Clinical trial results:
Personalised Electronic Record Supported OptimisatioN when ALone for Patients with Hypertension- Pilot Study for Remote Medical Management of Hypertension During the COVID-19 Pandemic

Summary

EudraCT number	2020-002494-10
Trial protocol	GB
Global end of trial date	19 November 2021

Results information

Result version number	v1 (current)
This version publication date	08 October 2023
First version publication date	08 October 2023
Summary attachment (see zip file)	Whose Dose is it Anyway ACC Abstract PERSONAL-COVIDBP (JACC published abstract Whose Dose is it Anyway March 8 2022.pdf) Personalized electronic record supported optimisation when alone for patients with hypertension- pilot study for remote medical management of hypertension during the Covid-19 pandemic (personal covidB (BIHS abstract 2022 PERSONAL-COVIDBP.docx)

Trial information

Trial identification

Sponsor protocol code	012665

Additional study identifiers

ISRCTN number	ISRCTN16393332
ClinicalTrials.gov id (NCT number)	NCT04559074
WHO universal trial number (UTN)	-
Other trial identifiers	IRAS number: 283209, REC number: 20/HRA/2988

Notes:

Sponsors

Sponsor organisation name	Queen Mary University of London
Sponsor organisation address	Mile End Road, London, United Kingdom, E1 4NS
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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	07 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2021
Global end of trial reached?	Yes
Global end of trial date	19 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary research objective is to assess how effective precision dosing of amlodipine is in managing blood pressure in participants with primary hypertension and inadequate blood pressure control. Amlodipine will be up-titrated in 1-2mg increments, under a remote medical management protocol during the COVID-19 pandemic. This study will involve the use of a digital diary on which home blood pressure recording will be entered by the participant. During the early part of the study blood pressure recordings will be assessed by the study team to see if the participant should stay on their existing medication regime- if blood pressure is okay- or if blood pressure is raised, participants will be sent liquid amlodipine in the post and the dose of this will be adjusted with the aim of better blood pressure control. The study aims to test the effect of this extra medication regime- both before and after.

Protection of trial subjects:

Subjects were remotely assessed for blood pressure control using home monitoring with a machine being supplied by the study team if required.
If readings between screening and baseline were elevated, subjects were allocated to intervention and sent liquid amlodipine bulk supply.
For intervention subjects regular 1-2 weekly reviews on BP with study team allowed titration of the dose of amlodipine from 1mg daily to 10mg daily, in 1-2mg steps.
For those subjects at baseline having adequate BP control, allocated to observation, they continued to measure BP each morning and evening for the three months of the trial. These subjects had remote visits every month or so with the study team to assess BP control on existing medication. For safety of the subjects, those in observation could qualify for the intervention part of the study if their 7-day average BP was above the entry level for the intervention group. 24 trial subjects from the observation group progressed to join the start of the intervention during the study period (for some this meant contributing data for the full 3 months of the intervention group and then another 14 weeks of intervention.)
In this way even subjects assessed at baseline to have adequate BP control still got regular remote BP checks and remote consultations. Subjects contributed BP data each morning and evening for the duration of the trial, completed medication dosing information and any covid-19 symptoms and likely amlodipine unwanted effects in the electronic dairy.

Background therapy:

Subjects had all had a diagnosis of hypertension and most were treated with medication at the time of screening.
Background BP lowering therapy was allowed with the exception of amlodipine 10mg, as this is the maximum licensed dose of amlodipine and could not be increased under the protocol, so such subjects were excluded from the trial.
Otherwise, subjects were taking CCB's (mostly amlodipine at doses <10mg daily), ACE inhibitors, ARB's, diuretics, alpha blockers, beta blockers, few on mineralocorticoid receptor antagonists.
Background BP therapy remained constant throughout the trial.

Evidence for comparator:

As the gradual titration of amlodipine liquid supplied to the intervention arm subjects, usually 1-2mg at a time, was going to take up to 12 weeks, then it was not possible to use a placebo for the comparison arm of the study (evidence of safety on placebo in BP trials is extensive but limited to 8 weeks). The placebo liquid was not available either. Therefore, there was no placebo comparison group in the study.

Actual start date of recruitment	23 October 2020
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	United Kingdom: 343
Worldwide total number of subjects	343
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)	208
From 65 to 84 years	134
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

UK only recruitment began screening on 23 Oct 2020 using clinic, GP, commercial radio advert and direct text from GP's (UMed Ltd). Recruitment closed 28 July 2021 having completed recruitment into the intervention arm, on which the designed power was based (planned for 200 in intervention, actual 205 subjects).

Pre-assignment

Screening details:

Consenting adult subjects with a diagnosis of hypertension were screened on their existing background BP medications, excluded if they were already on maximal amlodipine (10mg daily), did not have a suitable working smartphone, serious reactions to amlodipine, history suggestive of heart failure or aortic stenosis or inadequate contraception.

Period 1

Period 1 title	Intervention Trial
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Open label study

Arms

Arm title	Intervention

Arm description:

Eligible study participants with primary hypertension and inadequate BP control were invited to enrol into the intervention arm of the study, and receive an antihypertensive treatment regimen of precision dosing of liquid amlodipine by up-titration in daily dose in small increments of 1-2mg, under a remote medical management and smartphone app-enabled protocol during the COVID-19 pandemic.

Arm type	Experimental
Investigational medicinal product name	Amlodipine (type of calcium channel blocker)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Drug in liquid form to be taken orally once daily (AM) and not to exceed 10mg daily dose.

Number of subjects in period 1[1]	Intervention
Started	205
Baseline	205
Week 1	203
Week 2	203
Week 4	203
Week 6	200

Week 8	199
Week 10	198
Week 12	196
Week 14 (end of trial visit)	196
Completed	196
Not completed	9
Adverse event, non-fatal	1
Lost to follow-up	8

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: 205 subjects were enrolled into the Intervention arm, but the total number of patients enrolled into study (both Intervention arm and Observation arm) was 343. Note that 24 subjects who were originally enrolled into the Observation arm, were subsequently enrolled into the Intervention arm.

Period 2

Period 2 title	Observation study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Observation

Arm description:

Consenting participants with controlled blood pressure at baseline were invited to enrol into an observation arm. Participants in the observation arm did not receive study medication, but were medically managed and observed with a smartphone app-enabled protocol. If participants in the observation arm presented with uncontrolled blood pressure when reviewed at a study visit, they were invited to enrol into the intervention arm of the study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[2][3]	Observation
Started	162
Baseline	162
1 Month	157
2 Months	142
3 Months (end of study)	133
Completed	133
Not completed	29
Transferred to other arm/group	17
Lost to follow-up	12

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: 162 subjects were enrolled into the Observation arm, but the total number of patients enrolled into study (both Intervention arm and Observation arm) was 343. Note that 24 subjects who were originally enrolled into the Observation arm, were subsequently enrolled into the Intervention arm.

[3] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.

Justification: Subjects in the Observation arm were only able to transfer out and into the Intervention arm. No subjects who initially were enrolled into the Intervention cohort were subsequently enrolled into the Observation arm.

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Eligible study participants with primary hypertension and inadequate BP control were invited to enrol into the intervention arm of the study, and receive an antihypertensive treatment regimen of precision dosing of liquid amlodipine by up-titration in daily dose in small increments of 1-2mg, under a remote medical management and smartphone app-enabled protocol during the COVID-19 pandemic.	

Reporting group values	Intervention	Total	
Number of subjects	205	205	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	129	129	
From 65-84 years	75	75	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	60.05		
standard deviation	± 10.97	-	
Gender categorical Units: Subjects			
Female	68	68	
Male	137	137	
Ethnicity Units: Subjects			
Asian	25	25	
Black	20	20	
Mixed	1	1	
White	149	149	
Unknown/not reported	2	2	
Other	8	8	
Smoking status Units: Subjects			
Non-smoker	124	124	
Previous smoker	59	59	
Current smoker	21	21	
Unknown/not reported	1	1	
Diabetes Units: Subjects			
Yes	19	19	

No	186	186	
Kidney dysfunction Units: Subjects			
Yes	1	1	
No	204	204	
Peripheral arterial/vascular dysfunction Units: Subjects			
Yes	3	3	
No	202	202	
Hypercholesterolaemia Units: Subjects			
Yes	42	42	
No	163	163	
Previous stroke Units: Subjects			
Yes	0	0	
No	205	205	
Previous MI Units: Subjects			
Yes	3	3	
No	202	202	
Previous PCI Units: Subjects			
Yes	0	0	
No	205	205	
Number of antihypertensive medications on at baseline Units: Subjects			
None	49	49	
One	86	86	
Two or more	70	70	
Body Mass Index Units: kg/m2)			
arithmetic mean	28.85		
standard deviation	± 5.27	-	
Systolic blood pressure (home 7-day mean) Units: mmHg			
arithmetic mean	141.95		
standard deviation	± 9.75	-	
Diastolic blood pressure (home 7-day mean) Units: mmHg			
arithmetic mean	86.97		
standard deviation	± 8.09	-	
Heart rate (home 7-day mean) Units: beats per minute			
arithmetic mean	71.46		
standard deviation	± 10.88	-	

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

Eligible study participants with primary hypertension and inadequate BP control were invited to enrol into the intervention arm of the study, and receive an antihypertensive treatment regimen of precision dosing of liquid amlodipine by up-titration in daily dose in small increments of 1-2mg, under a remote medical management and smartphone app-enabled protocol during the COVID-19 pandemic.

Reporting group title	Observation

Reporting group description:

Consenting participants with controlled blood pressure at baseline were invited to enrol into an observation arm. Participants in the observation arm did not receive study medication, but were medically managed and observed with a smartphone app-enabled protocol. If participants in the observation arm presented with uncontrolled blood pressure when reviewed at a study visit, they were invited to enrol into the intervention arm of the study.

Primary: Change in systolic blood pressure from baseline to the end of the trial (Week 14)

End point title	Change in systolic blood pressure from baseline to the end of the trial (Week 14)[1]

End point description:

The timing of the final visit is approximately 14 weeks after their baseline visit in the intervention arm, but exact time-span varies slightly between subjects. Mean systolic blood pressure was calculated using all available home blood pressure measurements within the 7-day lead-up to baseline and the end of trial visit (Week 14) to represent baseline and end of trial mean systolic blood pressure for each study participant. Mean systolic blood pressure was also calculated in this way at each of the scheduled visits. The difference in mean systolic blood pressure between baseline and the end of trial visit (Week 14) was estimated from a linear mixed effects model, with each visit in the model as indicator variables for the fixed effects, with a random component for study participant.

End point type	Primary

End point timeframe:

From baseline (Day 0) to the end of trial visit (at Week 14).

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: The primary endpoint if the change in systolic blood pressure between baseline and the end of the trial, in the Intervention arm only. There is no comparator group. In order to enter statistical analysis into EudraCT, at least 1 comparator group needs to be specified, which is not relevant in this study.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: mmHg				
least squares mean (confidence interval 95%)	-11.02 (-11.99 to -10.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in diastolic blood pressure from baseline to the end of the trial (Week 14)

End point title	Change in diastolic blood pressure from baseline to the end of the trial (Week 14)

End point description:

The timing of the final visit is approximately 14 weeks after their baseline visit in the intervention arm, but exact time-span varies slightly between subjects. Mean diastolic blood pressure was calculated using all available home blood pressure measurements within the 7-day lead-up to baseline and the end of trial visit (Week 14) to represent baseline and end of trial mean diastolic blood pressure for each study participant. Mean diastolic blood pressure was also calculated in this way at each of the scheduled visits. The difference in mean diastolic blood pressure between baseline and the end of trial visit (Week 14) was estimated from a linear mixed effects model, with each visit in the model as indicator variables for the fixed effects, with a random component for study participant.

End point type	Secondary

End point timeframe:

From baseline (Day 0) to the end of trial visit (at Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: mmHg				
least squares mean (confidence interval 95%)	-6.50 (-7.10 to -5.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target less than 135 mmHg systolic and less than 85 mmHg diastolic blood pressure at the end of the trial (Week 14)

End point title	Achieving blood pressure target less than 135 mmHg systolic and less than 85 mmHg diastolic blood pressure at the end of the trial (Week 14)

End point description:

SBP<135 and DBP<85 mmHg at the end of the trial (Week 14)

End point type	Secondary

End point timeframe:

At the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[2]			
Units: Positive integers	102			

Notes:

[2] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving reduction of 5 or more mmHg systolic blood pressure by the end of the trial (Week 14)

End point title	Achieving reduction of 5 or more mmHg systolic blood pressure by the end of the trial (Week 14)

End point description:

Reduction in SBP ≥5 mmHg at the end of treatment (Week 14) as compared to baseline.

End point type	Secondary

End point timeframe:

Change in SBP at the end of treatment (Week 14) as compared to baseline.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[3]			
Units: Positive integer	136			

Notes:

[3] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving reduction of 10 or more mmHg systolic blood pressure by the end of the trial (Week 14)

End point title	Achieving reduction of 10 or more mmHg systolic blood pressure by the end of the trial (Week 14)

End point description:

End point type	Secondary

End point timeframe:

Change in SBP at the end of treatment (Week 14) as compared to baseline.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[4]			
Units: Positive integer	98			

Notes:

[4] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving reduction of 5 or more mmHg diastolic blood pressure by the end of the trial (Week 14)

End point title	Achieving reduction of 5 or more mmHg diastolic blood pressure by the end of the trial (Week 14)

End point description:

Reduction in DBP ≥5 mmHg at the end of treatment (Week 14) as compared to baseline.

End point type	Secondary

End point timeframe:

Change in DBP at the end of treatment (Week 14) as compared to baseline.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[5]			
Units: Positive integer	122			

Notes:

[5] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination of target blood pressure & specified reductions in blood pressure by the end of the trial (Week 14)

End point title	Achieving combination of target blood pressure & specified reductions in blood pressure by the end of the trial (Week 14)

End point description:

A combination of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

At the end of treatment (Week 14) as compared to baseline.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[6]			
Units: Positive integer	53			

Notes:

[6] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to achieving blood pressure control

End point title	Median time to achieving blood pressure control

End point description:

Using a Kaplan-Meier survival estimates approach, the median time to achieving blood pressure control, defined as an ABP <135 mmHg and a DBP <85 mmHg, was calculated.

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Weeks				
median (confidence interval 95%)	5.29 (3.86 to 6.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (Any of the main 6)

End point title	Self-reported side effects (Any of the main 6)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). The main 6 side effects were: headache, swelling, skin reaction, abdominal pain, fatigue or drowsiness, nausea or vomiting. This endpoint categorises any of these 6 reported side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[7]			
Units: Positive integers				
Mild or worse	161			
Moderate or worse	116			
Severe or worse	67			
Very severe	20			

Notes:

[7] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (headache)

End point title	Self-reported side effects (headache)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported headache side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[8]			
Units: Positive integer				
Mild or worse	112			
Moderate or worse	62			
Severe or worse	21			
Very severe	4			

Notes:

[8] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (swelling)

End point title	Self-reported side effects (swelling)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported swelling side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[9]			
Units: Positive integer				
Mild or worse	74			
Moderate or worse	41			
Severe or worse	19			
Very severe	6			

Notes:

[9] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (skin reaction)

End point title	Self-reported side effects (skin reaction)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported skin reaction side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[10]			
Units: Positive integer				
Mild or worse	51			
Moderate or worse	20			
Severe or worse	10			
Very severe	2			

Notes:

[10] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (abdominal pain)

End point title	Self-reported side effects (abdominal pain)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported abdominal pain side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[11]			
Units: Positive integer				
Mild or worse	48			
Moderate or worse	20			
Severe or worse	6			
Very severe	2			

Notes:

[11] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (fatigue or drowsiness)

End point title	Self-reported side effects (fatigue or drowsiness)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported fatigue or drowsiness side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[12]			
Units: Positive integer				
Mild or worse	122			
Moderate or worse	73			
Severe or worse	37			
Very severe	12			

Notes:

[12] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Self-reported side effects (nausea or vomiting)

End point title	Self-reported side effects (nausea or vomiting)

End point description:

Self-reporting of side effects was done via the digital diary, with each type of side effect scored on a visual analogue scale (VAS) from 0-100 (positive integers). This endpoint categorises self-reported nausea or vomiting side effects ever reported as mild or worse (over 0 on the VAS), moderate or worse (over 25 on the VAS), severe or worse (over 75 on the VAS), or very severe (over 75 on the VAS).

End point type	Secondary

End point timeframe:

From baseline to the end of the trial (Week 14)

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[13]			
Units: Positive integer				
Mild or worse	61			
Moderate or worse	26			
Severe or worse	11			
Very severe	5			

Notes:

[13] - Subjects who completed the trial. Note, subjects can appear in more than one category.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of adverse events at least possibly related to trial medication (amlodipine)

End point title	Number of adverse events at least possibly related to trial medication (amlodipine)

End point description:

The number of adverse events reported during the trial that were said to be at least possibly related to amlodipine.

End point type	Secondary

End point timeframe:

Within the trial follow-up period, from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Positive integer	377			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with reported adverse events at least possibly related to trial medication (amlodipine)

End point title	Number of subjects with reported adverse events at least possibly related to trial medication (amlodipine)

End point description:

The number of subjects with adverse events reported during the trial that were said to be at least possibly related to amlodipine.

End point type	Secondary

End point timeframe:

Within the trial follow-up period, from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: Positive integer	137			

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment having experienced unwanted side effects from amlodipine

End point title	Achieving blood pressure target at the end of treatment having experienced unwanted side effects from amlodipine

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having also ever experienced an unwanted side effect scored over 25 on the 0-100 VAS in the digital diary between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[14]			
Units: Positive integer				
Any of the main 6 side effects	82			
Headache	57			
Swelling	35			
Skin reaction	27			
Abdominal pain	23			
Fatigue or drowsiness	60			
Nausea or vomiting	27			

Notes:

[14] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment without having experienced unwanted side effects from amlodipine

End point title	Achieving blood pressure target at the end of treatment without having experienced unwanted side effects from amlodipine

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having never experienced an unwanted side effect scored over 25 on the 0-100 VAS in the digital diary between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[15]			
Units: Positive integer				
Any of the 6 main side effects	20			
Headache	45			
Swelling	67			
Skin reaction	75			
Abdominal pain	79			
Fatigue or drowsiness	42			
Nausea or vomiting	75			

Notes:

[15] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination of blood pressure target and response at the end of treatment having experienced unwanted side effects from amlodipine

End point title	Achieving combination of blood pressure target and response at the end of treatment having experienced unwanted side effects from amlodipine

End point description:

Number of subjects who achieved the combination of blood pressure target SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having also ever experienced an unwanted side effect scored over 25 on the 0-100 VAS in the digital diary between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[16]			
Units: Positive integer				
Any of the 6 main side effects	39			
Headache	28			
Swelling	17			
Skin reaction	14			
Abdominal pain	12			
Fatigue or drowsiness	31			
Nausea or vomiting	15			

Notes:

[16] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination of blood pressure target and response at the end of treatment without having experienced unwanted side effects from amlodipine

End point title	Achieving combination of blood pressure target and response at the end of treatment without having experienced unwanted side effects from amlodipine

End point description:

Number of subjects who achieved the combination of blood pressure target SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having never experienced an unwanted side effect scored over 25 on the 0-100 VAS in the digital diary between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[17]			
Units: Positive integer				
Any of the 6 main side effects	14			
Headache	25			
Swelling	36			
Skin reaction	39			
Abdominal pain	41			
Fatigue or drowsiness	22			
Nausea or vomiting	38			

Notes:

[17] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment having experienced an adverse event at least possibly related to amlodipine

End point title	Achieving blood pressure target at the end of treatment having experienced an adverse event at least possibly related to amlodipine

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having also experienced an adverse event that was said to be at least possibly related to amlodipine between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[18]			
Units: Positive integer	58			

Notes:

[18] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment having not experienced an adverse event at least possibly related to amlodipine

End point title	Achieving blood pressure target at the end of treatment having not experienced an adverse event at least possibly related to amlodipine

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having not experienced an adverse event that was said to be at least possibly related to amlodipine between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[19]			
Units: Positive integer	44			

Notes:

[19] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination of blood pressure target and reduction at the end of treatment having experienced an adverse event at least possibly related to amlodipine

End point title	Achieving combination of blood pressure target and reduction at the end of treatment having experienced an adverse event at least possibly related to amlodipine

End point description:

Number of subjects who achieved the combination blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having experienced an adverse event that was said to be at least possibly related to amlodipine between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[20]			
Units: Positive integer	25			

Notes:

[20] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination blood pressure target and reduction at the end of treatment having not experienced an adverse event at least possibly related to amlodipine

End point title	Achieving combination blood pressure target and reduction at the end of treatment having not experienced an adverse event at least possibly related to amlodipine

End point description:

Number of subjects who achieved the combination blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having not experienced an adverse event that was said to be at least possibly related to amlodipine between baseline and the end of the trial (Week 14).

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[21]			
Units: Positive integer	28			

Notes:

[21] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment having experienced a dose-limiting side effect during the study

End point title	Achieving blood pressure target at the end of treatment having experienced a dose-limiting side effect during the study

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having also experienced a dose-limiting side effect between baseline and the end of the trial (Week 14). A subject is said to have experienced a dose-limiting side effect at a titration consultation if they: do not have a dose up-titration; are not already at the highest dose (10mg), have

had a side effect recorded in the digital diary since last consultation of 25 or higher for any side effect, or have an AE that was deemed at least possibly related to amlodipine treatment since last consultation.

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[22]			
Units: Positive integer	54			

Notes:

[22] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving blood pressure target at the end of treatment having not experienced a dose-limiting side effect during the study

End point title	Achieving blood pressure target at the end of treatment having not experienced a dose-limiting side effect during the study

End point description:

Number of subjects who achieved the blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14) having not experienced a dose-limiting side effect between baseline and the end of the trial (Week 14). A subject is said to have experienced a dose-limiting side effect at a titration consultation if they: do not have a dose up-titration; are not already at the highest dose (10mg), have had a side effect recorded in the digital diary since last consultation of 25 or higher for any side effect, or have an AE that was deemed at least possibly related to amlodipine treatment since last consultation.

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[23]			
Units: Positive integer	48			

Notes:

[23] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination blood pressure target and reduction at the end of treatment having experienced a dose-limiting side effect during the study

End point title	Achieving combination blood pressure target and reduction at the end of treatment having experienced a dose-limiting side effect during the study

End point description:

Number of subjects who achieved the combination blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having also experienced a dose-limiting side effect between baseline and the end of the trial (Week 14). A subject is said to have experienced a dose-limiting side effect at a titration consultation if they: do not have a dose up-titration; are not already at the highest dose (10mg), have had a side effect recorded in the digital diary since last consultation of 25 or higher for any side effect, or have an AE that was deemed at least possibly related to amlodipine treatment since last consultation.

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[24]			
Units: Positive integer	27			

Notes:

[24] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving combination blood pressure target and reduction at the end of treatment having not experienced a dose-limiting side effect during the study

End point title	Achieving combination blood pressure target and reduction at the end of treatment having not experienced a dose-limiting side effect during the study

End point description:

Number of subjects who achieved the combination blood pressure target of SBP<135 and DBP<85 mmHg at the end of the trial (Week 14), a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of the trial (Week 14), having not experienced a dose-limiting side effect between baseline and the end of the trial (Week 14). A subject is said to have experienced a dose-limiting side effect at a titration consultation if they: do not have a dose up-titration; are not already at the highest dose (10mg), have had a side effect recorded in the digital diary since last consultation of 25 or higher for any side effect, or have an AE that was deemed at least possibly related to amlodipine treatment since last consultation.

End point type	Secondary

End point timeframe:

Blood pressure at the end of the trial (Week 14) and reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[25]			
Units: Positive integer	26			

Notes:

[25] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Experiencing a dose-limiting side effect

End point title	Experiencing a dose-limiting side effect

End point description:

The number of patients who experience a dose-limiting side effect. A subject is said to have experienced a dose-limiting side effect at a titration consultation if they: do not have a dose up-titration; are not already at the highest dose (10mg), have had a side effect recorded in the digital diary since last consultation of 25 or higher for any side effect, or have an AE that was deemed at least possibly related to amlodipine treatment since last consultation.

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[26]			
Units: Positive integer	112			

Notes:

[26] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point title	Number experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point description:

The number of patients who experience either unwanted side effect or an AE at least possibly related to amlodipine.

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event at least possibly related to amlodipine during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[27]			
Units: Positive integer	144			

Notes:

[27] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point title	Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point description:

Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and experiencing either unwanted side effect or an AE at least possibly related to amlodipine.

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[28]			
Units: Positive integer	70			

Notes:

[28] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and not experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point title	Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and not experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point description:

Achieving target of SBP<135 and DBP<85 mmHg at the end of treatment and not experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[29]			
Units: Positive integer	32			

Notes:

[29] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of treatment and experiencing either unwanted side effect or an AE at least possibly related

End point title	Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of treatment and experiencing either unwanted side effect or an AE at least possibly related

End point description:

Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of treatment and experiencing either unwanted side effect or an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[30]			
Units: Positive integer	34			

Notes:

[30] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of treatment and not experiencing either unwanted side effect or an AE at least possibly rel

End point title	Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of

	treatment and not experiencing either unwanted side effect or an AE at least possibly rel

End point description:

Achieving target combination of SBP<135 and DBP<85 mmHg at the end of treatment, a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg from baseline to the end of treatment and not experiencing either unwanted side effect or an AE at least possibly related to amlodipine.

End point type	Secondary

End point timeframe:

The reporting of unwanted side effect or adverse event during follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[31]			
Units: Positive integer	19			

Notes:

[31] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number reporting taking amlodipine on 80% or more days of follow-up

End point title	Number reporting taking amlodipine on 80% or more days of follow-up

End point description:

Number reporting taking amlodipine on 80% or more days of follow-up.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[32]			
Units: Positive integer	180			

Notes:

[32] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number reporting taking amlodipine on 80% or more days of follow-up and achieving the combination of target of SBP<135 and DBP<85 mmHg and a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg at the EOT

End point title	Number reporting taking amlodipine on 80% or more days of

	follow-up and achieving the combination of target of SBP<135 and DBP<85 mmHg and a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg at the EOT

End point description:

Number reporting taking amlodipine on 80% or more days of follow-up and achieving the combination of target of SBP<135 and DBP<85 mmHg and a reduction in SBP ≥10mmHg and a reduction in DBP ≥5mmHg at the EOT.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[33]			
Units: Positive integer	51			

Notes:

[33] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number reporting taking amlodipine on 80% or more days of follow-up and NOT achieving the combination of target of SBP<135 and DBP<85, a reduction in SBP ≥10mmHg, and a reduction in DBP ≥5mmHg at the EOT

End point title	Number reporting taking amlodipine on 80% or more days of follow-up and NOT achieving the combination of target of SBP<135 and DBP<85, a reduction in SBP ≥10mmHg, and a reduction in DBP ≥5mmHg at the EOT

End point description:

Number reporting taking amlodipine on 80% or more days of follow-up and NOT achieving the combination of target of SBP<135 and DBP<85, a reduction in SBP ≥10mmHg, and a reduction in DBP ≥5mmHg at the EOT

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[34]			
Units: Positive integer	129			

Notes:

[34] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[35]			
Units: Positive integer	79			

Notes:

[35] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[36]			
Units: Positive integer	57			

Notes:

[36] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[37]			
Units: Positive integer	78			

Notes:

[37] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[38]			
Units: Positive integer	58			

Notes:

[38] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[39]			
Units: Positive integer	84			

Notes:

[39] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point title	Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in SBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[40]			
Units: Positive integer	52			

Notes:

[40] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[41]			
Units: Positive integer	56			

Notes:

[41] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[42]			
Units: Positive integer	42			

Notes:

[42] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[43]			
Units: Positive integer	59			

Notes:

[43] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[44]			
Units: Positive integer	39			

Notes:

[44] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[45]			
Units: Positive integer	58			

Notes:

[45] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point title	Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in SBP ≥10mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[46]			
Units: Positive integer	40			

Notes:

[46] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[47]			
Units: Positive integer	62			

Notes:

[47] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing any unwanted side effects from amlodipine (reporting any of the 6 main side effects 25 or over on the VAS)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[48]			
Units: Positive integer	50			

Notes:

[48] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[49]			
Units: Positive integer	61			

Notes:

[49] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing a dose-limiting side effects from amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[50]			
Units: Positive integer	52			

Notes:

[50] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[51]			
Units: Positive integer	65			

Notes:

[51] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point title	Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point description:

Reduction in DBP ≥5mmHg from baseline to the end of treatment & without experiencing an AE at least possibly related to amlodipine

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	189[52]			
Units: Positive integer	47			

Notes:

[52] - Subjects who completed the trial and had at least 1 BP measurement at the end of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number making any diary entry on 80% or more days

End point title	Number making any diary entry on 80% or more days

End point description:

Number making any diary entry on 80% or more days.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[53]			
Units: Positive integer	187			

Notes:

[53] - Subjects who completed the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number making a BP diary entry on 80% or more occasions

End point title	Number making a BP diary entry on 80% or more occasions

End point description:

Number making a BP diary entry on 80% or more occasions. Patients were asked to record BP both AM and PM, and adherence for BP as calculated based on these 2 distinct occasions.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[54]			
Units: Positive integer	164			

Notes:

[54] - Subjects who completed the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number making a BP and side effect diary entry on 80% or more days

End point title	Number making a BP and side effect diary entry on 80% or more days

End point description:

Number making a BP and side effect diary entry on 80% or more days. Patients were asked to record BP both AM and PM, and adherence for BP as calculated based on these 2 distinct occasions.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the trial (Week 14).

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	196[55]			
Units: Positive integer	155			

Notes:

[55] - Subjects who completed the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Number achieving reduction in SBP of ≥5mmHg at the end of the study

End point title	Number achieving reduction in SBP of ≥5mmHg at the end of the study

End point description:

Number achieving reduction in SBP of ≥5mmHg at the end of the study.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	123[56]			
Units: Positive integer	34			

Notes:

[56] - Subjects who completed the trial and had at least 1 BP measurement at the end of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number achieving reduction in SBP of ≥10mmHg at the end of the study

End point title	Number achieving reduction in SBP of ≥10mmHg at the end of the study

End point description:

Number achieving reduction in SBP of ≥10mmHg at the end of the study.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	123[57]			
Units: Positive integer	10			

Notes:

[57] - Subjects who completed the trial and had at least 1 BP measurement at the end of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number achieving reduction in DBP of ≥5mmHg at the end of the study

End point title	Number achieving reduction in DBP of ≥5mmHg at the end of the study

End point description:

Number achieving reduction in DBP of ≥5mmHg at the end of the study.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	123[58]			
Units: Positive integer	18			

Notes:

[58] - Subjects who completed the trial and had at least 1 BP measurement at the end of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Patients who presented with uncontrolled BP (SBP≥135 or DBP≥85 mmHg) during the study

End point title	Patients who presented with uncontrolled BP (SBP≥135 or DBP≥85 mmHg) during the study

End point description:

Patients who presented with uncontrolled BP (SBP≥135 or DBP≥85 mmHg) during the study.

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	138[59]			
Units: Positive integer	24			

Notes:

[59] - Participants with BP readings and either completed or crossed over into intervention cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: Patients who did not present with uncontrolled BP during the study, and had moderate BP control at the end of the study (SBP≥120 and SBP<135 or DBP≥80 mmHg and DBP<85)

End point title	Patients who did not present with uncontrolled BP during the study, and had moderate BP control at the end of the study (SBP≥120 and SBP<135 or DBP≥80 mmHg and DBP<85)

End point description:

Patients who did not present with uncontrolled BP during the study, and had moderate BP control at the end of the study (SBP≥120 and SBP<135 or DBP≥80 mmHg and DBP<85)

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	138[60]			
Units: Positive integer	82			

Notes:

[60] - Participants with BP readings and either completed or crossed over into intervention cohort.

Statistical analyses

No statistical analyses for this end point

Secondary: Patients who did not present with uncontrolled BP during the study, and had good BP control at the end of the study (SBP<120 and DBP<80 mmHg)

End point title	Patients who did not present with uncontrolled BP during the study, and had good BP control at the end of the study (SBP<120 and DBP<80 mmHg)

End point description:

Patients who did not present with uncontrolled BP during the study, and had good BP control at the end of the study (SBP<120 and DBP<80 mmHg).

End point type	Secondary

End point timeframe:

During follow-up from baseline to the end of the study (3 months).

End point values	Observation			
Subject group type	Reporting group			
Number of subjects analysed	138[61]			
Units: Positive integer	32			

Notes:

[61] - Participants with BP readings and either completed or crossed over into intervention cohort.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of adverse events

End point title	Number of adverse events

End point description:

The number of adverse events reported during the trial for each trial arm.

End point type	Other pre-specified

End point timeframe:

Within the trial follow-up period, from baseline to the end of the trial (Week 14 for the intervention arm, and Month 3 for the observation arm).

End point values	Intervention	Observation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	162		
Units: Positive integer	469	28		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of subjects with reported adverse event

End point title	Number of subjects with reported adverse event

End point description:

The number of subjects with adverse events reported during the trial for each trial arm.

End point type	Other pre-specified

End point timeframe:

Within the trial follow-up period, from baseline to the end of the trial (Week 14 for the intervention arm, and Month 3 for the observation arm).

End point values	Intervention	Observation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	162		
Units: Positive integer	154	22		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from screening (when the electronic diary was uploaded by the participant) until the End of Treatment visit (or end of study visit for the observation cohort).

Adverse event reporting additional description:

Adverse events were collected by daily reporting on the electronic diary uploaded onto participant's smartphones, which informed the regular study calls from trails team staff at weekly/every two weeks frequency for the intervention group and monthly for the observation group).
Diary for intervention pts encouraged reporting of AE's.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.119

Reporting groups

Reporting group title	Intervention Group

Reporting group description:

Subjects with uncontrolled blood pressure at baseline were allocated to intervention and given small doses of amlodipine in addition to existing therapy at baseline.

Reporting group title	Observation study

Reporting group description:

subjects with controlled blood pressure were assigned to the observational group and were assigned to stay on baseline medication and be followed up for 3 months.

Serious adverse events	Intervention Group	Observation study	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 205 (2.44%)	1 / 162 (0.62%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast tumour malignant			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Unstable Angina			

subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STEMI			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrotic syndrome	Additional description: New diagnosis during study		
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Intervention Group	Observation study	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	154 / 205 (75.12%)	22 / 162 (13.58%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Hypotension			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	6 / 205 (2.93%)	0 / 162 (0.00%)	
occurrences (all)	6	0	
Chest discomfort			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	75 / 205 (36.59%)	2 / 162 (1.23%)	
occurrences (all)	78	2	
Feeling abnormal			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Gait disturbance			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	13 / 205 (6.34%)	0 / 162 (0.00%)	
occurrences (all)	14	0	
Malaise			
subjects affected / exposed	1 / 205 (0.49%)	1 / 162 (0.62%)	
occurrences (all)	1	1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Oedema			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	45 / 205 (21.95%)	0 / 162 (0.00%)	
occurrences (all)	46	0	
Pain			
subjects affected / exposed	3 / 205 (1.46%)	1 / 162 (0.62%)	
occurrences (all)	3	1	

Peripheral swelling			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Sensation of foreign body			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Swelling			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Temperature intolerance			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	

Dyspnoea			
subjects affected / exposed	12 / 205 (5.85%)	0 / 162 (0.00%)	
occurrences (all)	12	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Depressed mood			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Poor quality sleep			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Sleep disorder			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Investigations			
Heart rate irregular			
subjects affected / exposed	1 / 205 (0.49%)	1 / 162 (0.62%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	

Muscle strain			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	6 / 205 (2.93%)	0 / 162 (0.00%)	
occurrences (all)	6	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	11 / 205 (5.37%)	2 / 162 (1.23%)	
occurrences (all)	11	2	
Dizziness postural			
subjects affected / exposed	3 / 205 (1.46%)	1 / 162 (0.62%)	
occurrences (all)	3	1	
Dysgeusia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	55 / 205 (26.83%)	1 / 162 (0.62%)	
occurrences (all)	59	1	
Migraine			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Nerve compression			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			

subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Presyncope			
subjects affected / exposed	1 / 205 (0.49%)	1 / 162 (0.62%)	
occurrences (all)	1	1	
Sciatica			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Sleep deficit			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Vertigo			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Halo vision			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Visual impairment			
subjects affected / exposed	5 / 205 (2.44%)	1 / 162 (0.62%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			

subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	20 / 205 (9.76%)	0 / 162 (0.00%)	
occurrences (all)	23	0	
Abdominal pain upper			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Abdominal rigidity			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	5 / 205 (2.44%)	0 / 162 (0.00%)	
occurrences (all)	5	0	
Diarrhoea			
subjects affected / exposed	6 / 205 (2.93%)	0 / 162 (0.00%)	
occurrences (all)	6	0	
Dry mouth			
subjects affected / exposed	4 / 205 (1.95%)	0 / 162 (0.00%)	
occurrences (all)	4	0	
Dyspepsia			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Food poisoning			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	19 / 205 (9.27%)	0 / 162 (0.00%)	
occurrences (all)	22	0	
Paraesthesia oral			

subjects affected / exposed	2 / 205 (0.98%)	0 / 162 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Rash			
subjects affected / exposed	7 / 205 (3.41%)	0 / 162 (0.00%)	
occurrences (all)	7	0	
Skin reaction			
subjects affected / exposed	13 / 205 (6.34%)	0 / 162 (0.00%)	
occurrences (all)	13	0	
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	6 / 205 (2.93%)	0 / 162 (0.00%)	
occurrences (all)	6	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 205 (6.83%)	0 / 162 (0.00%)	
occurrences (all)	14	0	
Arthritis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	7 / 205 (3.41%)	0 / 162 (0.00%)	
occurrences (all)	7	0	
Costochondritis			

subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Fibromyalgia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Limb discomfort			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	4 / 205 (1.95%)	0 / 162 (0.00%)	
occurrences (all)	4	0	
Myalgia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Acute pulmonary histoplasmosis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	1 / 205 (0.49%)	3 / 162 (1.85%)	
occurrences (all)	1	3	
Diverticulitis			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	

Folliculitis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 205 (0.49%)	1 / 162 (0.62%)	
occurrences (all)	1	1	
Labyrinthitis			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 205 (0.49%)	2 / 162 (1.23%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	2 / 205 (0.98%)	3 / 162 (1.85%)	
occurrences (all)	2	3	
Tonsillitis			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 205 (0.00%)	1 / 162 (0.62%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Dehydration			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Gout			

subjects affected / exposed	3 / 205 (1.46%)	0 / 162 (0.00%)	
occurrences (all)	3	0	
Hyperglycaemia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	1 / 205 (0.49%)	0 / 162 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2021	SA01 The protocol, participant information sheet and consent form are updated to capture the following information. Post-screening visit, blood pressure is measured at home for 5 to 7 days, this is changed to "at least 7 days" to make it consistent with international expectations for home blood pressure studies. The minimum number of blood pressure readings required (24) is unchanged. Blood pressure criteria for entry into the Intervention part of the study are reduced to 135mmHg or above and/or 85mmHg and above, making the entry criteria consistent with international blood pressure guidelines. These changes are following expert feedback from the Trial Steering Committee (notably Professors McManus, Oxford and Poulter, Imperial). This may increase the proportion of participants who will be eligible for active added blood pressure treatment during the study, and also lowers the threshold for participants who are in the observational part of the study, but whose blood pressure might be improved by additional treatment (for safety participants can cross back into intervention if their blood pressure measurements become uncontrolled during the study). Permission is sought to transport IMP at room-temperature (then use within 3 months stored 2-8 in a refrigerator) rather than cold chain upright conditions, as advice from the manufacturer (Rosemont Pharmaceuticals) is that temperature stability data make this reasonable without loss of efficacy. During the COVID-19 pandemic cold-chain transport is at a premium and practical difficulties such as late deliveries have inconvenienced some participants. Where intolerance of small dose amlodipine occurs, smaller dose increments of 0.25mg and 0.5mg amlodipine may be used, where current or past intolerance makes this fit the patients need. A new statistician has joined the study delivery team, along with an administrative change of site telephone contact number for participants.

05 March 2021	SA02 Amendment is to add two further Participant Identifier Centre (PIC Site), to identify participants. The current existing PIC Sites are Barts NHS Health Trust and Salford NHS Trust. The third site is named as Wokingham Medical Practice, the fourth as The Homerton University Hospital. We are also updating an email contact address only in the Privacy Policy. We are also updating the consenting procedure and documentation of this to make this more robust: requesting to change change initial consent to not be conducted by a medically qualified person, this will be taken by site research staff, and we have updated the consent form to include a 2nd statement – of confirmation of consent at commencement of the intervention by a medically qualified person and must be completed whilst talking to the participant.

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.

Sponsor audit May 2021 identified potential issues of data integrity, inaccuracies in the protocol and patient eligibility. None of these affected participant safety. A protocol amendment written but was not submitted in error.

Notes: