Clinical trial results:
A Phase 2, Multicenter, Blinded, Sham Procedure-Controlled Trial of Renal Denervation by the Peregrine System Kit, in Subjects with Hypertension, in the Absence of Antihypertensive Medications

Summary

EudraCT number	2018-000036-96
Trial protocol	BE GB DE IE NL
Global end of trial date	19 January 2024

Results information

Result version number	v1 (current)
This version publication date	03 February 2025
First version publication date	03 February 2025
Summary attachment (see zip file)	Primary publication (Pathak_2023.pdf)

Trial information

Trial identification

Sponsor protocol code	CR0014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03503773
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ablative Solutions, Inc.
Sponsor organisation address	301 Edgewater Pl Suite 100, Wakefield, United States, MA 01880
Public contact	Clinical & Regulatory Affairs, Ablative Solutions, Inc., +1 4084212496, EU-Regulatory@ablativesolutions.com
Scientific contact	Clinical & Regulatory Affairs, Ablative Solutions, Inc., +1 4084212496, EU-Regulatory@ablativesolutions.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	19 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of renal denervation by alcohol-mediated neurolysis using the Peregrine Kit in hypertensive subjects, when used in the absence of antihypertensive medications, as evaluated by change in mean 24-hour ambulatory systolic blood pressure (SBP) from baseline to 8 weeks post-treatment.

Protection of trial subjects:

A Data Safety Monitoring Board (DSMB) regularly reviewed the safety data. The DSMB reviewed all 1 year data from all participants and the study had been unblinded to confirmed that there were no safety concerns, so the crossover phase of the trial was endorsed by the DSMB.
All participants received sedation and analgesia, which was applicable to the renal denervation (treatment) group and the sham control group.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 26
Country: Number of subjects enrolled	United Kingdom: 43
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 199
Country: Number of subjects enrolled	Ireland: 14
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	350
EEA total number of subjects	281

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)	212
From 65 to 84 years	138
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 350 participants provided informed consent and were enrolled and 106 of these participants were randomized and treated between 20 March 2019 and 28 December 2020. The trial was conducted in the EEA and the United States

Pre-assignment

Screening details:

Participants must have met all of the inclusion criteria to be eligible and undergo the procedure and with 3 office BP measurements with a mean office SBP of ≥ 140 mmHg and ≤ 180 mmHg AND mean office DBP ≥ 90 mmHg, and be willing to adhere to the no-medication regimen for at least 12 weeks (4 week run-in period and 8-week post-procedure.

Period 1

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

Blinding implementation details:

Participants received sedation, were blindfolded, and wore headsets (listening to music), so that they were unaware of any commentary from physicians or staff during the procedure.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment arm (renal denervation)

Arm description:

Double-blind phase where participants were randomized in a 1:1 ratio to one of the following 2 groups via central randomization (stratified by study site):
• Treatment Arm: renal denervation (using the Peregrine Kit) performed with alcohol (0.6 mL per treated renal artery) infused through the Peregrine Catheter (minimum treatment: the 2 main renal arteries [1 per side]; physician was also permitted to treat up to 1 additional accessory renal artery on each side. Thus, the planned maximum total dose was 4 × 0.6 mL = 2.4 mL).
• Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Arm type	Experimental
Investigational medicinal product name	Peregine Kit (Alcohol USP/renal denervation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intravenous use

Dosage and administration details:

The test product in this study is a co-packaged product, the Peregrine Kit, which includes the Peregrine Catheter and alcohol for injection. The catheter will be used to deliver a dose of 0.6 mL alcohol by direct infusion to the perivascular space of each renal artery in a single treatment session (i.e., a target dose of 1.2 mL). The 2 main renal arteries (1 on each side) will be treated. However, the treating physician is permitted to treat up to 1 additional accessory renal artery on each side (during the same treatment session) as well (depending on individual participant anatomy). Thus, the planned maximum total dose per participant is 4 × 0.6 mL = 2.4 mL.

Arm title	Sham control

Arm description:

Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1[1]	Treatment arm (renal denervation)	Sham control
Started	50	56
Completed	50	47
Not completed	0	9
Lost to follow-up	-	5
Crossover prior to Year 2	-	3
Did not attend follow-up visit	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 350 participants were enrolled, 244 participants were screen failures, and 106 participants were enrolled

Period 2

Period 2 title	Crossover phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Treatment arm (renal denervation)

Arm description:

Renal denervation (using the Peregrine Kit) performed with alcohol (0.6 mL per treated renal artery) infused through the Peregrine Catheter (minimum treatment: the 2 main renal arteries [1 per side]; physician was also permitted to treat up to 1 additional accessory renal artery on each side. Thus, the planned maximum total dose was 4 × 0.6 mL = 2.4 mL).

Arm type	Experimental
Investigational medicinal product name	Peregine Kit (Alcohol USP/renal denervation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intravenous use

Dosage and administration details:

The test product in this study is a co-packaged product, the Peregrine Kit, which includes the Peregrine Catheter and alcohol for injection. The catheter will be used to deliver a dose of 0.6 mL alcohol by direct infusion to the perivascular space of each renal artery in a single treatment session (i.e., a target dose of 1.2 mL). The 2 main renal arteries (1 on each side) will be treated. However, the treating physician is permitted to treat up to 1 additional accessory renal artery on each side (during the same treatment session) as well (depending on individual participant anatomy). Thus, the planned maximum total dose per participant is 4 × 0.6 mL = 2.4 mL.

Number of subjects in period 2[2]	Treatment arm (renal denervation)
Started	21
Completed	21

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 24 participants from the Sham Control group were re-screened for the Crossover Phase, 3 of whom were screen failures. The remaining 21 participants (from 15 study sites) crossed over and underwent alcohol-mediated renal denervation.

Baseline characteristics

Reporting groups	
Reporting group title	Randomized phase

Reporting group description: -

Reporting group values	Randomized phase	Total	
Number of subjects	106	106	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	54.1		
standard deviation	± 11.3	-	
Gender categorical Units: Subjects			
Female	28	28	
Male	78	78	
Type 2 diabetes Units: Subjects			
Yes	7	7	
No	99	99	
eGFR < 60 mL/min/1.73m2 Units: Subjects			
Yes	5	5	
No	101	101	
Smoking (current) Units: Subjects			
Yes	11	11	
No	95	95	
Peripheral vascular occlusive disease Units: Subjects			
Yes	2	2	
No	104	104	
Angiographically determined CAD Units: Subjects			
Yes	3	3	
No	103	103	

eGFR Units: mL/min/1.73m2 arithmetic mean standard deviation	 85.8 ± 13.4	 -	

End points

End points reporting groups

Reporting group title	Treatment arm (renal denervation)

Reporting group description:

Double-blind phase where participants were randomized in a 1:1 ratio to one of the following 2 groups via central randomization (stratified by study site):
- Treatment Arm: renal denervation (using the Peregrine Kit) performed with alcohol (0.6 mL per treated renal artery) infused through the Peregrine Catheter (minimum treatment: the 2 main renal arteries [1 per side]; physician was also permitted to treat up to 1 additional accessory renal artery on each side. Thus, the planned maximum total dose was 4 × 0.6 mL = 2.4 mL).
- Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Reporting group title	Sham control

Reporting group description:

Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Reporting group title	Treatment arm (renal denervation)

Reporting group description:

Renal denervation (using the Peregrine Kit) performed with alcohol (0.6 mL per treated renal artery) infused through the Peregrine Catheter (minimum treatment: the 2 main renal arteries [1 per side]; physician was also permitted to treat up to 1 additional accessory renal artery on each side. Thus, the planned maximum total dose was 4 × 0.6 mL = 2.4 mL).

Primary: Change from baseline to 8 weeks post-procedure in 24 hour ambulatory SBP

End point title	Change from baseline to 8 weeks post-procedure in 24 hour ambulatory SBP

End point description:

End point type	Primary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	144.6 (± 10.1)	147.0 (± 11.5)		

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Treatment arm (renal denervation) v Sham control

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2954
Method	ANCOVA

Secondary: Change from baseline to 8 weeks post-procedure in 24 hour ambulatory DBP

End point title	Change from baseline to 8 weeks post-procedure in 24 hour ambulatory DBP

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	90.0 (± 7.3)	90.1 (± 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean 24 hour ambulatory SBP at 6 months post-procedure

End point title	Change from baseline in mean 24 hour ambulatory SBP at 6 months post-procedure

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	134.1 (± 11.6)	135.1 (± 11.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean 24 hour ambulatory SBP at 12 months post-procedure

End point title	Change from baseline in mean 24 hour ambulatory SBP at 12 months post-procedure

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	137.6 (± 11.4)	133.7 (± 11.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean 24 hour ambulatory DBP at 6 months post-procedure

End point title	Change from baseline in mean 24 hour ambulatory DBP at 6 months post-procedure

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	83.0 (± 8.4)	83.4 (± 9.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean 24 hour ambulatory DBP at 12 months post-procedure

End point title	Change from baseline in mean 24 hour ambulatory DBP at 12 months post-procedure

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	85.6 (± 8.7)	81.0 (± 7.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean daytime ambulatory SBP at 8 weeks

End point title	Change from baseline in mean daytime ambulatory SBP at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	150.6 (± 10.5)	153.2 (± 12.0)		

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Treatment arm (renal denervation) v Sham control
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.323
Method	ANCOVA

Secondary: Change from baseline in mean daytime ambulatory SBP at 6 months

End point title	Change from baseline in mean daytime ambulatory SBP at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	139.7 (± 12.8)	140.6 (± 12.3)		

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Treatment arm (renal denervation) v Sham control

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.887
Method	ANCOVA

Secondary: Change from baseline in mean daytime ambulatory SBP at 12 months

End point title	Change from baseline in mean daytime ambulatory SBP at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	143.5 (± 12.6)	140.1 (± 12.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean daytime ambulatory DBP at 8 weeks

End point title	Change from baseline in mean daytime ambulatory DBP at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	95.2 (± 7.5)	94.7 (± 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean daytime ambulatory DBP at 6 months

End point title	Change from baseline in mean daytime ambulatory DBP at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	87.8 (± 9.2)	87.6 (± 9.0)		

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Treatment arm (renal denervation) v Sham control
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.959
Method	ANCOVA

Secondary: Change from baseline in mean daytime ambulatory DBP at 12 months

End point title	Change from baseline in mean daytime ambulatory DBP at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	90.4 (± 9.6)	86.0 (± 8.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory SBP at 8 weeks

End point title	Change from baseline in mean nighttime ambulatory SBP at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	134.4 (± 11.6)	136.9 (± 14.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory SBP at 6 months

End point title	Change from baseline in mean nighttime ambulatory SBP at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	125.4 (± 12.1)	125.6 (± 13.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory SBP at 12 months

End point title	Change from baseline in mean nighttime ambulatory SBP at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	127.8 (± 10.7)	123.1 (± 12.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory DBP at 8 weeks

End point title	Change from baseline in mean nighttime ambulatory DBP at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	81.5 (± 8.4)	82.5 (± 12.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory DBP at 6 months

End point title	Change from baseline in mean nighttime ambulatory DBP at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	75.5 (± 9.2)	75.8 (± 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean nighttime ambulatory DBP at 12 months

End point title	Change from baseline in mean nighttime ambulatory DBP at 12 months

End point description:

End point type	Secondary

End point timeframe:
12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	77.4 (± 7.8)	72.8 (± 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean office SBP at 8 weeks

End point title	Change from baseline in mean office SBP at 8 weeks

End point description:

End point type	Secondary

End point timeframe:
8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	155.4 (± 14.3)	160.6 (± 16.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean office SBP at 6 months

End point title	Change from baseline in mean office SBP at 6 months

End point description:

End point type	Secondary
End point timeframe: 6 months	

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	146.1 (± 16.4)	145.7 (± 14.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean office SBP at 12 months

End point title	Change from baseline in mean office SBP at 12 months
End point description:	

End point type	Secondary
End point timeframe: 12 months	

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	147.9 (± 18.5)	147.8 (± 15.1)		

Statistical analyses

Statistical analysis title	ANCOVA analysis
Comparison groups	Treatment arm (renal denervation) v Sham control

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.682
Method	ANCOVA

Secondary: Change from baseline in mean office SBP at 24 months

End point title	Change from baseline in mean office SBP at 24 months

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: mmHg				
arithmetic mean (standard deviation)	147.1 (± 20.0)	142.1 (± 14.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 8 weeks

End point title	Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	15	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 6 months

End point title	Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	31	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 12 months

End point title	Participants achieving target 24-hour ambulatory BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	22	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 8 weeks

End point title	Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 6 months

End point title	Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 6 months

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	14	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 12 months

End point title	Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	15	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 24 months

End point title	Participants achieving target office BP (SBP ≤ 140 mmHg and DBP ≤ 90 mmHg) at 24 months

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: participants	14	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean antihypertensive medications prescribed at 8 weeks

End point title	Mean antihypertensive medications prescribed at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: Number of medications				
arithmetic mean (standard deviation)	0.060 (± 0.240)	0.089 (± 0.288)		

Statistical analyses

No statistical analyses for this end point

Secondary: Major adverse events at 30 days

End point title	Major adverse events at 30 days

End point description:

End point type	Secondary

End point timeframe:

30 days

End point values	Treatment arm (renal denervation)	Sham control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	56		
Units: number of events	1	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in mean office SBP at 4 weeks (crossover)

End point title	Change from baseline in mean office SBP at 4 weeks (crossover)

End point description:

End point type	Other pre-specified

End point timeframe:

4 weeks

End point values	Treatment arm (renal denervation)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: mmHg				
arithmetic mean (standard deviation)	143.3 (± 14.3)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in mean office SBP at 6 months (crossover

End point title	Change from baseline in mean office SBP at 6 months (crossover

End point description:

End point type	Other pre-specified

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: mmHg				
arithmetic mean (standard deviation)	141.4 (± 18.6)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in mean office DBP at 4 weeks (crossover)

End point title	Change from baseline in mean office DBP at 4 weeks (crossover)

End point description:

End point type	Other pre-specified

End point timeframe:

4 weeks

End point values	Treatment arm (renal denervation)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: mmHg				
arithmetic mean (standard deviation)	88.3 (± 10.8)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from baseline in mean office DBP at 6 months (crossover)

End point title	Change from baseline in mean office DBP at 6 months (crossover)

End point description:

End point type	Other pre-specified

End point timeframe:

6 months

End point values	Treatment arm (renal denervation)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: mmHg				
arithmetic mean (standard deviation)	87.1 (± 11.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Treatment arm (renal denervation)

Reporting group description:

Double-blind phase where participants were randomized in a 1:1 ratio to one of the following 2 groups via central randomization (stratified by study site):
• Treatment Arm: renal denervation (using the Peregrine Kit) performed with alcohol (0.6 mL per treated renal artery) infused through the Peregrine Catheter (minimum treatment: the 2 main renal arteries [1 per side]; physician was also permitted to treat up to 1 additional accessory renal artery on each side. Thus, the planned maximum total dose was 4 × 0.6 mL = 2.4 mL).
• Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Reporting group title	Sham control

Reporting group description:

Sham Control Arm: only renal angiography performed. No renal denervation and no alcohol infusion has been performed.

Serious adverse events	Treatment arm (renal denervation)	Sham control	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 50 (20.00%)	10 / 56 (17.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			

subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the cervix			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 50 (4.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Mitral valve repair			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung neoplasm malignant			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Lumbar vertebral fracture			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 50 (2.00%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment arm (renal denervation)	Sham control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 50 (90.00%)	44 / 56 (78.57%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 50 (4.00%)	3 / 56 (5.36%)	
occurrences (all)	2	3	
Glomerular filtration rate decreased			
subjects affected / exposed	2 / 50 (4.00%)	6 / 56 (10.71%)	
occurrences (all)	2	6	

Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	6 / 50 (12.00%)	4 / 56 (7.14%)	
occurrences (all)	6	4	
Vascular disorders			
Dizziness			
subjects affected / exposed	2 / 50 (4.00%)	3 / 56 (5.36%)	
occurrences (all)	2	3	
Haematoma			
subjects affected / exposed	5 / 50 (10.00%)	2 / 56 (3.57%)	
occurrences (all)	5	2	
Hypertension			
subjects affected / exposed	3 / 50 (6.00%)	5 / 56 (8.93%)	
occurrences (all)	3	5	
Hypertensive crisis			
subjects affected / exposed	1 / 50 (2.00%)	3 / 56 (5.36%)	
occurrences (all)	1	3	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	3 / 50 (6.00%)	4 / 56 (7.14%)	
occurrences (all)	3	4	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 50 (22.00%)	7 / 56 (12.50%)	
occurrences (all)	11	7	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 50 (2.00%)	3 / 56 (5.36%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 50 (4.00%)	4 / 56 (7.14%)	
occurrences (all)	2	4	
Infections and infestations			
COVID-19			

subjects affected / exposed	5 / 50 (10.00%)	9 / 56 (16.07%)	
occurrences (all)	5	9	
Nasopharyngitis			
subjects affected / exposed	2 / 50 (4.00%)	4 / 56 (7.14%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	3 / 50 (6.00%)	0 / 56 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2018	Amendment before any participants were enrolled. Addition of serum creatinine sample and eGFR calculation for all participants prior to imaging at screening to exclude participants with eGFR ≤ 45 mL/min/1.73 m2 before undergoing any imaging; this eGFR value replaced the historical eGFR value to determine whether participant should have post-contrast serum creatinine measurement 48 to 96 hours after imaging at screening. Other study details updated.
05 September 2018	Response to a request by the UK Medicines and Healthcare products Regulatory Agency to clarify that, if required, the unblinding of a participant could be performed by the investigator without consultation with the medical monitor, and that the investigator has direct access to the code via the IWRS for this purpose.
24 October 2018	Response to requests from BfArM, UK Medicines and Healthcare Products Regulatory Agency. Updates made to the information reported from the post market study.
16 September 2019	Amended based on v4.0 to v5.0 to increase the time window for MRA/CTA images that could be reviewed by the core laboratory at screening from 6 months to 12 months prior to enrolment in order to minimize participants' radiation exposure to generate the current version of the protocol
01 July 2020	To include the United States as a study site
14 December 2022	To update the timeframe of the possible crossover from 6 months to 1 year post-procedure

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.

Recruitment and conduct of the study occurred during the COVID-19 pandemic.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37427416