zero to the Time of Last Measurable Concentration (AUClast) of REGN5381 in Serum[3]

End point description:

The pharmacokinetic analysis set (PKAS) included all participants who received any study drug and who had at least 1 non-missing result following the first dose of study drug.

End point type	Secondary

End point timeframe:

Up to Day 126

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo arms not included in this endpoint.

End point values	Group A: REGN5381 10 mg	Group A: REGN5381 30 mg	Group A: REGN5381 100 mg	Group A: REGN5381 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	4
Units: day*mg/L				
arithmetic mean (standard deviation)	5.12 (± 0.284)	35.3 (± 7.99)	241 (± 29.2)	583 (± 345)

End point values	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg	Group C: REGN5381 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	12	
Units: day*mg/L				
arithmetic mean (standard deviation)	47.2 (± 16.6)	221 (± 38.5)	897 (± 149)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-drug Antibodies (ADA)

End point title	Number of Participants with Anti-drug Antibodies (ADA)[4]

End point description:

The ADA status of each participant was classified as one of the following:
• Negative — If all samples were found to be negative in the ADA assay
• Pre-existing immunoreactivity — If the baseline sample was positive and all post baseline ADA titers were reported as less than 9-fold the baseline titer value
• Treatment-Boosted Response
• Treatment-Emergent Response
The ADA analysis set included all participants who received study drug and had at least 1 non-missing ADA result following the first study drug dose.

End point type	Secondary

End point timeframe:

Baseline up to Day 126

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo arms A and B combined

End point values	Group A: REGN5381 100 mg	Group A: REGN5381 300 mg	Group C: REGN5381 30 mg	Group C: REGN5381 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: participants				
Negative	6	3	3	3
Pre-existing Immunoreactivity	0	0	0	0
Treatment-Boosted Response	0	0	0	0
Treatment-Emergent Response	0	0	0	0

End point values	Group C: REGN5381 300 mg	Groups A and B: Placebo		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	12	22		

Units: participants				
Negative	11	22		
Pre-existing Immunoreactivity	0	0		
Treatment-Boosted Response	0	0		
Treatment-Emergent Response	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From date of informed consent up to end of study (Day 126)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	28.0
Reporting groups	
Reporting group title	Group_A Placebo
Reporting group description: -	
Reporting group title	Group_A R5381 - IV 10 mg
Reporting group description: -	
Reporting group title	Group_A R5381 - IV 30 mg
Reporting group description: -	
Reporting group title	Group_A R5381 - IV 100 mg
Reporting group description: -	
Reporting group title	Group_A R5381 - IV 300 mg
Reporting group description: -	
Reporting group title	Group_C Placebo
Reporting group description: -	
Reporting group title	Group_C R5381 - IV 30 mg
Reporting group description: -	
Reporting group title	Group_C R5381 - IV 100 mg
Reporting group description: -	
Reporting group title	Group_C R5381 - IV 300 mg
Reporting group description: -	

Serious adverse events	Group_A Placebo	Group_A R5381 - IV 10 mg	Group_A R5381 - IV 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Respiratory tract procedural complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Ischaemic hepatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	Group_A R5381 - IV 100 mg	Group_A R5381 - IV 300 mg	Group_C Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	2 / 4 (50.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Respiratory tract procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (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 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatobiliary disorders			
Ischaemic hepatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (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

Serious adverse events	Group_C R5381 - IV 30 mg	Group_C R5381 - IV 100 mg	Group_C R5381 - IV 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Injury, poisoning and procedural complications			
Respiratory tract procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (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
Hepatobiliary disorders			
Ischaemic hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (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

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

Non-serious adverse events	Group_A Placebo	Group_A R5381 - IV 10 mg	Group_A R5381 - IV 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)	1 / 3 (33.33%)	1 / 3 (33.33%)
Investigations			
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Group_A R5381 - IV 100 mg	Group_A R5381 - IV 300 mg	Group_C Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	3 / 4 (75.00%)	3 / 18 (16.67%)
Investigations			
Weight increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injury, poisoning and procedural			

complications			
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Non-serious adverse events	Group_C R5381 - IV 30 mg	Group_C R5381 - IV 100 mg	Group_C R5381 - IV 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	4 / 12 (33.33%)
Investigations			
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural			

complications			
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Catheter site discomfort			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2022	Amendment 1: The purpose of this amendment was to change references of this being a phase 1b study to phase 2a.
30 August 2022	Amendment 2: The main purpose of this amendment was to modify the protocol following feedback from various Health Authorities.
25 October 2022	Amendment 3: The main purpose of this amendment was to incorporate additional separate cohorts to include participants with left ventricular ejection fraction ≥50%, to include participants currently taking sacubitril/valsartan, and to test a dose of ≤300 mg REGN5381.
21 March 2023	Amendment 4: The purpose of this amendment was to modify the inclusion and exclusion criteria.
31 July 2023	Amendment 5: The main purpose of this amendment was to implement additional safety measures and incorporate additional study eligibility requirements to help mitigate potential risks.
09 February 2024	Amendment 6: The main purpose of this amendment was to implement changes to align with the latest EU-CTR guidelines and incorporate Health Authority recommendations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported